Zoonotic Tuberculosis

Third Edition

Mycobacterium bovis and Other Pathogenic Mycobacteria

EDITED BY
Charles O. Thoen
James H. Steele
John B. Kaneene

WILEY Blackwell

Zoonotic Tuberculosis

Zoonotic Tuberculosis

Mycobacterium bovis and Other Pathogenic Mycobacteria

Third edition

Editors

Charles O. Thoen,
James H. Steele,
and John B. Kaneene

WILEY Blackwell

This edition first published 2014 © 2014 by John Wiley & Sons, Inc.
Chapter 7 © 2014 UK Crown Copyright
Chapters 3, 8, 22, 23, 25, 29 © 2014 remains with the US Government

First edition, 1995 © Iowa State University Press
Second edition, 2006 © Blackwell Publishing Ltd.

Editorial Offices
1606 Golden Aspen Drive, Suites 103 and 104, Ames, Iowa 50014-8300, USA
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell.

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Blackwell Publishing, provided that the base fee is paid directly to the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923. For those organizations that have been granted a photocopy license by CCC, a separate system of payments has been arranged. The fee codes for users of the Transactional Reporting Service are ISBN-13: 978-1-1184-7429-7/2014.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book.

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting a specific method, diagnosis, or treatment by health science practitioners for any particular patient. The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. Readers should consult with a specialist where appropriate. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

Library of Congress Cataloging-in-Publication Data

Mycobacterium bovis infection in animals and humans.

Zoonotic tuberculosis : mycobacterium bovis and other pathogenic mycobacteria / editors, Charles O. Thoen, James H. Steele, and John B. Kaneene. – Third edition.
p. ; cm.
Preceded by: Mycobacterium bovis infection in animals and humans / [edited by] Charles O. Thoen, James H. Steele, Michael J. Gilsdorf. 2nd ed. 2006.
Includes bibliographical references and index.
ISBN 978-1-118-47429-7 (cloth)
I. Thoen, Charles O., editor of compilation. II. Steele, James H., editor of compilation. III. Kaneene, John B., editor of compilation. IV. Title.
[DNLM: 1. Tuberculosis. 2. Disease Eradication. 3. Mycobacterium bovis–pathogenicity. 4. Tuberculosis–veterinary. 5. Tuberculosis, Bovine. 6. Zoonoses–microbiology. WF 200]
RC311.19
616.99′5–dc23

2013042731

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: iStockphoto – cow-foued42, chimp-irvingnsaperstein, elk-JudiLen, elephant-johan63, milk-Sunget, background map - By Hans Braxmeier (http://www.maps-for-free.com/) [CC-BY-SA-2.5 (http://creativecommons.org/licenses/by-sa/2.5)], via Wikimedia Commons
Cover design by Modern Alchemy LLC

Set in 10/12.5pt Times by SPi Publisher Services, Pondicherry, India

1 2014

Contents

Contributors

Ehsan Abdalla, DVM, MS
College of Veterinary Medicine
Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

Andy Alhassan, DVM, PhD
Accra Veterinary Laboratory
Ministry of Food and Agriculture
Accra, Ghana

María Celia Antognoli, DVM, PhD
Veterinary Epidemiologist
National Surveillance Unit
Centers for Epidemiology and Animal Health
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

F. Olalekan Ayanwale, DVM, MPH, PhD
Extension Veterinarian/Health Specialist
Cooperative Extension Program
Tuskegee University
Tuskegee, Alabama

Raúl G. Barletta, PhD
Professor, School of Veterinary Medicine and Biomedical Sciences
University of Nebraska–Lincoln, USA

Jean-Jacques Bénet, DVM, PhD
Professor, Contagious Diseases
Unit EPIMAI
Ecole Nationale Vétérinaire d'Alfort
Maisons-Alfort, France

Mahesh Bhandari, DVM, MS
Department of Veterinary Microbiology and Preventive Medicine
College of Veterinary Medicine
Iowa State University
Ames, Iowa

Mariana Boadella, DVM, PhD
SaBio (Sanidad y Biotecnología)–Instituto de Investigación en Recursos Cinegéticos
Consejo Superior de Investigaciones Científicas
Universidad de Castilla–La Mancha
Ciudad Real, Spain

Asseged Bogale, DVM, MSc
Center for Computational Epidemiology, Bioinformatics and Risk Analysis
College of Veterinary Medicine, Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

María Laura Boschiroli, PhD, HDR
Unité de Zoonoses Bactériennes
Laboratoire de Maisons-Alfort (Santé Animale)
Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'environnement et du travail (ANSES)
Maisons-Alfort, France

Simeon I. B. Cadmus, DVM, MVPH, PhD
Tuberculosis and Brucellosis Research Laboratory
Department of Veterinary Public Health & Preventive Medicine
University of Ibadan
Ibadan, Nigeria

Paul P. Calle, DVM
Chief Veterinarian
Director, Zoological Health Program
Wildlife Conservation Society
Bronx, New York

Mark Camacho, DVM, MPH
Regional Epidemiologist (Tuberculosis)
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Huanchun Chen, PhD
Professor
State Key Laboratory of Agricultural Microbiology
College of Veterinary Medicine
Huazhong Agricultural University
Wuhan, China

Yingyu Chen, PhD
College of Agricultural Science and Technology
Huazhong Agricultural University
Wuhan, China

Laura Chiavacci, DVM
Istituto Zooprofilattico Sperimentale del Piemonte, della Liguria, e della Valle d'Aosta
Torino, Italy

Debra V. Cousins, PhD
Biosecurity Victoria
Department of Environment and Primary Industries
Victoria, Australia

Alessandro Dondo, DVM
Istituto Zooprofilattico Sperimentale del Piemonte, della Liguria, e della Valle d'Aosta
S.C. Diagnostica Generale—Sede Torino

Julian A. Drewe, BVetMed, CertZooMed, MSc, PhD, Dipl. ECZM, MRCVS
Lecturer in Veterinary Epidemiology
Royal Veterinary College
London, UK

Donald A. Enarson, MD
Director of Scientific Committees
International Union Against Tuberculosis and Lung Disease, France
Adjunct Professor of Medicine
University of Alberta, Canada
Extraordinary Professor of Paediatrics
Stellenbosch University, South Africa

Guillermo Agustín Reyes Escalona, DVM
Chief of the Bovine Tuberculosis and Brucellosis Section
SAGARPA-SENASICA
Mexico

Pat A. Frost, DVM
Veterinarian, Veterinary Resources
Texas Biomedical

Alfredo Garin, DVM
Chief, TB and Brucellosis Control Programs
Ministerio de Ganadería, Agricultura, y Pesca
Montevideo, Uruguay

Michael J. Gilsdorf, DVM, MS
President Veterinary Consultant Services
Sykesville, Maryland

Margaret Good, MVB, PhD, MRCVS
Veterinary Manager TB Eradication Programme
Department of Agriculture, Food and the Marine
Dublin, Ireland

Maria Goria, DBSc
S.C. Biotecnologie
Istituto Zooprofilattico Sperimentale del Piemonte, della Liguria, e della Valle d'Aosta
Torino, Italia

Eamonn Gormley, BA (Mod), PhD
Head of TB Diagnostics and Immunology
Research Centre
School of Veterinary Medicine
University College Dublin
Dublin, Ireland

Christian Gortazar, DVM, PhD
Professor
SaBio (Sanidad y Biotecnología)–Instituto de Investigación en Recursos Cinegéticos
Consejo Superior de Investigaciones Científicas
Universidad de Castilla–La Mancha
Ciudad Real, Spain

Aizhen Guo, PhD
Professor
State Key Laboratory of Agricultural Microbiology
College of Veterinary Medicine
Huazhong Agricultural University
Wuhan, China

José Alfredo Gutiérrez-Reyes, DVM
Zoosanitary Campaigns Director
SAGARPA-SENASICA
Mexico D.F., Mexico

Tsegaye Habtemariam, DVM, PhD
Dean, College of Veterinary Medicine,
Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

Noel Harrington, DVM, PhD
Veterinary Program Specialist
Domestic Disease Control Section
Canadian Food Inspection Agency
Ottawa, Ontario, Canada

C. William Hench, DVM
Senior Staff Veterinarian
National Tuberculosis Eradication Program
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Owen L. Henderson, DVM
Senior Staff Veterinarian
National Tuberculosis Eradication Program
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Eli Tonatiuh Selva Hernández, DVM
Agricultural Specialist
SAGARPA-SENASICA
Mexico

Krista Howden, DVM, DACVPM
Epidemiologist
Epidemiology and Surveillance Section
Canadian Food Inspection Agency
Edmonton, Alberta, Canada

María Susana Imaz, PhD
Instituto Nacional de Enfermedades Respiratorias
Emilio Coni
Santa Fe, Argentina

M. Tariq Javed, DVM, MSc (Hons), PhD, Postdoc (Spain)
Professor, Department of Pathology
Faculty of Veterinary Science
University of Agriculture Faisalabad
Pakistan

John B. Kaneene, DVM, PhD
Professor of Population Medicine
College of Veterinary Medicine
Michigan State University
East Lansing, Michigan

Isabel N. de Kantor, PhD
TB Consultant (retired)
World Health Organization
Buenos Aires, Argentina

Bruce Kaplan, DVM, Dipl. AVES
One Health Initiative
Sarasota, Florida

Hilton Klein, VMD, MS ACLAM, Dipl. ECLAM
Vice President, Regulatory, Science, and Innovation (retired)
Harlan Laboratories
Indianapolis, Indiana

Nick Kriek, BVSc, M MedVet (Path)
Professor
Faculty of Veterinary Science at Onderstepoort
Department of Paraclinical Sciences
University of Pretoria
South Africa

Dejan Krnjaic, DVM, PhD
Associate Professor
Faculty of Veterinary Medicine
University of Belgrade
Serbia

Adam J. Langer, DVM, MPH, Dipl. ACVPM
Epidemiologist, Outbreak Investigations Team
Surveillance, Epidemiology, and Outbreak Investigations Branch
Division of Tuberculosis Elimination
Centers for Disease Control and Prevention, USA

Philip A. LoBue, MD, FACP, FCCP
Acting Director
Associate Director for Science
Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention, USA

Jason Lombard, DVM, MS
Dairy Specialist / Veterinary Epidemiologist
National Animal Health Monitoring System (NAHMS)
USDA Animal and Plant Health Inspection Service, Veterinary Services
Centers for Epidemiology and Animal Health, Fort Collins, Colorado

Giuliana Moda, DVM
Executive Management Staff Health
European Planning Coordination
Regione Piemonte, Italy

Nora Morcillo, PhD
Laboratorio de Referencia Programa de Control de TB
Provincia de Buenos Aires, Hospital Cetrángolo
Vicente Lopez, Argentina

Simon J. More, BVSc, MVB, DipPM, PhD, MANZCVS, FANZCVS, Dipl. ECVPH, Dipl. ECBHM
Professor of Veterinary Epidemiology and Risk Analysis
Centre for Veterinary Epidemiology and Risk Analysis
UCD School of Veterinary Medicine
University College Dublin
Ireland

Gregory Banayah Mwinyelle, DVM, MS
Department of Pathobiology
College of Veterinary Medicine
Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

David Nganwa, DVM, MPH
Associated Professor
Department of Pathobiology
College of Veterinary Medicine
Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

Alecia Larew Naugle, DVM, PhD, Dipl. ACVPM (Epidemiology)
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Luis A. Paredes Noack, DVM
Bovine TB Control and Eradication Project
Servicio Agrícola Ganadero
División de Protección Pecuaria
Santiago, Chile

Graham Nugent, MS, PhD
Research Programme Leader
Landcare Research
Lincoln, New Zealand

Kathleen Orloski, DVM, MS, Dipl. ACVPM (Epidemiology)
Epidemiologist
National TB Eradication Program
Ruminant Health Programs
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Ivo Pavlik, DVM, Dr CSC
Associate Professor
Veterinary Research Institute
Brno, Czech Republic

Alejandro Perera Ortiz, DVM
USDA Animal and Plant Health Inspection Service, Veterinary Services/International Services, Fort Collins, Colorado

Dirk U. Pfeiffer, DrMedVet, PhD, MANZCVSc, Dipl. ECVPH
Professor, Royal Veterinary College
London, UK

Budimir Plavsic, DVM, MS
Head of Animal Health Department
Veterinary Directorate
Ministry of Agriculture, Forestry, and Water Management
Belgrade, Serbia

Katie Portacci, DVM, MPH, Dipl. ACVPM
Senior Risk Analyst
Center for Epidemiology and Animal Health
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

Suelee Robbe-Austerman, DVM, PhD
Head, Mycobacteria/Brucella Section
Diagnostic Bacteriology Laboratory
USDA Animal and Plant Health Inspection Service, Veterinary Services
Ames, Iowa

Eliana Roxo, DVM
Instituto Biológico
Secretaria da Agricultura e Abastecimento do Estado de São Paulo
Brazil

Luigi Ruocco, DVM
Department of Veterinary Public Health and Food Safety
Italian Ministry of Health, Italy

Mark Schoenbaum, DVM, PhD, Dipl. ACVPM (Epidemiology)
Regional Epidemiology Officer
Veterinary Services Western Regional Office
USDA Animal and Plant Health Inspection Service, Veterinary Services
Fort Collins, Colorado

María D. Sequeira, MSc
Instituto Nacional de Enfermedades Respiratorias (retired)
Santa Fe, Argentina

Jack Shere, DVM, PhD
Regional Director
USDA Animal and Plant Health Inspection Service, Veterinary Services
Raleigh, North Carolina

Michael Sheridan, MVB, MApplSc, MScMgmt, MRCVS
Deputy Chief Veterinary Officer
Department of Agriculture, Food, and the Marine
Dublin, Ireland

Noel H. Smith, MSc, PhD
Bovine Tuberculosis Genotyping Group
Animal Health and Veterinary Laboratories Agency (AHVLA)
Weybridge, Surrey, UK

Slavoljub Stanojevic, DVM
Director
Directorate of National Reference Laboratory
Ministry of Agriculture, Forestry, and Water Management
University of Belgrade, Serbia

James H. Steele*, DVM, MPH
Former Assistant Surgeon General
United States Public Health Service
Professor Emeritus
University of Texas School of Public Health, USA
*Deceased.

Berhanu Tameru, PhD
Center for Computing Epidemiology, Bioinformatics and Risk Analysis
College of Veterinary Medicine Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

María Alice da Silva Telles, MSc, MSH
TB Laboratory Consultant
World Health Organization, Global Laboratory Initiative
Sao Paulo, Brazil

Charles O. Thoen, DVM, PhD, Dipl. AVES
Professor of Veterinary Microbiology and Preventive Medicine
College of Veterinary Medicine
Iowa State University
Ames, Iowa

Pedro M. Torres, DVM, MSc
Chief, TB Control Program
Servicio Nacional de Sanidad y Calidad Agroalimentaria (SENASA)
Argentina

Claude Turcotte, DVM, MSc
Veterinary Microbiologist
Leader, Mycobacterial Diseases Centre of Expertise
Canadian Food Inspection Agency
Ontario Laboratory Fallowfield
Ottawa, Ontario, Canada

Estela Flores Velázquez, DVM, MSc
Sub Director of Animal Health Programs of Large Ruminants
SAGARPA-SENASICA
Mexico

Rishendra Verma, BSc, BVSc & AH, MVSc, MSc (Immunol, UK), MVM (Biosec, NZ), PhD
Joint Director and I/C Mycobacteria Laboratory
Centre for Animal Disease Research and Diagnosis
Indian Veterinary Research Institute
Izatnagar, India

Patrizia Vignetta, DVM
Health Directorate
Regione Piemonte
Torino, Italy

Saul T. Wilson, DVM, Dipl. AVES
Coordinator of International Programs, Emeritus Professor of Epidemiology
College of Veterinary Medicine Nursing and Allied Health
Tuskegee University
Tuskegee, Alabama

Han Sang Yoo, DVM, PhD
Professor of Infectious Diseases
College of Veterinary Medicine
Seoul National University
Republic of Korea

Kyoungjin J. Yoon, DVM, PhD, Dipl. ACVM
Professor of Veterinary Diagnostic and Production Animal Medicine
College of Veterinary Medicine
Iowa State University
Ames, Iowa

Simona Zoppi, DVM
Istituto Zooprofilattico Sperimentale del Piemonte, della Liguria e della Valle d'Aosta
Torino, Italy

Preface

Tuberculosis (TB), caused by the genus *Mycobacterium*, is a significant health problem in both humans and animals. The traditional picture of human tuberculosis is disease due to *M. tuberculosis* (MTB), which often presents as a chronic pulmonary infection that without treatment can progress to systemic infection and result in death.

Mycobacterial infections outside the respiratory system, or extrapulmonary TB, are documented but often underreported, since the majority of TB diagnostic tests are focused on pulmonary disease due to *M. tuberculosis*. In addition to MTB, *M. bovis* (BTB) is the agent most commonly associated with nonpulmonary TB and is a recognized public health problem in developing countries, where direct contact with livestock reservoir hosts of BTB and consumption of unpasteurized dairy foods and improperly cooked meat are important routes for the zoonotic transmission of BTB from animals to humans.

The primary reservoir host for BTB is domestic cattle; however, BTB has been reported in most mammalian species. It is important to emphasize that other domestic and wild animals have been recognized as potential reservoirs of *M. bovis* for cattle and human infection. The economic costs of BTB, from losses in livestock productivity (e.g., milk, meat, animal mortality) to losses in human productivity due to illness are greater in nonindustrialized countries where BTB control programs are absent or ineffective.

Despite the attention and investment given to address the global TB epidemic due to MTB, and the importance of human BTB infection in nonindustrialized countries, little has changed in understanding the role of BTB in the global TB epidemic in humans. The World Health Organization (WHO) lists BTB as one of seven neglected zoonoses that pose serious threats to public health, and the World Organization for Animal Health (Office International des Epizooties, OIE) has called for the control and eradication of BTB. Global awareness of the importance of BTB infection in humans has increased with the spread of HIV-AIDS: rates of BTB infection in HIV-AIDS patients are higher than those in the general population, and BTB/HIV-AIDS coinfections now constitute the majority of BTB cases in developing countries. Despite this growing awareness, the contribution of BTB to global rates of extrapulmonary TB and overall TB in humans is not well documented and requires additional research.

In order to address challenges associated with BTB in the global strategy to control TB, both human and animal health professionals must work together for effective prevention and control of zoonotic TB. The term *One Health* has been adopted to describe the unified human and veterinary medical approach to zoonoses. United approaches will be critical for future endeavors in the control of the global TB epidemic. This paradigm is ideally suited for control of BTB, since the epidemiology of BTB varies widely throughout the world, given differences in human, livestock, and wildlife populations; existing TB control programs; and environmental and socioeconomic conditions.

Sharing resources and increasing interaction between public health and veterinary medical scientists can raise awareness of the shared risk of BTB between humans and animals; in resource-limited situations, this method can maximize the use of existing infrastructure and reduce unnecessary duplication of effort in disease control programs. Shared research between human and animal health can speed the development of new diagnostic tools, potential novel vaccines for humans and livestock, and improved TB surveillance, control, and eradication programs.

Mycobacterium bovis BCG vaccines have been widely used in humans in high-burden countries. Although there is a long-standing debate whether they provide any protection against the adult form of TB, they do appear to provide some protection against disseminated TB and TB meningitis in children. BCG vaccines are not utilized in animals as they fail to protect against infection, and their ability to prevent progression to disease is uncertain. It is important to remember that when vaccine failures occur in humans, the patient presents for treatment, but animals with clinical disease that are contagious remain in the population and are reservoirs of infection for other animals. Therefore, vaccines for animals must be highly efficacious to be of practical value in the control of tuberculosis.

It is the purpose of this text to provide physicians, veterinarians, public health workers, allied health scientists, biomedical research workers, diagnosticians, and graduate students with current information on the significance of *M. bovis* in the elimination of TB in animals and humans. Updated information is presented on new molecular techniques utilized in identification of members of the *Mycobacterium tuberculosis* complex as well as application of molecular techniques useful in tracing outbreaks of tuberculosis.

This edition has added a new chapter describing how the One Health approach can be used for the prevention and control of TB in animals and humans and includes current updates on the status of *M. bovis* infection in animals and humans in industrialized and developing countries of the world. Six new chapters on the importance of zoonotic tuberculosis in countries in Africa are included. Utilization of One Health principles for interdisciplinary collaborations offers a valuable approach for all global regions.

This modernized information is and will be of significant value to public health officials, research workers, allied health scientists, state and federal regulatory veterinarians, medical and veterinary medical practitioners, and professionals interested in the importation of animals for herds and for collections of endangered species in zoos and animal parks.

The editors acknowledge financial support received from the United States Department of Agriculture, Animal and Plant Health Inspection Service–Veterinary Services. Finally, we wish to thank our publisher for assistance in transforming the manuscripts of individuals into a very nice book. A special thanks to Kendra Johnson for secretarial assistance and to the editors at Wiley Blackwell.

Donald A. Enarson, MD
James H. Steele, DVM, MPH
Philip A. LoBue, MD
Bruce Kaplan, DVM
Saul T. Wilson, DVM, MPH
John B. Kaneene, DVM, MPH, PhD
Charles O. Thoen, DVM, PhD

The findings and conclusions in this book are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Zoonotic Tuberculosis

Chapter 1

Tuberculosis in animals and humans

An introduction

Charles O. Thoen,[1] *Philip A. LoBue,*[2] *and Donald A. Enarson*[3]

[1]Iowa State University, USA

[2]Centers for Disease Control and Prevention, USA

[3]International Union Against Tuberculosis and Lung Disease, France

Tuberculosis is an important disease in animals and humans worldwide. It causes substantial morbidity, mortality, and economic loss. There is significant variation in terms of how different organisms of the *M. tuberculosis* complex affect specific animals, including humans. However, there are also important intersections between animals and humans with regard to TB. The best example is the occurrence of *M. bovis* disease in humans and domesticated and wild animals.

The tubercle bacillus infects an estimated 2 billion persons or approximately one third of the world's population, and it is estimated that 1.5 to 2 million people die from TB each year. Ninety-five percent of cases occur in people in developing countries. TB is one of the leading causes of infectious disease-related deaths worldwide [1]. The genus *Mycobacterium* includes several species that cause TB disease in humans and other animals. The *Mycobacterium tuberculosis* complex includes *M. tuberculosis*, *M. cannettii*, *M. africanum*, *M. bovis*, *M. pinnipedii*, *M. mungi*, *M. caprae*, and *M. microti*.

Significant progress has been made toward the elimination of TB caused by *M. tuberculosis* complex from humans in industrialized countries [2]. However, in many countries where TB programs have only recently been established, there has been only limited progress toward control of the disease. The development of drug-resistant (multidrug-resistant and extensively drug-resistant) strains has compromised the efficacy of TB treatment in humans and has markedly increased the cost associated with the use of multiple drug therapies [3]. Moreover, the susceptibility of human immunodeficiency virus (HIV)–infected individuals to *M. tuberculosis* complex is of major concern to public health officials in developing countries where the acquired immune-deficiency syndrome is rampant [4].

M. bovis accounts for only a small percentage of the reported cases of TB in humans; however, it is a pathogen of significant economic importance in wild and domestic animals

Zoonotic Tuberculosis: Mycobacterium bovis and Other Pathogenic Mycobacteria, Third Edition.
Edited by Charles O. Thoen, James H. Steele, and John B. Kaneene.
© 2014 John Wiley & Sons, Inc. Published 2014 by John Wiley & Sons, Inc.

around the globe, especially in countries where little information is available on the incidence of *M. bovis* infection in humans [5–7].

Tubercle bacilli were identified more than 130 years ago. However, a definitive understanding of the pathogenesis of the disease caused by the *M. tuberculosis* complex is deficient [8,9]. The tubercle bacillus enters the macrophage by binding to cell surface molecules of the phagocyte. Ingestion of the tubercle bacillus by phagocytes into the phagosome or intracytoplasmic vacuole protects the organism from the natural defenses in the serum. Following ingestion of the bacillus, lysosomes fuse with the phagosome to form phagolysosomes, and it is there that the phagocytes attempt to destroy the bacillus [10]. However, virulent bacilli have the ability to escape killing. Virulent mycobacteria survive inside a mononuclear phagocyte by inhibiting phagosome fusion with preformed lysosomes, thereby limiting acidification. It has been suggested that the pathogenicity of *M. tuberculosis* complex is a multifactorial phenomenon. However, in cases in which the host response is unable to destroy the bacillus due to conditions that compromise immune function, resulting in low CD4+ T-cell counts, such as immune suppression due to chemotherapy, stress, or HIV, reactivation may occur, resulting in the release of bacilli and transmission of infection.

The susceptibility of different host species varies for the *M. tuberculosis* complex, depending on the route of exposure, the dose of organisms, and the virulence of the strain [11]. Humans, nonhuman primates, and guinea pigs are very susceptible to *M. tuberculosis*. Cattle, rabbits, and cats are susceptible to *M. bovis* and are quite resistant to *M. tuberculosis*. Wild hoofed stock is generally susceptible to *M. bovis*, but few reports are available on the isolation of *M. tuberculosis* [12–14]. Swine and dogs are susceptible to both *M. bovis* and *M. tuberculosis* [15].

In humans, TB is a pulmonary and systemic disease caused by *M. tuberculosis* complex species, predominantly *M. tuberculosis*. TB infections occur when susceptible individuals inhale droplet nuclei containing tubercle bacilli and the droplet nuclei reach the alveoli of the lungs. The tubercle bacilli that reach the alveoli are ingested by alveolar macrophages and the majority of these bacilli are destroyed or inhibited. A small number multiply intracellularly and are released when the macrophages die. If alive, these bacilli may spread through the lymph or bloodstream to more distant tissues and organs, including areas in which TB disease is most likely to develop: the apices of the lungs, the kidneys, the brain, the bones, and through the lymphatic system to regional lymph nodes. This process of dissemination primes the immune system for systemic responses.

Because of the primed immune system, extracellular bacilli attract macrophages and other immunologically active cells. The immune response kills most of the bacilli, and the remaining bacilli are confined through the formation of granulomas. At this point, latent TB infection (LTBI) has been established, which may be detected using the Mantoux tuberculin skin test or interferon-gamma release assays. Within weeks after infection, the immune system is usually able to halt the multiplication of the tubercle bacilli, preventing further progression.

In some people, the tubercle bacilli overcome the defenses of the immune system and begin to multiply, resulting in the progression from LTBI to TB disease. This process may occur soon after or many years after infection. Unless treated, approximately 3%–5% of persons who have been infected with *M. tuberculosis* will develop TB disease in the first

2 years after infection, and another 2%–5% will develop disease at some time later in life. Thus, approximately 5%–10% of persons with normal immune systems who are infected with *M. tuberculosis* will develop TB disease at some point in their lives. Immunocompromised persons have a much higher risk of progression from infection to disease. For example, HIV-infected persons not receiving antiretroviral therapy have an 8% annual risk of progression [16].

TB continues to be an important disease both in humans and animals. It causes substantial morbidity, mortality, and economic loss worldwide. There is significant variation in terms of how different organisms of the *M. tuberculosis* complex affect specific animals, including humans. However, there are also important intersections between animals and humans with regard to TB. Perhaps the best example is the occurrence of *M. bovis* disease in humans and domesticated and wild animals.

M. bovis persists in humans, causing pulmonary and extrapulmonary disease. Unlike transmission of *M. bovis* from cattle to humans, the role of human-to-human airborne transmission in the spread of *M. bovis* has been somewhat controversial [17]; the predominant view has been that human-to-human transmission is a rare event and that it is only likely to occur in populations that are particularly susceptible to TB (e.g., HIV-infected persons). However, reports of clusters of cases with social and molecular epidemiologic links with patients with pulmonary *M. bovis* have suggested that human-to-human transmission does occur, even in nonimmunosuppressed persons [18].

Investigations are needed to elucidate the relative importance of *M. bovis* as regards TB incidence in humans, especially in developing countries [1]. Efforts should be concentrated in countries where HIV infection is widespread, as HIV-infected individuals are more susceptible to mycobacterial disease. Eradication of *M. bovis* in cattle and pasteurization of dairy products are the cornerstones of the prevention of human disease [19]. Standard public health measures used to manage patients with contagious *M. tuberculosis* should be applied to contagious patients with *M. bovis* to stop person-to-person spread. Finally, measures should be developed to identify and control *M. bovis* infection in wild animals, as these animals may be important reservoirs of infection for domesticated food-producing animals.

It is important to emphasize that pathogenic tubercle bacilli have a wide host range; several species of the genus *Mycobacterium* infect humans as well as wild and domestic animals. There is therefore a need for medical and veterinary medical professionals to cooperate in disease outbreaks [20]. This concept has been promoted previously [21]. However, this is of increasing importance in TB control in the twenty-first century because of the occurrence of drug-resistant *M. tuberculosis* complex strains and the immunosuppression of host responses from multiple causes, resulting in increased susceptibility to tubercle bacilli.

Acknowledgment

Published with permission from the Journal of International Union Against Tuberculosis and Lung Disease (Int J Tuberc Lung Dis 14[9]:1075–1078 © 2010) prepared from serialization of article: Thoen, C. O., P. A. LoBue, D. A. Enarson, J. B. Kaneene, and I. N. de Kantor. 2009. Tuberculosis: a re-emerging disease in animals and humans. *Vet Ital* 45:135–181.

Note

This chapter was originally printed in part as the first of an educational series on *Mycobacterium bovis* as a zoonotic disease and its implications for tuberculosis control in human populations. This series was offered as a reminder that tuberculosis is a disease with an animal reservoir and that therefore ultimate eradication must recognize this animal reservoir and incorporate strategies to deal with it in the global strategy for the control and elimination of tuberculosis in humans. We believe that this has been neglected in the current strategy and needs to be acknowledged and incorporated, however minimally, in future revisions of the global strategy.

References

1. World Health Organization. 2009. Global tuberculosis control 2009: epidemiology, strategy, finances. WHO/HTM/TB/2009.411. Geneva, Switzerland: WHO.
2. Enarson, D. A., and H. L. Rieder. 1995. The importance of Mycobacterium bovis to the tuberculosis epidemic in humans. In: C. O. Thoen and J. H. Steele, eds. *Mycobacterium bovis infection in animals and humans*, 1st ed. (pp. xix–xxii). Ames, IA, USA: Iowa State University Press.
3. Zignol, M., M. S. Hosseini, and A. Wright, et al. 2006. Global incidence of multidrug-resistant tuberculosis. *J Infect Dis* 194:479–485.
4. Tiruviluamala, P., and L. B. Reichman. 2002. Tuberculosis. *Annu Rev Public Health* 23:403–426.
5. Thoen, C. O., P. LoBue, and I. N. de Kantor. 2006. The importance of Mycobacterium bovis as a zoonosis. *Vet Microbiol* 112:339–345.
6. de Kantor, I N., and V. Ritacco. 2006. An update on bovine tuberculosis programs in Latin American and Caribbean countries. *Vet Microbiol* 112:111–118.
7. Thoen, C. O., P. A. LoBue, D. A. Enarson, J. B. Kaneene, and I. N. de Kantor. 2009. Tuberculosis: a re-emerging disease in animals and humans. *Vet Ital* 45:135–181.
8. Cole, S. T., R. Brosch, J. Parkhill, et al. 1998. Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence. *Nature* 393:537–544.
9. Brosch, R., S. V. Gordon, M. Marmiesse, et al. 2002. A new evolutionary scenario for the Mycobacterium tuberculosis complex. *Proc Natl Acad Sci* 99:3684–3689.
10. Olsen, I., R. G. Barletta, and C. O. Thoen. 2010. Mycobacterium. In: C. L. Gyles, J. F. Prescott, J. G. Songer, and C. O. Thoen. *Pathogenesis of bacterial infections in animals*, 4th ed. (pp. 113–139). Ames, IA, USA: Wiley-Blackwell.
11. Thoen, C. O. 1994. Tuberculosis in wild and domestic mammals. In: B. R. Bloom, ed. *Tuberculosis: pathogenesis, protection and control* (pp. 157–162). Washington, DC: American Society for Microbiology Press.
12. Francis, J. *Tuberculosis in animals and man*. 1958. London, UK: Cassell: p. 357.
13. Lomme, J. R., C. O. Thoen, E. M. Himes, J. W. Vincent, and R. E. King. 1976. Mycobacterium tuberculosis: infection in two East African oryxes. *J Am Vet Med Assoc* 169:912.
14. Schmitt, S. M., D. J. O'Brien, C. S. Bruning-Fann, and S. D. Fitzgerald. 2002. Bovine tuberculosis in Michigan wildlife and livestock. *Ann NY Acad Sci* 969:262–268.
15. Thoen, C. O. Tuberculosis. 2012. In: J. J. Zimmerman, L. A. Karriker, A. Ramirez, K. J. Schwartz, and G. W. Stevenson, eds. *Diseases of swine*, 10th ed. (pp. 856–865). Ames, IA, USA: Wiley-Blackwell.

16. Selwyn, P. A., D. Hartel, V. A. Lewis, et al. 1989. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *N Engl J Med* 230:545.
17. LoBue, P. Public health significance of *M. bovis*. In: C. O. Thoen, J. H. Steele, and M. J. Gilsdorf, eds. *Mycobacterium bovis infection in animals and humans*, 2nd ed. (pp. 6–12). Ames, IA, USA: Blackwell.
18. Evans, J. T., P. Sonnenberg, E. Grace Smith, et al. 2007. Bovine tuberculosis: multiple human-to-human transmission in the UK. *Lancet* 14:1270–1276.
19. Ashford, D. A., L. Voelker, and J. H. Steele. 2006. Bovine tuberculosis: environmental public health preparedness considerations for the future. In: C. O. Thoen, J. H. Steele, and M. J. Gilsdorf, eds. *Mycobacterium bovis infection in animals and humans*, 4th ed. (pp. 305– 315). Ames, IA, USA: Blackwell.
20. Moda, G., and M. Valpreda. 1994. Bovine tuberculosis eradication: need of collaboration between physicians and veterinarians. *Alpe Adria Microbiol J* 3:296–297.
21. Thoen, C. O., D. E. Williams, and T. C. Thoen. 2008. Discovery of streptomycin for treatment of tuberculosis. *One Health Newsletter* 1:5–6.

Chapter 2

One Health approach for preventing and controlling tuberculosis in animals and humans

John B. Kaneene,[1] *Bruce Kaplan,*[2] *James H. Steele,*[3] *and Charles O. Thoen*[4]

[1]Michigan State University, USA
[2]One Health Initiative, USA
[3]University of Texas, USA
[4]Iowa State University, USA

The term *One Health*, previously referred to as *One Medicine* in the 20th century, is now used to describe the unified human and veterinary approach to zoonoses [1,2]. Part of the unified human and veterinary medical approach of One Health is a worldwide strategy for expanding coequal, all-inclusive multidisciplinary and interdisciplinary collaborations and communications directed to the development of disease control and prevention programs, as well as biomedical clinical research investigations. Understanding the effects of zoonoses on socioeconomic well-being; addressing social, cultural, and economic conditions that facilitate spread and maintenance of disease; and development of programs with active stakeholder input and participation are critical to the success of One Health [3,4]. In addition, utilization of the One Health approach currently has (and will in the future) expanded the scientific knowledge base, improved medical education and clinical care, and developed effective disease control programs in both human and animal populations, resulting in the protection and saving of untold millions of lives today and in future generations.

History of the One Health approach

Associations between animal and human diseases have been observed in ancient civilizations to the present [5]. Parallels in the progression of disease between humans and domestic animals, and the historic use of animals as sentinels for human disease [6], acknowledge these associations. The evidence of “shared risk” in humans and animals in recent history include Minamata disease (mercury poisoning in humans and cats), anthrax

Zoonotic Tuberculosis: Mycobacterium bovis and Other Pathogenic Mycobacteria, Third Edition.
Edited by Charles O. Thoen, James H. Steele, and John B. Kaneene.
© 2014 John Wiley & Sons, Inc. Published 2014 by John Wiley & Sons, Inc.

in livestock and humans, and West Nile virus in humans and animals [6]. Further, studies of human and animal ethnopharmacology have found commonality in the descriptions, symptoms, and treatments for humans and animals in traditional medicine, as well as the fact that many remedies were used to treat both humans and animals [7].

Some of the earliest applications of the concept of associations between human and animal disease were prompted by veterinarians in the United States. Dr. J. Law, a professor of veterinary medicine at Cornell University, advised the U.S. Board of Health on the effects of zoonoses on public health in 1880 [5]. The focus of early proponents of veterinary public health impacting human public health involved hazards of milk from diseased cows in the 1880s, from diseases including tuberculosis (TB), typhoid fever, diphtheria, and brucellosis [5]. Actions to control milk-borne diseases included pasteurization after production and control of bovine TB and brucellosis in cattle through Grade A milk requirements for cattle herd health status [5]. The success of this program has resulted in the near eradication of these diseases as foodborne hazards in the United States.

Acceptance of the One Health approach

In the first decade of the 21st century, the One Health concept was promoted by the veterinary medical community through the American Veterinary Medical Association (AVMA) [5,8], which established a unique One Health collaborative liaison with the American Medical Association (AMA) in 2006. In 2007, the AMA passed a landmark One Health resolution, and the AVMA officially established the One Health Initiative Task Force (OHITF) to develop strategies to enhance collaboration between human and veterinary medical professionals. The OHITF produced a strategic framework for reducing risks of infectious diseases at the human-animal-ecosystem interface, and developed the recommendations that formed the bases of the current One Health Initiative [9]. As a result, the One Health Commission (OHC) was officially chartered in 2009 for the wide spectrum purpose of promoting One Health in the United States and worldwide.

After support of the One Health concept by the AVMA, AMA, U.S. Centers for Disease Control and Prevention (CDC), and the American Society for Microbiology, it has been embraced by the World Health Organization (WHO), the World Organisation for Animal Health (Office International des Epizooties—OIE), the United Nations Food and Agriculture Organization (FAO), UNICEF, the United Nations System Influenza Coordination, and the World Bank. The World Bank has specifically recognized the importance of One Health and its economic benefits [10, 11]. Other major organizations promoting One Health include the U.S. Department of Agriculture (USDA), the U.S. National Environmental Health Association (NEHA), the European Union, the American Academy of Pediatrics, and many others. Recognition of the importance of One Health has also expanded beyond the medical and economic sciences: in the United States, The National League of Cities has formally recognized and supported the work of the OHITF and has acknowledged how the success of the One Health Initiative will rely on leadership, communication skills, and cooperation.

One Health is now being embraced by many different countries to address different zoonotic diseases, and One Health principles are an important part of global health training