

Fabrizio Bruschi *Editor*

Helminth Infections and their Impact on Global Public Health

 Springer

Helminth Infections and their Impact on Global Public Health

Fabrizio Bruschi
Editor

Helminth Infections and their Impact on Global Public Health

 Springer

Editor
Fabrizio Bruschi
Dipartimento di Ricerca Traslazionale, N.T.M.C.
Università di Pisa
Pisa, Italy

ISBN 978-3-7091-1781-1 ISBN 978-3-7091-1782-8 (eBook)
DOI 10.1007/978-3-7091-1782-8
Springer Wien Heidelberg New York Dordrecht London

Library of Congress Control Number: 2014938100

© Springer-Verlag Wien 2014

This work is subject to copyright. All 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. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

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.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

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

A Linda

Preface

The helminths are comprised of two distantly related taxa, the roundworm Nematelminthes and the flatworm Platyhelminthes, the latter being divided into cestodes (tapeworms) and trematodes (flukes). Although these groups diverged evolutionarily many hundreds of millions of years ago, their patterns of transmission, infection, and pathogenesis are in many ways similar. Furthermore, the host immune responsiveness to these pathogens follows a typical pattern which is dominated by a Type 2 (Th2) profile with a significant regulatory (Treg) component.

It was estimated that approximately one-third of the almost three billion people who live in extremely poor conditions (less than two US dollars per day) in developing regions of sub-Saharan Africa, Asia, and the Americas are infected with one or more helminths. Despite this, helminth diseases are among the *neglected tropical diseases*.

According to the Global Burden of Disease 2010 Project, more than 14 million of disability-adjusted life years due to disability plus mortality are ascribable to helminths, but since these are inclined to give chronic infections, their impact on the quality of life, estimated with the more appropriate parameter quality-adjusted life years, is certainly enormous. We should take into account that helminths can affect also livestock, with a following worsening of malnutrition in poor countries.

We may then conclude that this world is still a *wormy* one, according to the definition of Norman Stoll in 1947.

The aim of this book is that to give an overview of the impact of helminth infections on the global public health, providing informations not only on the epidemiology, immunology and immunopathology, clinical and laboratory diagnosis, treatment, and prognosis but also on the present and future perspectives of control.

Helminths not only cause diseases but they also undermine the future of next generations in endemic areas; then the control of such infections is strategic for the development of these geographic regions.

This book deals with two general chapters, one on the systematics and biology of helminths and one on paleoparasitology of helminth infections which shows how

the mankind has encountered these pathogens for thousands of years, obliging to change the habits to reduce their impact on the health status.

Then, chapters are specifically devoted to the most relevant helminths which affect the human population such as *Schistosoma*, *Fasciola*, and *Opisthorchis*, among trematodes; *Echinococcus* and *Taenia* spp., among cestodes and soil-transmitted helminths; and *Trichinella*, *Toxocara*, *Anisakis*, *Angiostrongylus*, *Strongyloides*, and lymphatic and tissue as well as zoonotic filariae, among nematodes.

Finally, a chapter on the possible exploitation of helminth-derived molecules for the treatment of human immune-mediated diseases shows how the improvement of the knowledge of the host–parasite interplay might open new ways to medicine in the future.

The reviewing work by Claudio Bandi, Jong-Yil Chai, Jorge Correale, Nilanthi de Silva, Hubert Ferté, Albis Gabrielli, Ray Gamble, Eisaku Kimura, Arne Levsen, Rick M. Maizels, Pedro Moro, K. Darwin Murrell, Alessandra Nicoletti, Karl Reinhard, Evan W. Secor, and Fernando Simon Martin is greatly appreciated.

This book is dedicated to Carlo Urbani, the Italian WHO officer well known to have given the first alarm of SARS outbreak in 2003 and dead because of that 10 years ago. He was a physician, tropicalist, and also a renowned parasitologist who gave an important contribution to the knowledge of *Schistosoma mekongi*, showing how the basic research is strictly related to field applications.

Pisa, Italy

Fabrizio Bruschi

Contents

1 Diversity and History as Drivers of Helminth Systematics and Biology	1
Dante S. Zarlenga, Eric P. Hoberg, and Jillian T. Detwiler	
2 Paleoparasitology of Helminths	29
Gino Fornaciari and Raffaele Gaeta	
3 Schistosomiasis	49
Ahmad Othman and Rashika El Ridi	
4 Fascioliasis	93
S. Mas-Coma, M.D. Bargues, and M.A. Valero	
5 Clonorchiasis and Opisthorchiasis	123
Eduardo Pozio and Maria Angeles Gomez-Morales	
6 Echinococcosis	153
Francesca Tamarozzi, Enrico Brunetti, and Dominique A. Vuitton	
7 Taeniosis and Cysticercosis	201
Elizabeth Ferrer and Teresa Gárate	
8 Trichinellosis	229
Fabrizio Bruschi and Jean Dupouy-Camet	
9 Soil-Transmitted Helminthiasis	275
Albis Francesco Gabrielli, Antonio Montresor, and Lorenzo Savioli	
10 <i>Strongyloides stercoralis</i> and Strongyloidosis	299
Masataka Korenaga and Fabrizio Bruschi	
11 Anisakiasis	325
Simonetta Mattiucci and Stefano D'Amelio	

12 Lymphatic and Tissue Filariasis 367
Marc P. Hübner, Laura E. Layland, and Achim Hoerauf

13 *Dirofilaria* Infections in Humans and Other Zoonotic Filarioses . . . 411
Claudio Genchi, Claudio Bandi, Laura Kramer, and Sara Epis

14 Toxocariasis 425
Clare M. Hamilton, Ayako Yoshida, Elena Pinelli,
and Celia V. Holland

15 Angiostrongyloidosis 461
Shih-Chan Lai

16 Can the Study of Helminths Be Fruitful for Human Diseases? 479
Justyna Rzepecka and William Harnett

List of Contributors

Claudio Bandi Department of Veterinary Sciences and Public Health, Università degli Studi di Milano, Milan, Italy

M.D. Bargues Departamento de Parasitología, Facultad de Farmacia, Universidad de Valencia, Burjassot, Valencia, Spain

Enrico Brunetti Division of Infectious and Tropical Diseases, WHO Collaborating Centre for Clinical Management of Cystic Echinococcosis, University of Pavia, San Matteo Hospital Foundation, Pavia, Italy

Fabrizio Bruschi Department of Translational Research, N.T.M.S., Università di Pisa, Pisa, Italy

Stefano D'Amelio Department of Public Health and Infectious Diseases, Section of Parasitology, Sapienza – University of Rome, Rome, Italy

Jillian T. Detwiler Department of Biological Sciences, Faculty of Science, University of Manitoba, Winnipeg, MB, Canada

Jean Dupouy-Camet Centre National de Référence des Trichinella, Service de Parasitologie et Mycologie Médicale, Hôpital Cochin, Université Paris Descartes, Paris, France

Rashika El Ridi Zoology Department, Faculty of Science, Cairo University, Cairo, Egypt

Sara Epis Department of Veterinary Sciences and Public Health, Università degli Studi di Milano, Milan, Italy

Elizabeth Ferrer Instituto de Investigaciones Biomédicas “Dr. Francisco J. Triana Alonso” (BIOMED) and Departamento de Parasitología, Universidad de Carabobo Sede Aragua, Maracay, Venezuela

Gino Fornaciari Division of Paleopathology, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Albis Francesco Gabrielli Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

Raffaele Gaeta Division of Paleopathology, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Teresa Gárate Instituto de Salud Carlos III, Centro Nacional de Microbiología, Servicio de Parasitología, Majadahonda, Madrid, España

Claudio Genchi Department of Veterinary Sciences and Public Health, Università degli Studi di Milano, Milan, Italy

Clare M. Hamilton Moredun Research Institute, Edinburgh, Scotland

William Harnett Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK

Eric P. Hoberg Animal Parasitic Diseases Laboratory, Agricultural Research Service, USDA, Beltsville, MD, USA

Achim Hoerauf Institute of Medical Microbiology, Immunology and Parasitology, University Hospital Bonn, Bonn, Germany

Celia V. Holland Department of Zoology, School of Natural Sciences, Trinity College Dublin, Dublin 2, Ireland

Marc P. Hübner Institute of Medical Microbiology, Immunology and Parasitology, University Hospital Bonn, Bonn, Germany

Masataka Korenaga Department of Parasitology, Kochi Medical School, Kochi University, Nankoku, Kochi, Japan

Laura Kramer Department of Veterinary Science, Università degli Studi di Parma, Parma, Italy

Shih-Chan Lai Department of Parasitology, Chung Shan Medical University, Taichung, Taiwan

Laura E. Layland Institute of Medical Microbiology, Immunology and Parasitology, University Hospital Bonn, Bonn, Germany

S. Mas-Coma Departamento de Parasitología, Facultad de Farmacia, Universidad de Valencia, Burjassot, Valencia, Spain

Simonetta Mattiucci Department of Public Health and Infectious Diseases, Section of Parasitology, Sapienza – University of Rome, Rome, Italy

Antonio Montresor Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

Maria Angeles Gomez Morales Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy

Ahmad Othman Medical Parasitology Department, Faculty of Medicine, Tanta University, Tanta, Gharbiya, Egypt

Elena Pinelli Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands

Edoardo Pozio Department of Infectious, Parasitic and Immunomediated diseases, Istituto Superiore di Sanità, Rome, Italy

Justyna Rzepecka Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK

Lorenzo Savioli Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

Francesca Tamarozzi WHO Collaborating Centre for Clinical Management of Cystic Echinococcosis, University of Pavia, Pavia, Italy

M.A. Valero Departamento de Parasitología, Facultad de Farmacia, Universidad de Valencia, Burjassot, Valencia, Spain

Dominique A. Vuitton WHO Collaborating Centre for Prevention and Treatment of Human Echinococcosis, University of Franche-Comté and University Hospital, Besançon, France

Ayako Yoshida Department of Infectious Diseases, University of Miyazaki, Miyazaki, Japan

Dante S. Zarlenga Animal Parasitic Diseases Laboratory, Agricultural Research Service, USDA, Beltsville, MD, USA

Chapter 1

Diversity and History as Drivers of Helminth Systematics and Biology

Dante S. Zarlenga, Eric P. Hoberg, and Jillian T. Detwiler

Abstract Over the years, we have come to recognize that evolution is a dynamic process and a fundamental organizing principle for exploring diversity and the biosphere. Basic knowledge of systematics and phylogenetics within an evolutionary context is essential for gaining a flexible understanding of contemporary parasite diversity and developmental pathways and how these are influenced by environmental perturbation and anthropogenic forcing. Further, an appreciation for historical processes as determinants of modern day geographic patterns and host associations is needed to explore the outcomes of environmental perturbation on parasite evolution. Collectively, these data lead to better predictive capacity for future changes in the distribution patterns and roles that parasites play in animal and human health. In this chapter we highlight how insights from the past and knowledge of current parasite assemblages expose the impacts that accelerated climate warming, habitat perturbation, erosion of biodiversity, and changes in host adaptation have had on the ebb and flow of zoonotic infectious diseases. We further look at how molecular and biochemical studies have advanced systematics, taxonomic stability, and diagnostic capability and are guiding future progress toward understanding parasites, parasitism, and their relationships to global public health.

D.S. Zarlenga (✉)

Animal Parasitic Diseases Laboratory, Agricultural Research Service, USDA, Beltsville, MD 20705, USA

e-mail: Dante.Zarlenga@ARS.USDA.GOV

E.P. Hoberg

US National Parasite Collection, Agricultural Research Service, USDA, Beltsville, MD 20705, USA

J.T. Detwiler

Department of Biological Sciences, Faculty of Science, University of Manitoba, Winnipeg, MB, Canada R3T 2N2

1.1 Introduction

Systematics is the foundation for biology. It provides a basic evolutionary map to discover, characterize, and interpret global diversity and our place in the biosphere. It also allows us to explore questions related to host associations, life history, genetics, and patterns of infection and disease, the cornerstones of epidemiology. Systematics reflects the intersection of phylogeny (evolutionary or genealogical relationships of organisms) and taxonomy (a standard nomenclature, the process of species delimitation, and the theory and practice of classification). Significantly, it brings history on the table and links evolution, ecology, and biogeography.

Many operational definitions or “species concepts” have arisen over time, and these concepts have become more convoluted as the number and types of characters and methodologies have increased, including the use of biochemical and genetic information. Scientists seeking to establish and validate helminth systematics are seemingly disadvantaged in that they lack fossil records to support present-day classifications. Instead, they must reconstruct evolutionary history that gave rise to assemblages of considerable diversity predicated on examining characters from extant organisms only. However, with concepts of phylogenies in hand, host and parasite associations can be explored over time and across a global arena that is under dynamic change. Episodic change or perturbation at all levels of history, linking evolutionary and ecological time, introduces uncertainty but also drives the overall structure of complex biological systems including those represented by hosts and parasites (Hoberg and Brooks 2013).

Heisenberg, a German theoretical physicist, conveyed pioneering insight on quantum mechanics, uncertainty and indeterminacy. In his 1927 paper on the Uncertainty Principle, he commented on the relationship between the position and the momentum of photons and the future behavior of an atomic particle. In his discussion he indicated that “. . . it is not the conclusion that is wrong (determining future behavior) but the premise (predictability). . . .” He determined that our observations have a direct effect on perceived behavior of quanta or, more generally, on outcomes. His discussion of observer effects on measuring and conveying scientific data is most applicable when trying to understand the concepts of classification, evolution, and the ever-changing role that the environment plays on diversification.

Many philosophies have been put forth on the natural order of things. Smart (1959) suggested that biology is a dynamic entity that neither creates nor refutes but is a manifestation or technological application of the laws of physics and chemistry:

. . . in the (physical type sciences) we are interested in laws, whereas in (the biological type sciences) we are interested in the natural history of structure. . . and in the explanation of why things with this natural history function as they do.

Smart’s premise was there could be no “laws of nature” that guide biological species because any biological laws like the laws of physics would by definition disallow deviation. Michael Ghiselin (1974) further suggested that biological species and monophyletic taxa are not nominal classes but actual individuals

where multiplicity is not required to define a class. Thus, it behooves us to think of and investigate evolution, speciation, and taxonomy as ongoing processes, producing a more fluid and mutable understanding of species in both space and time. Stable classifications require ample sampling, a valid comparative context, and inclusive consideration of what currently surrounds us, all of which are prone to human interpretation, frailty, and change, much as Heisenberg discovered in the movement of subatomic particles.

A wealth of reviews, chapters, and articles has been written on the taxonomy and systematics of helminths. Inasmuch as specific topics and detailed presentations of the biology of each parasite group constitute other portions of this book, we offer a look at helminth phylogeny from a different perspective. We endeavor to examine why “history matters.” A deeper understanding of the historical arena on global to landscape scales contributes to our knowledge of complex host–parasite assemblages. Geographic patterns, host associations, and historical determinants (abiotic and biotic) are foundations for examining the outcomes of perturbation and allow us to predict and anticipate future changes in the distribution of parasites through niche modeling (Peterson 2011) and, by extension, their potential impact on human and animal health (Hoberg and Brooks 2013; Brooks and Hoberg 2013). We highlight how past and current evidence provides a window to explore a future of dynamic change caused by accelerated climate warming, habitat perturbation, erosion of biodiversity, the dissemination of invasive species, changes in host adaptation, and the emergence of zoonotic infectious diseases. Highlighted are recent advancements in molecular identification and population genetics to underscore the value of well-engineered population research to advancing sound taxonomy. Finally, we consider how studies on genomics and phylogenomics have begun to better inform us on the broader “tree of life.” In so doing, we hope to help advance and guide future progress in understanding parasitology and its relationship to global public health.

1.2 Complexities Surrounding Helminth Systematics

Helminths that typically utilize humans either as primary or intermediate hosts are represented by roundworms (phylum Nematoda), flukes (Digenea), and tapeworms (Eucestoda), the latter two belonging to the phylum Platyhelminthes. There are no members of the phylum Acanthocephala that commonly parasitize humans. Body form and symmetry among the primary helminths vary widely, although each major phylum is characterized by a general plan and structure. The nematodes are dioecious (either male or female). Those which infect people commonly include gastrointestinal parasites such as hookworms and ascarids (geo-helminths) and lymphatic parasites such as those that cause onchocerciasis and filariasis. All nematodes possess cylindrical bodies, a fluid-filled pseudocoelom, and a complete tubular digestive system in all stages of development. The body is relatively impervious to the external environment because of an outer cuticle that is

synthesized at the end of each larval stage and just prior to molting. In contrast, the Platyhelminthes or flatworms have a soft, solid-tissue body circumscribed by a plasma membrane or tegument. Unlike other bilaterians, the flatworms have neither a coelom nor a complete digestive tract. Specialized organs for circulatory or respiratory systems are to some extent reduced. In the absence of circulatory and respiratory systems, oxygen and other nutrients must diffuse across a permeable tegument. All Platyhelminthes are hermaphroditic except for blood flukes (schistosomes), which are dioecious. In their adult, sexually mature stage, all helminths are considered to be macroparasites and relatively large (>1 mm long), though some adult tapeworms can be measured in meters rather than millimeters. Although there are numerous biological and developmental characters that link these groups, faunal and morphological diversity abounds.

Revealing the complex tapestry of human helminths and infection relies on clear definitions of faunal diversity, species, and populations. Diversity, encompassing spatial, ecological, and genealogical aspects, can be considered in hierarchical patterns relative to scale. It extends from regional faunas to species, cryptic diversity (e.g., cryptic morphospecies), and populations (Hoberg 1997; Pérez-Ponce de León and Nadler 2010). As a gateway to fine-scale relationships, variation in local haplotype diversity is ephemeral and serves as an indicator for landscape epidemiology (analyses of ecosystems) and regional processes. It is the foundation for understanding patterns of emergence (Thompson 2005). Landscape evaluations are essential for understanding basic determinants for occurrence, emergence, and disease. The distribution of disease is often heterogeneous, local, and circumscribed within a more extensive spatial range for a parasite or host–parasite assemblage (Audy 1958; Hoberg 2010). Thus, it becomes important to use molecular phylogenetic and phylogeographic methods to understand the genetic variation within populations, genetic differentiation between populations, and the extent of gene flow among populations (Avisé 2000; Criscione et al. 2005; Huyse et al. 2005; Nieberding et al. 2008).

These relationships for spatial and temporal scale highlight the importance of phylogeny and hierarchical order in framing hypotheses and constraining explanations for species diversity, faunal structure, and history. In recent years, we have seen a transformation in how we view the nature of species and a shift from typological and authoritative approaches that characterized much of the twentieth century (Brooks and McLennan 2002) to those that involve hypothesis testing. Modern-day hypotheses emerged from an evolutionary species concept (historical and phylogenetic definitions of species) followed by secondary evaluation relying on aspects of biogeography, ecology, and reproductive isolation (biological species concept) (see Brooks and McLennan 2002; Wiley and Lieberman 2011). Thus, species delineation and the process of speciation (the mechanisms involved in the origins of species) are linked, where history (phylogeny) allows the recognition of species followed by testable hypotheses based upon the biological species concept (Brooks and McLennan 2002; Nadler 2002). Recent examples are analyses exploring diversity among species of *Taenia* and *Echinococcus* (Hoberg 2006; Nakao

et al. 2007, 2009, 2013a, b; Lavikainen et al. 2008), and studies of species richness in *Trichinella* (Zarlenga et al. 2006; Pozio et al. 2009).

1.2.1 *Helminth Parasites and the World Stadium*

The impact of parasites occurs at the junction of human populations, ecosystem structure, and globalization in a matrix increasingly determined by climatological forces of anthropogenic origin and environmental perturbation (Patz et al. 2000, 2007, 2008; Brooks and Hoberg 2007; Weaver et al. 2010; Brooks and Hoberg 2013). Despite thousands of years of medical and veterinary intervention, helminth parasites remain a considerable regional concern for people, their domestic food animals, and free-ranging vertebrate species. Over the past 10,000–15,000 years, the evolution of agriculture, animal domestication, urbanization, and transformation of natural habitats have all been driving forces for the emergence of helminth and other diseases (Daszak et al. 2000; Patz et al. 2008; Rosenthal 2008; Hoberg 2010; Kuris 2012). These historical processes are equivalent to those in a present-day regime of accelerating environmental change (Brooks and Ferrao 2005; Hoberg and Brooks 2008, 2013). Although the tipping points represented by a burgeoning human population and the development of agriculture and animal domestication have had a direct influence on the occurrence of parasites in humans, many host–parasite associations for extant parasites have considerably deeper origins extending into the Pliocene and Pleistocene (Hoberg and Brooks 2013).

Although parasites are often obscure, they represent in excess of 40–50 % of the organisms on Earth. They are integral components of all ecosystems and have considerable involvement in at least 75 % of trophic links within food webs (Dobson et al. 2008; Lafferty et al. 2008; Kuris et al. 2008). Significantly, 61 % of all pathogens are zoonotic, derived primarily through interactions with free-ranging vertebrate species (Daszak et al. 2000). Human pathogens (primarily viruses and bacteria) are often associated with wildlife (Taylor et al. 2001; Cleaveland et al. 2001; Wolfe et al. 2007). This intricate web of interactions establishes the significance of human parasites as mediators of health and well-being, food sustainability, food security and safety, socioeconomic development, and, more broadly, ecological structure and services that contribute to continuity and connectivity in the biosphere (Patz et al. 2007, 2008; Polley 2005; Weaver et al. 2010).

Based on global estimates, between 75,000 and 300,000 species of helminths infect terrestrial and aquatic vertebrates (Dobson et al. 2008). Among these, 287 are known to occur in humans, 95 % of which are zoonotic (Cleaveland et al. 2001; Taylor et al. 2001). An alternative estimate places this number at 305 helminth species in humans, with 83 identified as prevalent, and 39 able to cause substantial morbidity or mortality (Ashford and Crewe 2003; Kuris 2012) (Table 1.1). Among this larger assemblage, 39 species have patterns of circulation and transmission that are solely dependent on human hosts. Overall, only 44 % of the most prevalent

Table 1.1 Helminth species characteristic of people across the world including those dependent on humans for transmission and some prominent zoonotic parasites [Based on Ashford and Crewe (2003) with modifications from Jenkins et al. (2013) and Nakao et al. (2013b)]

Platyhelminthes-

Digenea (11 human-dependent species)

Schistosomatidae-

Schistosoma haematobium^a

Schistosoma intercalatum^a

Schistosoma japonicum^b

Schistosoma mansoni^{a?}

[+ species of *Schistosoma* (8), *Gigantobilharzia* (2), *Trichobilharzia* (4)]^c

Echinostomatidae-

Echinostoma echinatum^b

[+ species of *Acanthoparyphium* (2), *Artyfechinostoma* (2), *Echinocasmus* (5), *Echinostoma* (11), *Hypoderaeum* (1)]^c

Gymnophallidae-

[*Gymnophalloides seoi*]^c

Fasciolidae-

Fasciolopsis buski^b

[+ species of *Fasciola* (2)]^c

Gastrodiscidae-

Gastrodiscus hominis^b

Heterophyidae-

Heterophyes heterophyes^{b?}

[+ species of *Apophallus* (1), *Centrocestus* (5), *Cryptocotyle* (1), *Haplorchis* (5), *Heterophyes* (5), *Metagonimus* (4), *Stictodora* (3)]^c

Opisthorchidae-

Clonorchis sinensis^{a?}

Opisthorchis felineus^{b?}

[+ species of *Metorchis* (2)]^c

Paragonimidae-

Paragonimus westermani^b

[+ species of *Paragonimus* (8)]^c

Troglorematidae-

[*Nanophyetus salmincola*]^c

Eucestoda (6 human-dependent species)

Diphyllobothriidae-

Diphyllobothrium latum^b

[+ species of *Diphyllobothrium* (15), *Diplogonoporus* (3), *Pyramicocephalus* (1), *Schistocephalus* (1), *Spirometra* (4)]^c

Anoplocephalidae-

Inermicapsifer cubensis^b

[+ species of *Bertiella* (2), *Raillietina* (2)]^c

Dilepididae-

[*Dipylidium caninum*]^c

Hymenolepididae-

Rodentolepis nana^a

[+ *Hymenolepis diminuta*]^c

(continued)

Table 1.1 (continued)

Taeniidae-
Taenia asiatica^a
Taenia saginata^a
Taenia solium^a
[+ species of *Echinococcus* (6), *Taenia* (7)]^c

Mesocestoididae-
[species of *Mesocestoides* (2)]^c

Nematoda (22 human-dependent species)

Strongyloididae-
Strongyloides fuelleborni fuelleborni^b
Strongyloides fuelleborni kellyi^a
Strongyloides stercoralis^a

Ancylostomatidae-
Ancylostoma duodenale^a
[+ species of *Ancylostoma* (4)]^c
Necator americanus^a

Chabertiidae-
Oesophagostomum bifurcum^b
Ternidens deminutus^b

Trichostrongylidae-
Trichostrongylus colubriformis^b
Trichostrongylus orientalis^b

Angiostrongylidae
[species of *Parastrongylus* (2)]^c

Oxyuridae-
Enterobius gregorii^a
Enterobius vermicularis^a

Ascaridae-
Ascaris lumbricoides^a
[+ species of *Baylisascaris* (1), *Toxocara* (2), *Toxascaris* (1)]^c

Anisakidae-
[species of *Anisakis* (2), *Pseudoterranova* (1)]^c

Dracunculidae-
Dracunculus medinensis^a

Gnathostomatidae-
[species of *Gnathostoma* (6)]^c

Gongylonematidae-
[*Gongylonema pulchrum*]^c

Onchocercidae-
Brugia malayi^b
Brugia timori^a
Loa loa^a
Mansonella ozzardi^a
Mansonella perstans^a
Mansonella streptocerca^a
Onchocerca volvulus^a
Wuchereria bancrofti^a

(continued)

Table 1.1 (continued)

[+ species of <i>Dirofilaria</i> (5)] ^c
Trichuridae-
<i>Trichuris trichiura</i> ^b
[+ <i>Calodium hepaticum</i> , <i>Eucoleus aerophilus</i> , <i>Paracapillaria philippinensis</i>] ^c
Diectophymidae-
[<i>Diectophyme renale</i>] ^c
Trichinellidae-
[<i>Trichinella spiralis</i> , <i>T. britovi</i> , <i>T. murrelli</i> , <i>T. nativa</i> , <i>T. nelsoni</i> , <i>T. pseudospiralis</i>] ^c
Acanthocephala (Ø human-dependent species)
<i>Macracanthorhynchus hirudinaceus</i> ^c
<i>Macracanthorhynchus ingens</i> ^c
<i>Moniliformis moniliformis</i> ^c

^aParasites completely dependent on human transmission

^bParasites that occur among humans and other definitive hosts, and for which people are not required for transmission, but may be involved in circulation

^cParasites that represent prominent regional to local zoonoses, and in which humans are not involved in transmission or circulation

? = exact relationship as obligate human parasite requires elucidation

Ø = denotes “none”

micro- and macroparasites are considered zoonotic. This more conservative estimate denotes parasites as zoonotic because they cannot be sustained in humans as definitive hosts (consistent with $R_0 < 1$) and includes helminths for which humans may be infected by larval stages such as the metacestodes of certain taeniid tapeworms (species of *Taenia* and *Echinococcus*) or larvae of nematodes such as *Baylisascaris*, *Anisakis* and *Pseudoterranova*, and *Toxascaris* and *Toxocara* (Polley 2005; Kuris 2012). Consequently, species of *Taenia* utilizing people as definitive hosts (*T. saginata*, *T. solium*, and *T. asiatica*), but requiring domestic ungulates for transmission, are not regarded as zoonotic. Among these, only *T. solium* is considered highly pathogenic as the causative agent of human neurocysticercosis.

Approximately 25 % of the world’s population is infected with helminth parasites. Among these, there are 100–150 million suffering substantial morbidity. Not all parasites exact equivalent costs in human health as they vary in virulence, prevalence, abundance, and pathogenicity (Kuris 2012). For example, the soil-transmitted *Ascaris lumbricoides*, *Trichuris trichiura*, *Necator americanus*, and *Ancylostoma duodenale* are cosmopolitan and cause greater morbidity in humans than any other parasitic disease except malaria (Murray and Lopez 1996; Weaver et al. 2010). Further, the distribution of diseases and the impact of parasitic helminths are often heterogeneous. Local factors related to history, climate, land use, food habits, demographics, human behavior, and sanitation play prominent roles as determinants of human infections (Patz et al. 2007; Kuris 2012; Brooks and Hoberg 2013; Hoberg and Brooks 2013). An emerging challenge is seen in the disruption of socioeconomic controls on the occurrence and impact of infection. Warfare, changing climate as it affects food distribution and water resources, movement of refugees, and a breakdown in medical infrastructure all facilitate

new patterns of infection and disease (Patz et al. 2007, 2008; Weaver et al. 2010; Brooks and Hoberg 2013).

1.2.2 *Host-Switching Drives Helminth Evolution*

History is a defining factor in exploring and understanding contemporary distributions and disease risks posed by helminth parasites in human populations. Traditionally, explanations for host occurrence, biogeography, and diversity have been linked to coevolutionary histories (cospeciation/association by common descent of host and parasite lineages) (Brooks and McLennan 1993, 2002; Brooks and Hoberg 2013) wherein parasite faunas of humans and other vertebrates are largely derived from historical ancestor–descendant relationships with other primates (Kuris 2012). This coevolutionary/cospeciation perspective extends to present-day ideas with regard to the difficulty for parasites to undergo host-switching with unrelated vertebrate lineages (Brooks and Ferrao 2005). It behooves us to explore this apparent paradox for cospeciation, host specificity, and colonization in the arena of pathogenic human parasites and emerging infectious diseases (Agosta et al. 2010; Brooks and Hoberg 2013).

A prevailing assumption describing complex host–parasite assemblages is that parasites coevolve with their hosts (Brooks and Ferrao 2005 and earlier papers cited therein). The interdependence of these phenomena discounts host-switching by otherwise narrowly distributed helminths. A challenge to this orthodoxy is that host-switching is common, has directly influenced parasite faunal structure for humans, and is the basis for what are recognized as emerging infectious diseases (Cleaveland et al. 2001; Wolfe et al. 2007; Brooks and Hoberg 2013). Cospeciation as the driving force behind complex host–parasite associations and faunas has had limited explanatory power. It has also hindered studies on geographic expansion, ecological perturbation, and host colonization as prominent processes in faunal assembly and diversification. Invasion is pervasive; episodes leading to the breakdown of ecological isolation and barriers to host colonization have important implications for the distribution and evolution of helminth faunas and emerging infectious diseases (Wolfe et al. 2007; Hoberg 2010; Brooks and Hoberg 2013; Hoberg and Brooks 2013).

Whereas coevolutionary history can explain some helminth faunas in great apes and humans (e.g., pinworms, species of *Enterobius*, and hookworms, species of *Oesophagostomum*) (Brooks and Ferrao 2005), the reality is considerably more complex and fascinating. A contemporary helminth fauna in humans has been cumulative, serving to indicate the rich temporal, spatial, and ecological connectivity that *Homo sapiens* have had across the biosphere in space and time (Hoberg et al. 2001; Hoberg 2006). The diverse helminth fauna among humans denotes dynamic and episodic shifts in climate, habitat, and ecological structure during the late Pliocene and Quaternary (Hoberg et al. 2012). These changes occurred in migratory/dispersal capacity and in foraging behavior among our initial hominoid

(Brooks and Ferrao 2005; Folinsbee and Brooks 2007) and immediate human ancestors (Hawdon and Johnston 1996; Jenkins et al. 2013), and among our contemporary worldwide population. Emphasized is the importance of history and scale, and the connectivity of processes for geographic and host colonization in evolutionary and ecological time. Many human parasites have origins linked more to shared trophic relationships and host-switching among carnivorans than to associations with other mammals and birds that are either carnivores or piscivores (Hoberg et al. 2001; Ashford and Crewe 2003; Kuris 2012). As such, geographic proximity and ecological structure and continuity among foraging guilds are key drivers of parasite acquisition and diversification. Events such as these account for numerous host-specific parasites in humans such as species of *Taenia*.

Shared trophic resources are also the basis for many contemporary zoonotic infections, and less involved in the process of parasite speciation (Kuris 2012). For example, species of *Diphyllobothrium* and diphyllobothriid tapeworms known to parasitize marine mammals at high latitudes of the Nearctic also parasitize humans (Jenkins et al. 2013). Also, the considerable diversity of heterophyid, echinostomatid, and other trematodes transmitted through freshwater and marine fishes and crustaceans promotes their circulation among assemblages of vertebrates, including humans, throughout the world (Marty and Andersen 2000).

1.2.3 Anthropogenic Translocation of Parasitic Helminths

Sorting out which parasites are our coevolutionary legacies (distributed out of Africa or other regions with hominid expansion), and which were acquired through ecological dynamics, provides a nuanced understanding of the mechanisms involved in faunal assembly. Contemporary global expansion (from Africa and Eurasia into North America) has led to a breakdown of geographic and ecological isolation and an increasingly broad exposure of humans to “exotic” helminths and other parasites (Daszak et al. 2000; Harcourt 2012; Jenkins et al. 2013). Global invasion and secondary distribution of parasites (anthropogenic translocation) coincided with early Eurasian trade routes, European expansion, colonial occupations, and the slave trade. As a result, a rich temporal (chronological) and spatial (geographic from landscape to regions) mosaic for acquisition, introduction, and establishment of helminth assemblages has emerged (Hoberg 2010; Hoberg et al. 2012). In a contemporary setting, anthropogenic drivers increasingly influence invasion and the distribution of parasites and pathogens with attendant threats across a matrix linking environments, economies, and societies (Pimentel et al. 2005). The character and evolution of geographic expansion for both free-living and parasitic species have also been influenced by a series of thresholds and tipping points in human history beginning with our expansion out of Africa nearly 40–60 Kya. Further, the advent of agriculture and animal husbandry 10–11 Kya, the age of European exploration ensuing around the year 1500, and the industrial revolution have all represented irreversible points of change for people and our

interface with the environment (Riccardi 2007; Hoberg 2010; Hoberg and Brooks 2013). Today, human influence is a pervasive force in evolution as seen in natural systems and in the diverse assemblages of pathogens in both free-ranging and domesticated hosts (Palumbi 2001). These emerged from a burgeoning population and a transition from a slow and large world dominated by isolation and local effects to a rapid and small world resulting from globalization, homogenization, and integration of fragmented environmental networks (Hoberg 2010; Hoberg and Brooks 2013).

1.3 Defining Diversity

Accurate definitions of diversity are vital to understanding the role of parasites in human and animal diseases. In addition, defining diversity is critical to studying epidemiology, developing management practices to limit transmission, and designing treatment regimes to reduce, mitigate, or eliminate infections. Over the past 200 years, species-level identification of specimens has relied on comparative morphology and is often dependent on examining fully developed adult worms. This is best exemplified by the challenges in diagnosing zoonotic helminths in human infections (Jenkins et al. 2013). In the absence of mature or gravid specimens, authoritative morphological identification has often not been possible due to the absence of reliable structural attributes in other parasitic stages. It was not until the advent and application of reliable and rapid molecular-based diagnostic methodologies (Polley and Thompson 2009; Jenkins et al. 2013) that these problems have begun to resolve themselves. Although molecular-based diagnostics can now supplant preparation and microscopic examination of whole specimens, such approaches remain directly tied to definitive identification of adult parasites through linkage to a morphospecies name and concept. Validation of molecular data from multiple authoritatively identified adults, held as archival vouchers in museum collections, is the gateway for applying sequences and appropriate molecular markers to diagnosing life history stages including eggs and larvae.

Continued reliance on archival museum collections as resources for biodiversity, informatics and our study of the biosphere, including history and structure, is apparent (Cook et al. 2013). Museum collections and specimens are the self-correcting records for biodiversity that document the geographic occurrence and host associations for parasites. As such, they remain highly relevant to understanding diversity and the changing patterns of distribution over time. Deposition and full documentation of specimens and their environmental niche in appropriate archives should be the expectation from ongoing programs for host–parasite surveys and strategic monitoring for particular spectrums of pathogens (Hoberg 2010; Cook et al. 2013). In this manner the influence of accelerated climate change, ecological perturbation, human activities and invasion, and other factors that determine the distribution of pathogens and disease may be tracked in space and time through the application of comparative baselines. Specimens combined with