Akio Yamada · Laura H. Kahn
Bruce Kaplan · Thomas P. Monath
Jack Woodall · Lisa Conti *Editors*

Confronting Emerging Zoonoses

The One Health Paradigm

Springer

Confronting Emerging Zoonoses

Akio Yamada • Laura H. Kahn • Bruce Kaplan
Thomas P. Monath • Jack Woodall • Lisa Conti
Editors

Confronting Emerging Zoonoses

The One Health Paradigm

Springer

Editors
Akio Yamada
Department of Veterinary Medical Science
Graduate School of Agricultural and Life Sciences
The University of Tokyo
Tokyo, Japan

Bruce Kaplan
Sarasota, FL, USA

Jack Woodall
Rio de Janeiro, Brazil

Laura H. Kahn
Woodrow Wilson School of Public and International Affairs
Princeton University
Princeton, NJ, USA

Thomas P. Monath
Hookipa BioTech AG
Townsend, MA, USA

Lisa Conti
Florida Department of Agriculture and Consumer Services
Tallahassee, FL, USA

ISBN 978-4-431-55119-5 ISBN 978-4-431-55120-1 (eBook)
DOI 10.1007/978-4-431-55120-1
Springer Tokyo Heidelberg New York Dordrecht London

Library of Congress Control Number: 2014950637

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

According to the United Nations, the global population is estimated to reach 8.1 billion in 2025 and increase to 9.6 billion in 2050. In developing countries, the population is projected to increase to 8.2 billion in 2050. Sustainably supporting these unprecedented populations will require integrating a "One Health" approach in medicine, public health, and agriculture.

In a recent presentation by Jimmy Smith, the Director General of the International Livestock Research Institute, it was projected that total livestock production would increase 92 % by 2050. To feed these enormous numbers of humans and livestock, 61 million hectares of additional cropland would be needed worldwide. Direct and indirect interactions between different species of animals, including humans, are anticipated to increase, leading to the emergence of more zoonotic pathogens. These novel pathogens might have the capacity for interhuman spread and even pandemic potential among humans. To mitigate the burden of emerging infectious zoonotic diseases, efficacious monitoring of diseases of wild and domesticated animals would be required. This interspecies disease surveillance would enable early disease detection at the interface of humans, livestock, and wildlife and would promote rapid response capabilities.

Although emerging infectious diseases pose health threats to people regardless of their economic status, the poor in many developing countries suffer the brunt of the burden from "neglected zoonotic diseases." In these countries, the poor depend upon small livestock like goats and poultry for their livelihoods, but many of these animals harbor zoonotic diseases. Industrialized countries, in contrast, have much better biocontainment capabilities in their livestock production. Prevention is critical but is often hampered by the diversion of necessary resources for diseases with higher priorities in the human medical communities such as heart disease, cancer, and diabetes.

Furthermore, the provincial silo approach to zoonotic and neglected diseases makes matters more difficult because prevention and response measures are not implemented using a collaborative, interdisciplinary One Health approach. These diseases, which affect all species, require that disciplines with expertise in different

areas work together. One Health is a concept that underpins the multidisciplinary or transdisciplinary approaches to zoonotic diseases. This is equally applicable to other health and health care categories that fall under the One Health Umbrella (http://www.onehealthinitiative.com/OneHealth2) such as comparative medicine/translational medicine.

Contributors to this book provide an overview of the current understandings of zoonotic and emerging infectious diseases using examples where the One Health approach was successfully applied. The book also highlights some of the challenges societies face in confronting several specific zoonotic diseases. A chapter is included on comparative medicine to demonstrate the broad scope of the One Health concept.

This book is dedicated to those studying zoonotic diseases and comparative medicine in both human and veterinary medicine, to those involved in the prevention and control of zoonotic infections, and to those in the general public interested in the visionary field of One Health.

Akio Yamada
Laura H. Khan
Bruce Kaplan
Thomas P. Monath
Jack Woodall
Lisa Conti

Contents

Part III The Successes and Challenges of Implementing One Health

Part I
The Importance of a One Health Approach to Emerging Zoonotic Diseases

Chapter 1
The Origin of Human Pathogens

Gabriel Trueba

Abstract Modern human infectious diseases are thought to have originated in domestic animals during the Neolithic period or afterwards. However, recent genetic, phylogeographic and molecular clock analyses of microbial genomes point to a much older Paleolithic origin (2.5 million to 10,000 years ago) and suggest that many of these pathogens coevolved with ancestral hominids in Africa. Another group of human pathogens seems to have derived recently from non-human hominids.

Keywords Evolution • Molecular clock • Phylogeny • Zoonosis

1.1 Introduction

Some scientists contend that many modern human infectious diseases arose during the Neolithic period or afterwards due to close contact with domestic animals and their pathogens (Diamond 1999; Pearce-Duvet 2006; Wolfe et al. 2007). There is indeed evidence of a recent origin of measles virus from bovine rinderpest virus (Furuse et al. 2010), and bubonic plague (*Yersinia pestis*) from *Y. pseudotuberculosis*, a zoonotic bacterium carried by rodents (Cui et al. 2013). As a consequence of this view, the origins of many human infectious diseases, such as tuberculosis, malaria, smallpox, and pertussis have focused on domestic animals and environments outside of Africa. However, the combination of genetics, molecular clock analysis and phylogeography provide evidence that some of these diseases arose much earlier in the Paleolithic period and probably when our hominid ancestors were still isolated in Africa (Forster 2004). Some of these findings are in agreement with paleontological and archeological discoveries.

G. Trueba (✉)
Instituto de Microbiología Universidad, San Francisco de Quito, Quito, Ecuador
e-mail: gtrueba@usfq.edu.ec

A. Yamada et al. (eds.), *Confronting Emerging Zoonoses*,
DOI 10.1007/978-4-431-55120-1_1

1.2 Older Origins

Tuberculosis was the typical example of a disease thought to have originated in the Neolithic period and transmitted from cattle to humans (Diamond 1999). This scenario implied that the human *Mycobacterium tuberculosis* bacterium derived from a bovine *M. bovis* ancestor.

Recent analyses of genomic deletions and nucleotide polymorphisms suggests that the ancestor of *M. tuberculosis* Complex (MTCP) may actually have originated from a group of smooth mycobacteria found in humans in East Africa (Gutierrez et al. 2005; Wirth et al. 2008). Molecular clock analysis of strains belonging to MTCP indicates that the common ancestor may have existed 2.6–2.8 million years ago (Gutierrez et al. 2005). This ancient date places the origin of the disease at a time when our hominid ancestors were living in Africa. Furthermore, there is evidence of a genetic bottleneck of *M. tuberculosis* occurring about 40,000 years ago, possibly the result of the human migration out of African to Eurasia (Gutierrez et al. 2005; Wirth et al. 2008). In congruence with the molecular data, tuberculosis lesions and mycobacterial DNA have been found in pre-Columbian Americans (Stone et al. 2009) who most likely did not have contact with domesticated cattle. Furthermore, rather than evolving from bovines as originally hypothesized, recent analyses of genome deletions and phylogeny suggest that *M. bovis* (and other animal adapted MTCP mycobacteria) derived from a mycobacteria more similar to the human adapted *M. tuberculosis* than to *M. bovis*. These studies clearly contradict the notion that the human *M. tuberculosis* derived from *M. bovis* (Smith et al. 2009; Garnier et al. 2003; Wirth et al. 2008). Nevertheless the evolutionary relationship between *M. tuberculosis* and *M bovis* seems to be complex; current evidence suggest that the most recent common ancestor of MTCP may have evolved into two groups: *M. tuberculosis* and a group of mycobacteria infecting different animal species; *M. bovis* may have emerged from the group of animal adapted mycobacteria (Smith et al. 2009).

The presence of *M. bovis* in badgers and its possible connections with livestock have been investigated using whole genome sequencing analysis and showed that the transmission of *M. bovis* between cattle and badgers is recent, however the direction of the transmission remains unresolved (Biek et al. 2012).

Another mycobacterial disease, leprosy was first recorded in humans around 600 B.C. in India (Stone et al. 2009). Based on historic documents, it was thought that this disease was later brought to Europe during Greek military campaigns (Stone et al. 2009). In support of this recent origin is an absence of leprosy in pre-Columbian Americans (Stone et al. 2009), and little genetic variation among isolates of *Mycobacteria leprae* (Gómez-Valero et al. 2007; Monot et al. 2005), the causative agent of this infectious disease. By contrast, phylogeography using single nucleotide polymorphism (SNP) analyses point to *M. leprae* originating in Africa during the Paleolithic (Monot et al. 2005; Monot et al. 2009). This ancient date suggests that the current presence of little genomic variation may be due to a recent bottleneck (Monot et al. 2009; Monot et al. 2009), possibly due to *M. leprae*'s low

rate of infection (Smith 1904). This low infection rate could also explain the absence of leprosy in pre-Columbian Americans, even though their ancestors may have themselves been infected. Interestingly, a mycobacterial species (*M. lepromatosis*) has been discovered recently in Mexico and the Caribbean. However, this bacterium seems to have diverged around 10 million years ago from *M. leprae* and may have been brought to the American continent by the first human immigrants (Han et al. 2009). Molecular clock analysis suggests that the ancestor of *M. leprae* diverged from *M. tuberculosis* around 66 million years ago, prior to the origins of the genus *Homo*, 2.5 million years ago (Forster 2004). Analysis of non-synonymous nucleotide substitutions suggests that *M. leprae* underwent genomic decay between 10 to 20 million years ago (Gómez-Valero et al. 2007; Monot et al. 2009). See Sect. 1.4 below.

Other diseases whose origins have been subjected to major debates are human treponematoses, which include syphilis (caused by *Treponema pallidum* subsp. *pallidum*), bejel (caused by *T. pallidum* subsp. *endemicum*), yaws (caused by *T. pallidum* subsp. *pertenue*) and pinta (caused by *T. pallidum* subsp. *carateum*) (Scolnik et al. 2003). The genomes of the four subspecies display very few differences, suggesting a recent common *Treponema* ancestor. However *T. pallidum* seems to be a pathogen that has co-evolved with human ancestors; typical yaws-like lesions have been found in prehistoric human bones and ancestral hominids, indicating a Paleolithic origin of treponematosis (Rothschild and Rothschild 1996).

Most of the debate has focused on the origins and spread of syphilis. Recent phylogenetic and SNP analyses of treponemal genes suggest that a New World lineage of *T. pallidum* subsp. *pertenue* may be the origin of the subspecies *pallidum* (Harper et al. 2008). Also there are interesting parallelisms between human treponematosis and similar infections in primates (please see Sect. 1.4) The change from casual to venereal route of transmission in *Treponema pallidum* remains a puzzle. However, non-venereal *T. pallidum* subsp. *pertenue* has been found to cause chancre-like (syphilis-like) lesions in Guyanese indigenous people (Scolnik et al. 2003). *Neisseria gonorroheae*, another venereal pathogen, may have evolved from a linage of *Neisseria meningitides* (upper respiratory tract inhabitant) during the Neolithic (Saunders et al. 1999) and it may be related to the emergence of large villages. In this case there is no evidence of recent zoonotic origin of pathogenic of human *Neisseria* which may suggest co-evolution within hominids.

Bordetella pertussis, the etiologic agent of whooping cough, was thought to have originated recently from *Bordetella bronchiseptica* infecting domestic animals such as pigs and dogs (Diamond 1999; Pearce-Duvet 2006; Wolfe et al. 2007). Although analysis of DNA sequences of multiple loci (MLST) indicated that *B. pertussis* evolved from *B. bronchiseptica* (Diavatopoulos et al. 2005), recent molecular clock estimations suggest that the divergence time between *B. pertussis* and *B. bronchiseptica* associated with domestic animals was 1.1 to 5.6 million years ago (Diavatopoulos et al. 2005), before the origin of *Homo sapiens*, 0.2 million years ago (Forster 2004) and therefore also before the domestication of pigs and dogs. Genomic decay in *B. pertussis* may have been the result of evolution among ancestral hominids and adaptation to these hosts (Diavatopoulos et al. 2005; Bentley and Parkhill 2004). Additionally, human strains of *B. parapertussis*

(a bacterium causing less severe whooping cough in humans) have diverged from animal *B. bronchiseptica* 0.7 to 3.5 million years ago and from a different clade than *B. parapertussis* isolated from domestic animals, however a recent report suggests that strains of *B. parapertussis* of human and ovine origins may be more closely related than previously described (Park et al. 2012)

Some *B. bronchisepica* infecting humans seem to belong to different lineages from those infecting domestic animals whereas other clades appear to be zoonotic (Diavatopoulos et al. 2005). Human pathogenic *Bordetella* may have originated from related bacteria infecting other animals during the Paleolithic period (Diavatopoulos et al. 2005).

Variola (Smallpox) virus was also thought to have originated in domestic animals (Diamond 1999; Pearce-Duvet 2006; Wolfe et al. 2007). However correlation of phylogenetic analysis and historical records indicate that variola virus belongs to a different lineage than cowpox virus (Li et al. 2007). Recent analysis suggests that this virus originated in an African rodent during the Paleolithic period (Li et al. 2007), however other authors have presented evidence of a more recent divergence (approximately 3,500 years ago) between the virus from the African rodent and the variola virus (Babkin and Babkina 2012).

1.3 Evidence of Co-evolution with African Primates

Mycobacterium leprae has been found in wild primates showing signs of leprosy (Hubbard et al. 1991; Clark-Curtiss and Walsh 1989). The significance of non-human primate leprosy is unknown because of lack of genetic information of the etiologic agents. At this point it is not possible to decipher if these primates, like armadillos (Truman et al. 2011), contracted *M. leprae* from humans or vice versa, or whether this bacterium belongs to a distinct but phylogenetically related linage (co-evolution within primates). While it is unknown whether this leprosy from non-human primates could be passed to humans, there is some evidence that leprosy from armadillos could be zoonotic in some regions (Truman et al. 2011).

Similarly, *T. pallidum* subsp. *pertenue* infection rates are high in both humans and primates in yaws-endemic areas of West Africa (Centurion-Lara et al. 2006). A simian yaws-like skin disease caused by a variant closely related to the human *T. pallidum* subsp. *pertenue*, which does not appear to be the result of recent cross infection from humans, has been described (Harper et al. 2008; Centurion-Lara et al. 2006), although inoculation with the simian strain can cause a yaws-like infection in humans suggesting that cross species transference is also possible (Harper et al. 2008). Additionally, *T. pallidum* subsp.*pertenue* has been reported to cause genital ulcerations in African primates (Knauf et al. 2011) and the tropism to genital epithelia of these non-human primate strains could be an example of

parallel evolution. These data suggest that skin treponematosis may have evolved within African primates and ancestral hominids.

Other microorganisms which may have co-evolved with African hominids are herpesviruses (McGeoch et al. 2005), papillomaviruses (Gottschling et al. 2007), *Helicobacter pylori* (Linz et al. 2007), *Streptococcus pneumoniae* (Kilian et al. 2008), *Taenia solium*, *T. saginata* (Hoberg et al. 2001), and even human intestinal microbiota (Ochman et al. 2010).

1.4 Evolving to Human-Specific Pathogens

Pathogen crossing of host-species barriers is a common occurrence in natural environments (zoonosis and anthroponosis). However, acquiring traits enabling efficient transmission within a given host species is a more unusual event. Evolutionary adaptation of many bacterial pathogens to a specific host transmission may be accompanied by a trade off which reduces the competence to cross host species barriers and often involves genome decay (Bentley and Parkhill 2004).

Adaptation to transmission within a new host (i.e. human to human transmision) seems to occur more frequently in pathogens infecting phylogenetically related hosts (Davies and Pedersen 2008; Holmes 2008). Molecular similarities between cells from closely related animal species may facilitate this adaptation process (Holmes 2008). The recent evolution of the human pathogens such as hepatitis B virus (Simmonds and Midgley 2005; Vartanian et al. 2002; Tatematsu et al. 2009), HIV (Keele et al. 2006), HTLV (Wolfe et al. 2005), falciparum malaria (Liu et al. 2010) from African primates follows this pattern (Fig. 1.1). Close contact of modern humans with their genetically closer hominid species such as *Homo neanderthalensis* (Green et al. 2010) (or other archaic humans) may have also played a role in the introduction of some of these infectious diseases to modern humans (Fig. 1.1). For instance, the possible emergence of the typhoid fever agent *S. enterica* serovar Typhi (Kidgell et al. 2002) and *E. coli* (Pupo et al. 2000) roughly coincides with the time estimates of the interaction between *Homo sapiens* and *H. neanderthalensis* (Green et al. 2010).

Close contact with phylogenetically distant animals can also result in the evolution of new host-specific pathogens; animal pathogens becoming human pathogens (measles, bubonic plague, smallpox, and swine and avian influenza) and human pathogens becoming pathogens of other animal species (taeniasis, tuberculosis and infectious gastritis).