Infectious Diseases in Primates

Behavior, Ecology and Evolution

Charles L. Nunn
Sonia Altizer

OSEE

Oxford Series in Ecology and Evolution

Infectious Diseases in Primates

Oxford Series in Ecology and Evolution
Edited by Paul H. Harvey and Robert M. May

The Comparative Method in Evolutionary Biology
Paul H. Harvey and Mark D. Pagel
The Causes of Molecular Evolution
John H. Gillespie
Dunnock Behaviour and Social Evolution
N. B. Davies
Natural Selection: Domains, Levels, and Challenges
George C. Williams
Behaviour and Social Evolution of Wasps:
The Communal Aggregation Hypothesis
Yosiaki Itô
Life History Invariants: Some Explorations of Symmetry in Evolutionary Ecology
Eric L. Charnov
Quantitative Ecology and the Brown Trout
J. M. Elliott
Sexual Selection and the Barn Swallow
Anders Pape Møller
Ecology and Evolution in Anoxic Worlds
Tom Fenchel and Bland J. Finlay
Anolis Lizards of the Caribbean:
Ecology, Evolution, and Plate Tectonics
Jonathan Roughgarden
From Individual Behaviour to Population Ecology
William J. Sutherland
Evolution of Social Insect Colonies: Sex Allocation and Kin Selection
Ross H. Crozier and Pekka Pamilo
Biological Invasions: Theory and Practice
Nanako Shigesada and Kohkichi Kawasaki
Cooperation Among Animals: An Evolutionary Perspective
Lee Alan Dugatkin
Natural Hybridization and Evolution
Michael L. Arnold
Evolution of Sibling Rivalry
Douglas Mock and Geoffrey Parker
Asymmetry, Developmental Stability, and Evolution
Anders Pape Møller and John P. Swaddle
Metapopulation Ecology
Ilkka Hanski
Dynamic State Variable Models in Ecology: Methods and Applications
Colin W. Clark and Marc Mangel
The Origin, Expansion, and Demise of Plant Species
Donald A. Levin
The Spatial and Temporal Dynamics of Host-Parasitoid Interactions
Michael P. Hassell
The Ecology of Adaptive Radiation
Dolph Schluter
Parasites and the Behavior of Animals
Janice Moore
Evolutionary Ecology of Birds: Life Histories, Mating Systems and Extinction
Peter Bennett and Ian Owens
The Role of Chromosomal Change in Plant Evolution
Donald A. Levin
Living in Groups
Jens Krause and Graeme D. Ruxton
Stochastic Population Dynamics in Ecology and Conservation
Russell Lande, Steinar Engen, and Bernt-Erik Sæther
The Structure and Dynamics of Geographic Ranges
Kevin J. Gaston
Animal Signals
John Maynard Smith and David Harper
Evolutionary Ecology: The Trinidadian Guppy
Anne E. Magurran
Infectious Diseases in Primates: Behavior, Ecology and Evolution
Charles L. Nunn and Sonia Altizer

Infectious Diseases in Primates

Behavior, Ecology and Evolution

CHARLES L. NUNN
Max Planck Institute for Evolutionary Anthropology, Germany and University of California, USA

SONIA ALTIZER
University of Georgia, USA

OXFORD
UNIVERSITY PRESS

OXFORD
UNIVERSITY PRESS
Great Clarendon Street, Oxford OX2 6DP

Oxford University Press is a department of the University of Oxford.
It furthers the University's objective of excellence in research, scholarship,
and education by publishing worldwide in

Oxford New York

Auckland Cape Town Dar es Salaam Hong Kong Karachi
Kuala Lumpur Madrid Melbourne Mexico City Nairobi
New Delhi Shanghai Taipei Toronto

With offices in

Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
South Korea Switzerland Thailand Turkey Ukraine Vietnam

Oxford is a registered trade mark of Oxford University Press
in the UK and in certain other countries

Published in the United States
by Oxford University Press Inc., New York

First published 2006

British Library Cataloguing in Publication Data
Data available

Library of Congress Cataloging in Publication Data

Nunn, Charles L.
Infectious Diseases in Primates : Behavior, Ecology and Evolution /
Charles L. Nunn, Sonia M. Altizer.
p. cm.
ISBN-13: 978–0–19–856585–7 (alk. paper)
ISBN-13: 978–0–19–856584–0 (alk. paper)
1. Primates—Diseases. 2. Communicable diseases.
3. Communicable diseases—Environmental aspects.
I. Altizer, Sonia M. II. Title.
RC112.N85 2006
616.9—dc22 2006000425

Typeset by Newgen Imaging Systems (P) Ltd., Chennai, India
Printed in Great Britain
on acid-free paper by
Biddles Ltd., King's Lynn

ISBN 0–19–856584–4 978–0–19–856584–0
ISBN 0–19–856585–2 (Pbk.) 978–0–19–856585–7 (Pbk.)

10 9 8 7 6 5 4 3 2 1

Preface

During the past 25 years, primatologists have remarkably advanced knowledge of primate behavior, ecology, and evolution, providing a deeper understanding of factors driving variation in primate social systems and expanding our perspectives on human evolution. Research in disease ecology over the past several decades has simultaneously identified a number of core principles through a combination of theory and data analysis. Despite this progress—and perhaps even because of it—several gaps have become increasingly obvious. From the perspective of primate biology, we know surprisingly little about the role of infectious diseases in the lives of nonhuman primates in their natural environments. From an epidemiological perspective, important questions involve the role of variation in host social interactions and behavior on the dynamics of infectious diseases.

As a well-studied clade of social animals, primates offer the opportunity to explore how host behavior and ecology can alter the spread of infectious diseases, and to examine the hypothesis that parasites are a potent selective force on host sociality. Addressing these issues requires combining ecological and evolutionary perspectives together with details on primate traits that are likely to influence disease risk and characteristics of the parasites themselves. The idea that parasites are important in the lives of social animals such as primates is not a new one. Yet common wisdom and new hypotheses have yet to be explored in a synthetic framework that examines variation among individuals, groups, populations, and even species. With this in mind, our goal in writing this book is to identify key questions in a framework that integrates existing knowledge of host–parasite interactions with what we know about primate sociality and behavior, while also examining the implications of this knowledge for primate conservation and understanding of human evolution.

We are deeply indebted to Janis Antonovics, Colin Chapman, and Bill Freeland, who gave generously of their time reviewing chapters and provided excellent feedback that greatly improved the first draft of the manuscript. We also recognize Janis for detailed comments on all chapters, and for training us earlier in our careers in the fundamentals of evolutionary biology and inspiring us to study the complex interactions between hosts and parasites. We thank Ian Sherman, Paul Harvey, and Bob May for being open to the ideas presented in this book and for encouraging us to pursue them. Pete Richerson, Tim Caro, Monique Borgerhoff Mulder, Christie Henry,

Michael Pereira, and Michael Sanderson generously gave advice and additional encouragement to pursue the book project.

Several graduate students and postdoctoral researchers at Emory University and the University of California at Berkeley provided important comments and critiques of chapters. At UC Berkeley, we wish to acknowledge students in the "primate disease seminar," including Paul Cross, Sadie Ryan, Andrew Ritchie, Mariah Hopkins, Mike Wasserman, Adrian Dokey, Jessie Standish, and Denise Bonilla. At Emory, we thank Roman Biek, Jaap de Roode, Kristin Harper, Catherine Bradley, Liz Harp, Elizabeth Lindsey, and Nick Vitone. Students and researchers at other institutions provided crucial comments leading to reformulation or revision of several chapters. For this, we thank Michael Huffman, Matt Bonds, Britta Mueller, Barbara Fruth, Leslie Knapp, and Pete Thrall.

Members of the working groups that we co-organized at the National Center for Ecological Analysis and Synthesis (NCEAS) and Conservation International provided helpful feedback at many stages, and with their support and encouragement, we pursued a number of new and exciting projects, with many of the completed research projects described in this book. We thank in particular John Gittleman, Amy Pedersen, Andrew Cunningham, Andy Dobson, Pete Thrall, Janis Antonovics, Kate Jones, Wes Sechrest, Mary Poss, Vanessa Ezenwa, Peter Daszak, and Patrik Lindenfors. All of these individuals gave their time to two or more meetings of the working groups, and they played integral roles in developing projects within these groups.

We thank our colleagues who graciously volunteered photographs or advice on images, including Dawn Kitchen, Ken Glander, Frances White, Alan Dixson, Dewald Keet, Craig Packer, Katharine Milton, Britta Müller, Brian Byrd, Joyce Parga, Kerstin Mätz-Rensing, AnaPatricia Garcia, Michael Huffman, Zhang Peng, Matt Bonds, Kate Jones, Joost Philippa, Catherine Bradley, Martha Robbins, Vanessa Ezenwa, Peter Kappeler, Ulrike Walbaum and Roland Regoes. Noel Rowe deserves particular mention for his assistance with finding "just the right image," including photos for the front and back cover. Peter Walsh kindly provided unpublished manuscripts. Special recognition goes to Liz Harp and Laura Gold who helped extensively in locating photographs and organizing images for several of the chapters, and Joann Chang and Corine Graham for locating articles, obtaining permission to use figures, and organizing references. Anja Herb, Claudia Nebel and Claudia Feige provided help compiling the completed manuscript.

Deep thanks are extended to Sheila Patek and Andy Davis. Sheila provided the initial encouragement to pursue this book project, and patiently provided moral support during the book-writing project. She also provided extensive feedback on topics to cover, advice on proposal preparation, and comments on early versions of the first chapters. Andy assisted with extensive proofing of the manuscript, provided bibliographic support, and inspired revisions of multiple chapters. Andy also supplied patience and continued support during the final stages of writing and revisions.

Charlie also wishes to thank his parents, John and Janet Nunn, and Dorothy McIntyre, for providing a learning environment, education, and support that ultimately made this work possible. Ken Korey at Dartmouth College taught Charlie about

evolution and revealed the pleasures of academic pursuits. Carel van Schaik introduced Charlie to primate socioecology, changed his career path toward behavioral evolution, and inspired him to push the boundaries of our knowledge about primate behavior and ecology. Sonia thanks her parents, Chris and Jim, for encouraging writing, creativity, and academic scholarship, and her Aunt Carole who cultivated an interest in science and nature.

In terms of financial and research support, the authors acknowledge the National Science Foundation (#DEB-0212096), National Center for Ecological Synthesis and Analysis, Conservation International, the University of California (Davis and Berkeley), and Emory University. More recently, we are grateful to the Max Planck Institute for Evolutionary Anthropology and the Institute of Ecology at the University of Georgia for opportunities to extend our research in new directions by providing resources and a dynamic, collaborative environment. We appreciate the support that has been extended to us, and we look forward to developing collaborations with new colleagues.

Charlie Nunn and Sonia Altizer

October 14, 2005

This page intentionally left blank

Contents

I

Questions, terminology, and underlying principles

1.1 Introduction

Parasites are ubiquitous in the lives of primates, and infectious diseases can cause devastating mortality in wild populations, including recent deaths arising from Ebola hemorrhagic fever and anthrax infections in African apes (Walsh et al. 2003b; Leendertz 2004). An incredible diversity of parasites inhabits primate hosts, including sexually transmitted viruses, insect-borne protozoa that cause malaria, and helminths responsible for schistosomiasis and tapeworm infections. More than 50 different parasite species have been documented in some free-ranging primate species, such as olive and yellow baboons (Nunn et al. 2003a), and an individual primate may shed hundreds or thousands of parasite infectious stages over the course of a single day (Pitchford and Visser 1975; Müller-Graf et al. 1996; Nizeyi et al. 1999).

Many of these infectious agents, such as simian immunodeficiency viruses (SIVs), are relatively benign in their natural hosts, and thus have virtually undetectable effects on primate fitness. Others, such as Ebola, have caused alarming declines in primate populations and therefore play a major role in conservation efforts (Chapman et al. 2005a). Still other parasites, including intestinal worms and blood-borne protozoa, have more cryptic effects on primate survival or fecundity in the short term, but taken together their cumulative impacts could be enormous. Not to be overlooked are the myriad of ways that parasites affect patterns of primate behavior, including foraging decisions, behavioral defenses to insect vectors, and mating and social interactions.

Behavioral ecologists have highlighted a variety of ecological and social factors that underlie primate mating and social systems, including predation, resource competition, and inter-sexual conflict (Wrangham 1980; Dunbar 1988; van Schaik 1989, 1996; Smuts and Smuts 1993). Infectious disease represents another potential ecological force in primate social evolution, but the role of parasites in primate socioecology has received remarkably little attention compared to other factors. This omission is extraordinary given that social animals such as primates are expected to be at unusually high risk from infectious diseases, in part because greater contact rates among individuals in social networks should facilitate the spread of infectious disease (Møller et al. 1993; Altizer et al. 2003b). Primates are an ideal group for investigating the links between parasites and socioecology because much is known about

their basic biology, including life history traits, diet, habitat use, and mating patterns (Smuts et al. 1987; Lee 1999; Kappeler and Pereira 2003). This extensive knowledge base makes it possible to investigate the effects of parasites against the background of other ecological forces that influence social systems.

The goal of this book is to examine the links between parasitism and primate behavior, ecology and evolution. Although we focus on primates, many of the principles and approaches developed here apply to a wide range of animals, including other mammals, birds, and insects. A question central to this book is "what factors influence disease risk"? In other words, what intrinsic host characteristics and environmental parameters determine the number and types of parasites infecting wild animals at the individual, population, and species levels? A second and related question is "how can animals reduce this risk"? Data exist to test a broad range of hypotheses related to these two questions, although further research is needed to link many of these predictions with real-world data and to experimentally investigate key hypotheses. Given recent theoretical and empirical developments in wildlife epidemiology, this is an exciting and dynamic time to investigate these questions. We cannot yet hope to provide a definitive treatise; instead, we identify key hypotheses concerning the role of infectious disease in primate mating and social systems, synthesize existing evidence for these hypotheses, and identify future directions for testing predictions through field, comparative, and theoretical approaches.

We also explore the implications of infectious disease in nonhuman primates for both public health and conservation concerns. Humans are clearly the best studied of all primate species in terms of infectious diseases, and pathogens continue to impact human health around the world. The origins of multiple pathogens that crossed into humans both recently and thousands of years ago can be traced to nonhuman primates, with examples including malaria and several retroviral diseases, the best known of which is HIV/AIDS. Understanding the links between parasites and primate socioecology should provide new insights to human health in a broad ecological and evolutionary context, expanding the domain of Darwinian medicine (Ewald 1980; Nesse and Williams 1996; Stearns 1999; Trevathan et al. 1999), and generating new hypotheses to test across human societies at a global scale (Low 1987; Guegan et al. 2001; Guernier et al. 2004). Furthermore, epidemiological insights drawn from studies of infectious diseases in humans can advance our understanding of disease spread in nonhuman primates, which is critical for conserving endangered primates increasingly at risk from emerging pathogens and other anthropogenic threats (Wallis and Lee 1999; Walsh et al. 2003b).

To set the stage for the rest of the book, in this introductory chapter we begin by defining key terms and providing a historical overview of previous research on the interplay between ecological factors and primate sociality. To emphasize the ecological impacts of infectious diseases and their potential role as selective agents, we conclude the chapter by reviewing the effects of parasites on host fitness in wild primate populations.

1.2 Essential terminology: parasite, disease, and disease risk

1.2.1 What is a parasite?

The word parasite has different meanings depending on the discipline in which it is used and how it is applied. In this book, we use the ecological definition of a parasite as any organism that lives on and draws nutrients from another living organism (the host), usually to the host's detriment. Parasites not only drain material resources from their hosts, but can also exploit host metabolism and behavior. Combes (2001) refers to host–parasite relationships as "durable interactions", in contrast to predator–prey relationships that are of shorter duration and result in death of the prey. The definition of parasite we use excludes some groups of organisms that have a close association with primate hosts, such as symbiotic bacteria that aid digestion of leaves in colobines (Bauchop and Martucci 1968). This definition also excludes mosquitoes and other highly mobile arthropods that feed on blood or other host resources. As with predators, their associations with hosts tend to be ephemeral at the level of individual animals; hence, these biting insects are more accurately described as "micro-predators" (Bush et al. 2001). However, many blood-feeding arthropods play an important role as vectors for parasites that infect primate hosts, including vector-borne protozoa, nematodes, and viruses. As such, many behavioral defenses against parasitism target arthropod vectors that are responsible for the spread of these parasites.

An important distinction made by Anderson and May (1979, 1991) is that parasitic organisms can be categorized either as microparasites or as macroparasites. Microparasites are often referred to as pathogens or disease-causing microbes and include viruses, bacteria, protozoa, and fungi, whereas macroparasites typically include worms (helminths) and arthropods. The distinction between micro- and macroparasites is useful to ecologists and epidemiologists, as these groups differ in the degree of within-host replication, factors affecting their population dynamics, and how they are measured in natural populations. Later chapters address these fundamental differences in more detail, and also consider additional classifications of parasites, with special attention to parasite characteristics that govern their transmission within populations and between species.

1.2.2 Parasite and disease

The terms "parasite" and "disease" are often used interchangeably, yet it is incorrect to do so. Disease refers to the pathology caused by infection, including outward physical signs and internal or behavioral changes, whereas parasites are the disease-causing organisms. A related term is pathogen, which refers to any disease-causing agent, although this term is most commonly used for microbial parasites (viruses and bacteria). In this book, we primarily use the term parasite to refer to all infectious

organisms that can potentially harm their hosts, but occasionally substitute related words when appropriate (e.g. pathogen, infectious agent).

Although not all infections are pathogenic, parasitic organisms can cause a staggering array of pathologies in primate hosts (e.g. Kuntz 1982). These manifestations might result directly from activities of the parasite, as in the painful migration of warble flies through the flesh of large mammals (Bush et al. 2001; Colwell 2001), or as diarrhea resulting from reduced intestinal water absorption caused by *Giardia* (Olson and Buret 2001). Physiological consequences of parasite infection in the host usually fall into one of three categories—those that benefit the parasite, those that benefit the host, and those that are byproducts of infection and benefit neither host nor parasite (Ewald 1980; Dawkins 1982; Holmes and Zohar 1994; Thompson 1994b). For example, several arthropod-borne parasites clog the insect vector's digestive systems and impair their ability to obtain a full blood meal, thereby increasing the biting rate of these vectors to the parasites' advantage (and to the detriment of the host, Koella et al. 1998). On the other hand, a rise in host body temperature (fever) following infection can interfere with the growth of some parasites and facilitate a more intense immune response, in this case to the host's advantage (Ewald 1994a).

In some situations, pathology produced by the host's body in the context of infection actually can be harmful to host survival and reproductive success. Consider, for example, the famous images of elephantiasis of the lower extremities (lymphatic filariasis; Fig. 1.1). These horrifying pathologies are the result of complex, long-term immune responses to the mosquito-transmitted nematodes *Brugia malayi* and *Wuchereria bancrofti* (Bush et al. 2001). Interestingly, *B. malayi* is documented to occur in free-living Southeast Asian monkeys (Laing et al. 1960; Mak et al. 1982), but in these species the parasite does not cause the striking pathology found in humans (Orihel and Seibold 1972).

Parasites that induce detrimental pathology in hosts are more likely to regulate populations than those with weaker effects on host fitness (Scott and Dobson 1989). But it is important to keep two caveats in mind. First, when parasites affect host survival alone, standard host–parasite models (Anderson and May 1979, 1991) predict that parasites with low or intermediate effects on hosts will depress host density to a greater extent than parasites that cause high host mortality. This occurs because extremely harmful parasites are likely to kill their hosts before new transmission events occur, highlighting the kinds of insights that emerge when questions are addressed from a rigorous epidemiological modeling perspective—an approach described in later chapters. Thus, an important point to emerge from models is that parasites with low or moderate effects on hosts should not be overlooked when assessing sources of disease risk and potential causes of wildlife declines (McCallum 1994; McCallum and Dobson 1995). This point especially applies to parasites that affect host fecundity (or, in extreme cases sterilize their hosts), as theory predicts that such parasites can limit host recruitment and cause extreme reductions in host population size.

Second, counter to conventional wisdom, the most frequently observed parasites are not necessarily the ones most responsible for population declines (Anderson

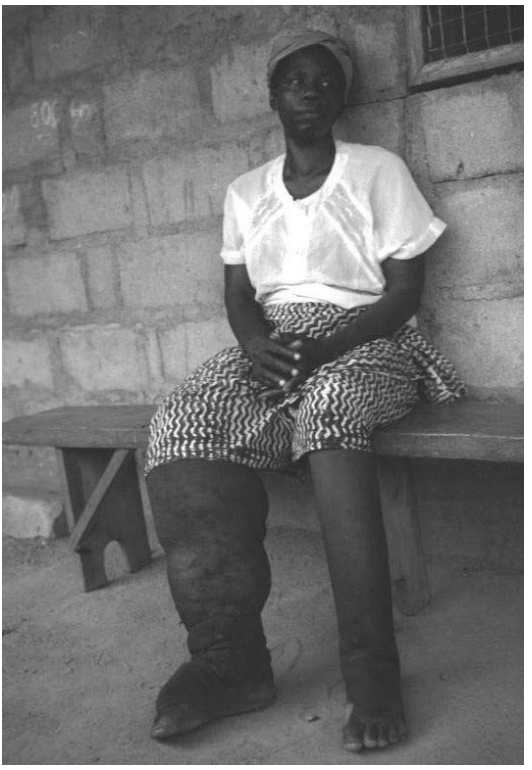


Fig. 1.1 Woman in Ghana exhibits elephantiasis of the right leg and oedema of the left leg. Reprinted from the World Health Organization (WHO/TDR/Crump, image 9902944).

and Gordon 1982). Mathematical models predict that highly transmissible micro- or macroparasites with little or no fitness effects should be relatively common at the population level. In this case, the general host population will show relatively high levels of infection, and the parasite will be found incidentally among a large number of animals that die. Thus, high rates of parasitism in morbid or dead hosts do not necessarily indicate that the parasite in question is having a major impact on the population (McCallum and Dobson 1995). Later in this chapter and subsequent chapters, we discuss more appropriate ways to measure population-level impacts of parasites (Gulland 1992; Hudson et al. 1998b).

1.2.3 What is disease risk and how is it measured?

Throughout this book we refer to "disease risk" as the probability of acquiring an infectious disease. In using this term, we are approaching questions from the host's perspective, as the parasite would view this as an opportunity rather than a risk.

In most cases, we consider disease risk without factoring in the effects of parasites on individual host fitness or population size, in large part because these impacts are presently unknown for the vast majority of parasites in wild primates. In future studies, infectious disease risk could be quantified as some combination of the probability of acquiring an infectious disease and its fitness impact on the host.

At least two questions related to disease risk are of fundamental importance. First, what factors influence the risk of acquiring an infectious disease at the individual, population, and species levels, and second, how does this risk influence the evolution of host behavioral or immune defenses? Biologists have addressed components of these questions in primates (Freeland 1976; Nunn et al. 2000; Tutin 2000), and in other vertebrates (Møller et al. 1993; Altizer et al. 2003b) and invertebrates (Schmid-Hempel 1998; Wilson et al. 2003). In reviewing past work and developing new hypotheses, we distinguish between two measures of disease risk. *Intrinsic disease risk* refers to the probability that an individual host encounters or acquires an infectious disease, whereas *observed patterns of infection* involve the presence and severity of infection at the individual level, or rates of occurrence at the population level. This distinction between intrinsic risk and infection rate should be familiar to primatologists, as it follows similar distinctions in the literature on intrinsic risk versus observed rates of predation in primates (Cowlishaw 1997; Hill and Dunbar 1998; Janson 1998; Nunn and van Schaik 2000).

Different questions sometimes require different measures of disease risk. In this book we refer to three ways of quantifying disease risk.

1. *Quantitative measures of immune and behavioral defenses* can be used to assay levels of risk, based on the reasoning that increased disease risk should select for increased expression and mobilization of host defenses (Harvey et al. 1991; Møller and Saino 1994). These defenses can include behavioral avoidance or physical removal of parasites by preening or grooming, innate or generalized immune defenses, and the adaptive arm of the immune system, including antigen-specific responses (Roitt et al. 1998). For example, Fig. 1.2 shows results from a study that used counts of circulating white blood cells to assay disease risk across a large number of primate species. This figure shows that more promiscuous primate species have higher white blood cell counts, consistent with the hypothesis that risk of acquiring sexually transmitted diseases (STDs) increases when individuals have more mating partners (Nunn et al. 2000; Nunn 2002a; Anderson et al. 2004). Because immune response was not measured directly, these counts are more likely to reflect variation in innate or baseline defenses.

2. Another gauge of risk concerns the *number of parasite species to which a host is exposed*. Empirical measures include observed parasite community diversity within single host populations, or parasite species richness at the level of host species or broader taxonomic scales (e.g. Morand and Poulin 2000; Nunn et al. 2003a). A related measure acknowledges that pathogens might "spillover" from one host species to individuals of another species (Daszak et al. 2000; Cleaveland et al. 2001; Haydon et al. 2002a; Fenton and Pedersen 2005). Such risk can be quantified using

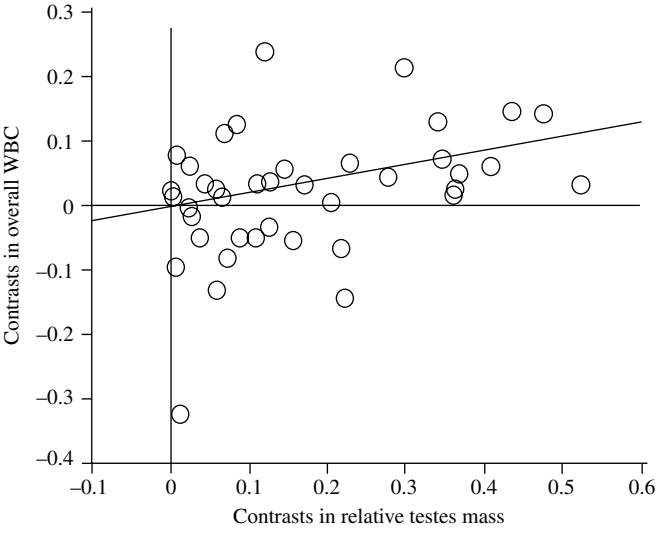


Fig. 1.2 Variation in overall white blood cell counts in relation to mating promiscuity in primates. Mating promiscuity was measured as testes mass after controlling for body mass; as a measure of sperm competition, relative testes mass quantifies female mating promiscuity. Data points represent independent contrasts based on the phylogeny of Purvis (1995). Altered slightly from figure 5 in Nunn, C. L. 2002. A comparative study of leukocyte countsand disease risk in primates. Evolution 56:177–190. Reproduced with permission from the Society for the Study of Evolution.

information on the parasites known to occur across multiple host species within a focal host's habitat or geographic range, such as those found in geographically overlapping (sympatric) host populations.

3. Finally, it is possible to quantify observed levels of infection in a population based on the *prevalence, intensity*, and *abundance* of parasites. Prevalence refers to the proportion of individuals in a population or sub-group that are infected with a parasite. A related term, *incidence*, refers to the rate at which new cases occur, or the change in prevalence over a specified time interval. An individual's infection status can be determined based on direct isolation of the parasite itself, physical signs of infection, or using serum antibodies produced by the host in response to infection, also called seroprevalence. Estimates of seroprevalence should be interpreted cautiously, however, because these antibodies could indicate past exposure rather than current levels of infection. Intensity of infection refers to the number of parasites (i.e. parasite load) within infected hosts only, and abundance measures the mean parasite load of the entire host population. As such, these latter two measures might indicate the total population size of parasites themselves and their quantitative impacts in draining host resources and damaging host tissues.

1.3 Ecological drivers of primate sociality

Socioecologists investigate the ecological basis of social and mating systems, largely through field and comparative studies (Struhsaker 1969; Crook 1970; Sterck et al. 1997; Lee 1999; Harcourt 2001). In terms of primate socioecology, models for ecological determinants of primate mating and social systems initially grew from the pioneering work of Crook and Gartlan (1966). These authors proposed that the environment and sexual selection determined "grades" of primate sociality. Under this scenario, grades were identified as discrete transitions from nocturnal, solitary primates that consume insects, to diurnal species living in socially structured groups in more open environments. The emergence of sociobiology in the 1970s (Wilson 1975; Trivers 1985; Segerstråle 2000) pointed to a larger number of factors influencing primate socioecology, including infanticide as a male reproductive tactic that is costly to females (Hrdy 1974; Hausfater and Hrdy 1984).

Throughout the 1960s and 1970s, long-term field studies of baboons, chimpanzees, gorillas, and langurs provided further insights to primate sociality and ecology (e.g. Altmann and Altmann 1970; Hrdy 1977; Fossey 1983; Goodall 1986), including the role of communication, resource acquisition, predation, and infanticide. Pioneering comparative studies of trait evolution focused on the functional basis of variation across species, including studies by Clutton-Brock et al. (1976, 1977, 1980), Milton and May (1976), and Mitani and Rodman (1979). These studies identified the primary axes of variation in primate socioecology, namely body size, sex ratio, home range size, diet, group size, and life history features. Results of these studies revealed some of our core knowledge of the traits that vary among primate species, including that sexual dimorphism increases when male intrasexual competition for mates increases; that ranging patterns correlate with diet, group size, defense of the home range, and body mass; and that life history traits correlate with body mass (see also Nunn and van Schaik 2001).

This book uses several terms to describe broad aspects of primate sociality. *Social organization* is commonly used to describe the size, composition, and spatial distribution of groups; it specifies how individuals in a population are organized into social units (Kappeler and van Schaik 2002). Key dimensions of social organization in primates include group size, number of adult males and females, age structure, and measures of territoriality (e.g. the defensibility index, Mitani and Rodman 1979). *Social structure* addresses how individuals interact within primate groups, focusing on patterns of individual behavior and the type and frequency of interactions, such as aggression, grooming, cooperative breeding, and food sharing (Kappeler and van Schaik 2002). *Mating system* describes patterns of mating contact among individuals, with categories that include monogamy, polygyny (one male mating with multiple females), polygnyandry (both sexes having multiple partners), and polyandry (one female mating with multiple males, see Clutton-Brock 1989 for an overview). Finally, the *social system* combines both social organization and social structure to describe overall patterns of interaction in the context of group size and composition. Embedded within this framework is the important issue of dispersal, with one or both sexes typically emigrating (Moore 1984; Pusey and Packer 1987).

Modern views of primate socioecology focus on factors that influence different components of social systems, particularly the size and composition of groups, relationships among individuals, and intergroup dispersal. Four main ecological forces have been proposed as key drivers of primate social evolution: resource competition, predation, inter-sexual conflict, and infectious disease. In what follows, we briefly review the major conceptual models that were built around these ecological factors. Further details are available in Smuts et al. (1987), Dunbar (1988), Janson (1992, 2000), Sterck et al. (1997), Isbell and Young (2002), and Nunn and van Schaik (2000).

1.3.1 Between-group resource competition

Wrangham (1980) first proposed that females living in social groups experience a major advantage in competing with other groups for resources. This early and influential model of primate social systems proposed that larger groups of females dominated smaller groups at preferred feeding sites, thus obtaining greater food rewards. Wrangham's model was used to explain the evolution of "female-bonded" kin groups in which related individuals remained in differentiated networks of social relationships rather than living alone. Although between-group competition might provide an advantage to larger groups when population densities are high, more recent studies suggest that resource competition probably does not represent a primary selective force driving the formation of female social relationships (Cheney 1992; Cowlishaw 1995; Sterck et al. 1997; Matsumura 1999). Instead, predation and competition among females *within* groups, as discussed next, probably play a larger role.

1.3.2 Predation and within-group competition

In response to Wrangham's (1980) model of primate socioecology, van Schaik (1983, 1989) proposed that female primates form groups to reduce their risk of predation (following on previous researchers, for example, Alexander 1974). Several studies supported this general hypothesis (Krause and Ruxton 2002). For example, van Schaik et al. (1983) found a significant association between group size and the ease with which animals detected a (human) predator. Similarly, in a comparative study of cercopithecoid primates, Hill and Lee (1998) found that group size increased in populations that experienced greater predation risk.

Once individuals form groups to counter predation risk, the effects of *within-group feeding competition* were hypothesized to influence female relationships within groups (van Schaik 1989; Janson 1992). The intensity of competition will increase when food patches are small, distributed patchily, or when female spatial clumping is high for other reasons (Janson 1988b). Where the potential for within-group contest competition is high, female-bonded groups show decided dominance relationships, alliances with relatives, and female philopatry (van Schaik 1989; Isbell 1991; Sterck et al. 1997), as supported by cumulative evidence from detailed

behavioral studies (e.g. Mitchell et al. 1991; Barton et al. 1996; Isbell and Pruetz 1998; Koenig et al. 1998).

1.3.3 Inter-sexual conflict

Recent attention has focused on male behavior as a selective force affecting female sociality, although it has long been recognized that the social context might be as important as ecological factors in influencing primate mating and social systems (Clutton-Brock and Harvey 1976; Wrangham 1979). Males can use sexual coercion, involving actual or threatened force, to increase their access to mates and to reduce the probability that females mate with other males (see also Clutton-Brock and Parker 1995). Sexual coercion by male primates includes forced copulation, infanticide to shorten the time to fertility, and herding behavior (a form of mate-guarding) to prevent females from copulating with other males. Infanticide in particular has been proposed as a major force on primate behavior (Hrdy 1974; Hausfater and Hrdy 1984; van Schaik and Janson 2000). Females can counter male coercion by forming special relationships with "protector" males and other females (Smuts 1985; Palombit et al. 1997). Thus, female counterstrategies to infanticide can generate variation in mating and social systems, including patterns of male–female associations (van Schaik and Kappeler 1997), female coalitions (Treves and Chapman 1996), and possibly even the evolution of monogamy (van Schaik and Dunbar 1990; cf. Palombit 2000).

1.3.4 Infectious disease

In a series of pioneering papers in the late 1970s, Freeland proposed that primate social interactions and behavior have evolved in ways that reduce the risks of acquiring infectious diseases (Freeland 1976, 1977, 1979, 1980). As one example, Freeland (1977) hypothesized that multi-species associations, in which individuals from different primate species aggregate together, reduce individual rates of attack by blood-sucking flies (Fig. 1.3) in a process analogous to the encounter-dilution effect used by animals to reduce predation by living in groups (see Mooring and Hart 1992; Krause and Ruxton 2002). He even used himself as a human "guinea pig" by sitting on a platform 20 m above the forest floor from dawn until dark, recording the number of bites to his bare arms and legs throughout the day. Freeland was interested in a wide variety of links between primate socioecology and disease risk, proposing, for example, that variation in rates of exchange of individuals between groups was influenced by variation in disease risk (Freeland 1979), and that primate arboreal ranging patterns were linked to avoidance of fecal-contaminated pathways (Freeland 1980). More recently, Loehle (1995) reinvigorated discussion about disease and social barriers to transmission across a wide variety of animals (including primates), with hypotheses linked directly to modes of parasite transmission.

Freeland's proposals remain provocative and interesting, but largely untested. Many of his hypotheses require careful consideration of alternative ideas, because

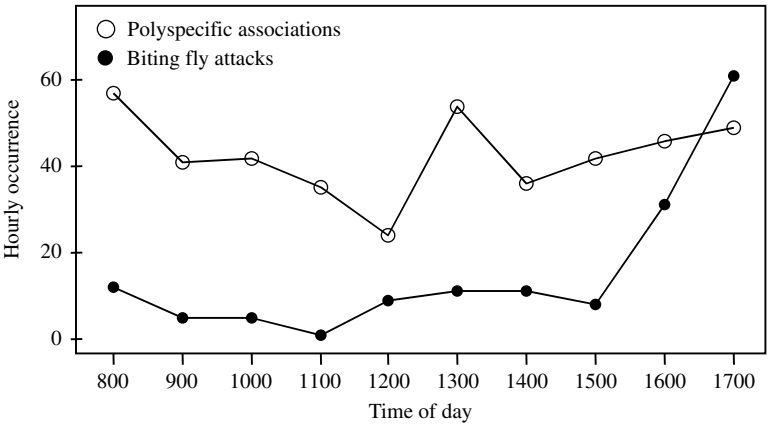


Fig. 1.3 One of the earliest studies of primate social behavior in relation to infectious disease risk. Plot shows polyspecific associations and biting fly attacks in Kibale, Uganda (data from Freeland 1977). Open circles show the occurrence of polyspecific associations by a group of mangabeys (*Cercocebus albigena*), with associations defined as the presence of an individual of another species within 20 m of the nearest mangabey. Closed circles are the occurrence of biting fly attacks (mosquitoes and other insects) measured on humans at the site. Spearman rank correlation=0.63, which is significant ($P < 0.05$) in a one-tailed test.

other ecological and social factors make predictions similar to those involving disease risk. The case of dispersal between groups provides an intuitive and accessible example of how alternative hypotheses could also account for behavioral patterns that might be linked with disease. Thus, Freeland (1976) noted that in many primate species, animals must endure a lengthy process to disperse from one group and assimilate into a new one. As an explanation, he proposed that individuals are forced to undergo a period of harassment prior to successfully transferring into a new group, during which time any latent infections might be expressed (with stressful challenges used to identify infectious immigrants). But an alternative hypothesis asserts that primates exclude potential immigrants to reduce competition for mates (among males) or resources (among both sexes)—and this might even be a more plausible explanation for resistance by group members to potential immigrants.

At one level, the consequences of sociality and group living for infectious disease seem relatively straightforward, in that animals living in close proximity or with high contact rates should experience higher rates of parasite transmission. Thus, more social primate species should have higher parasite prevalence and more diverse parasite communities relative to species that are solitary or live at low density, and they should also experience more intense selection for behavioral or immune defenses (Møller et al. 1993, 2001). This link between population density and greater disease risk emerges from models of directly-transmitted micro- and

macroparasites (Anderson and May 1979, 1991). In fact, the relationship between disease risk and group size was noted by Alexander (1974) in an early review of the evolution of social behavior.

Several researchers of primate socioecology have tested hypotheses concerning disease risk and primate social systems. For example, Hausfater and Watson (1976) investigated the parasite loads of individual baboons based on social rank, finding that higher-ranking males exhibited increased levels of parasitism with intestinal helminths. In another influential paper, Hausfater and Meade (1982) investigated patterns of habitat use and parasitism in baboons. They proposed that risks from fecal-borne parasites that accumulate in the soil influence baboon ranging patterns and movement between sleeping sites. These and other papers represent some of the first attempts to formulate and test hypotheses for the links between infectious disease and the behavior and demography of free-living primates.

Compared to the rapid proliferation of studies addressing the socioecological consequences of predation, resource competition, and inter-sexual conflict, studies of parasites in relation to group living in primates have proceeded at a slow trickle. In many cases, authors offered lip service to the possibility that parasites influence primate socioecology, often citing one of Freeland's publications, but then moved on to examine another ecological factor in greater depth. This tendency to focus on other ecological factors probably reflects the challenges of quantifying parasitism or disease risk. As we show in the chapters that follow, tests of hypotheses involving infectious diseases are now more feasible (see also Heymann 1999; Janson 2000).

A brief history of infectious disease in primate socioecology would be incomplete without mentioning medicinal plant use as a way that primates can lower their parasite loads or alleviate the symptoms of disease (Chapter 5). Following a provocative paper by Janzen (1978), Wrangham and Nishida (1983) proposed that chimpanzees (*Pan troglodytes*) consume the leaves of *Aspilia* spp. for their pharmacological effects. Similarly, Phillips-Conroy (1986) proposed that baboons consume the leaves and berries of *Balanites aegyptiaca* to eliminate infection with schistosomes, based on evidence that consumption of the plant was more common in areas where schistosomiasis was most likely to occur (although a follow-up study in captive mice failed to support the proposed mechanism; Phillips-Conroy and Knopf 1986). A large number of studies in the late 1980s and 1990s have investigated the use of medicinal plants and consumption of soil in chimpanzees and other primates (Huffman 1997, 2006).

Finally, a publication by two evolutionary ecologists produced reverberations in a wide range of fields, including primatology. Hamilton and Zuk (1982) proposed that parasites are important in female mate choice, and that secondary sexual traits in males signal their infection loads or ability to resist parasites. This hypothesis predicted that within species, the brightest males should have the lowest parasite loads, but across species, those in which males have the most exaggerated traits should experience the greatest disease risk. In primate males, expression of good health could involve color signals, such as the bright faces of mandrills (*Mandrillus*

Fig. 1.4 The typical bright red color of a bald-headed uakari (*Cacajao calvus*) has been proposed to signal the absence of parasitic infection and an individual's ability to resist parasites. This captive individual's head is notably pale (less red) and likely to indicate sickness. Photo by N. Rowe, Primate Conservation, Inc.

sphinx) or rhesus macaques (*Macaca mulatta*, Waitt et al. 2003), or even more vividly, the bright red head of the bald uakari (*Cacajao calvus*, Fig. 1.4; Ayres 1986). The Hamilton and Zuk hypothesis continues to play a pivotal role in the interplay between social evolution and disease risk, as have Hamilton's other hypotheses on parasites and evolution (1987, 1990). Similarly, Møller and his colleagues have had a tremendous impact in understanding how infectious disease interacts with social evolution and sexual selection (Møller et al. 1993, 1999), particularly in birds (Møller et al. 1998b, 2001).

As noted by Heymann (1999), Janson (2000), and Kappeler and van Schaik (2002), infectious disease represents one of the last frontiers in our understanding of primate socioecology. Perhaps more importantly from a broader biological perspective, the great wealth of knowledge about primates can inform our understanding of disease risk more generally. Freeland's pioneering papers on disease risk, although commonly cited, tended to focus on infectious disease to the exclusion of other ecological forces. A more refined view is that disease risk is oneecological force among many that shape primate mating and social systems. One aim of this book is to flesh out some of the speculations and proposals of Freeland, Loehle, and Hamilton as they apply to primate socioecology. Primates are an excellent test case for evaluating the role of infectious disease, given that much is known about their parasites and the behavioral and ecological features thought to influence parasitism.

1.4 Fitness consequences of parasites in wild primate populations

If predation and resource competition influence primate behavior, then evidence for the fitness consequences of these ecological interactions should be apparent in natural populations. By similar reasoning, if infectious disease acts as a significant ecological force on primate behavior, we expect to find evidence for parasites in natural populations, and these parasites should increase mortality rates and/or reduce fecundity in primate hosts. Evidence of parasite-mediated mortality in wild primates is available; studies of parasite effects on primate mating success and fertility are less common, but measuring these parameters is feasible in the course of most long-term primate field studies. Most examples attesting to negative effects of parasites on wild primates come from three main sources of information: long-term field studies, focused studies of endemic disease in wild populations, and reports of epidemics in wildlife (Table 1.1; see also Young 1994; Heymann 1999; Wallis and Lee 1999; Cowlishaw and Dunbar 2000).

First, long-term behavioral field studies provide indirect evidence that infectious diseases cause or contribute to death in primate hosts, including studies of vervet monkeys (Cheney et al. 1988), chacma baboons (Barrett and Henzi 1998), gorillas (Fossey 1983), and chimpanzees (Goodall 1986). For example, Cheney et al. (1988) found that illness accounted for more deaths than predation in one troop of vervet monkeys (*Cercopithecus aethiops*), with lower-ranking animals suffering more from parasite infections. Similarly, Goodall's (1986) study of the Gombe chimpanzees (*Pan troglodytes*) revealed that individuals were afflicted by a range of seemingly harmful diseases, including gastrointestinal disorders, a paralysis resembling polio, respiratory diseases, and cutaneous fungal infections.

Second, more direct studies of endemic parasites in natural primate populations have demonstrated large numbers of deaths from parasite infections (Table 1.1). In a 68-month study of mantled howler monkeys (*Alouatta palliata*), for example, mortality increased with the intensity of botfly larvae infections (*Alouattamyia baeri*, Milton 1996). A particularly striking example was provided by Brain and Bohrmann (1992). In their study of chacma baboons (*Papio ursinus*), they discovered that some individuals harbored more than 400 ticks. These authors attributed over 50% of infant mortality to tick infestations, with some infants unable to nurse because so many ticks were attached to their muzzles. Primate mortality has less commonly been attributed to infections with intestinal nematodes (Kreis 1932), although severe infections with these and other gut parasites are likely to cause diarrhea, emaciation, and malaise (Orihel and Seibold 1972; Huffman et al. 1997). Most deaths and extreme pathology resulting from parasitic worms occur when hosts harbor large numbers of parasites (Thompson 1994b), or when individual parasites migrate to an organ outside the usual physical domain for that parasite species (Orihel and Seibold 1972). Parasite effects could also be more pronounced in nutritionally or socially stressed animals, when females experience costs associated with reproduction,

or when multiple parasite species co-infect a single host (Hart 1994; Woolhouse et al. 2001).

Finally, some of the most striking evidence for the effects of infectious disease comes from population declines associated with epidemics (Table 1.1). Recently, Ebola hemorrhagic fever has decimated populations of African apes (Formenty et al. 1999a; Walsh et al. 2003b; Leroy et al. 2004a). In many other cases, primate populations crash as the result of disease, but the infectious agent remains unknown, as in the case of a siamang (*Hylobates syndactylus*) population that declined from an unknown disease that appears to have spread through social contact (Palombit 1992; R. Palombit and N. Lerche, personal communication). Similarly, Pope (1998) described an outbreak of disease in red howler monkeys (*Alouatta seniculus*) that caused an 85% decline in the size of the population over a 4-year period. The agent causing this epidemic remains unknown (T. Pope, personal communication). The virus that causes yellow fever is a possible causal agent of the decline, with this virus causing other population declines among New World monkeys (Kumm and Laemmert 1950; Felsenfeld 1972; Yuill and Seymour 2001). On a 1966 collecting trip in Panama, for example, Galindo and Srihongse (1967) reported on the apparent extinction of mantled howler monkeys at one field site (Rio Mono), which they attributed to an epidemic of yellow fever that caused higher mortality in howlers, as compared to other monkey species in the area.

Few studies of primates have systematically investigated the effects of parasites on individual reproduction, but anecdotal evidence suggests that high levels of parasitism reduce an individual's reproductive success. Thus, Cheney et al. (1988) reported that a pathogen in vervet monkeys resulted in "blackened, shriveled testicles" (p. 389), which seems likely to have reduced the reproductive success of individuals unfortunate enough to have acquired this unknown parasite! Anecdotal reports of a *Treponema*-like venereal disease in captive and wild baboons involve gruesome lesions leading to severe secondary infections, genital disfigurement, and even death among males (Bouloux and Cirera 1972; Fribourg-Blanc 1972; Wallis and Lee 1999; Hogan 2003, A. Collins, personal communication). In captive breeding colonies, outbreaks of sexually transmitted viruses in baboons (Simian Agent 8, synonymous with Herpes simplex virus-1) caused female scarring so severe that genital tracts of some individuals required surgical repair (Levin et al. 1988). Female captive rhesus monkeys became infected with RhPV-1, a virus similar to oncogenic human papillomavirus, after mating with a male who later developed penile carcinoma. A retrospective study of this captive population revealed that over one-third of the females developed mild-to-severe clinical signs, including warty lesions, neoplasia, and cancer of the cervix (Ostrow et al. 1990).

Infectious diseases can also impact host fitness indirectly, even among individual animals that do not become infected. For example, by affecting the demography of groups, especially in the aftermath of epidemics, infectious disease outbreaks can alter opportunities for coalitions, reduce predator avoidance capabilities, and decrease levels of competition over mates and resources within groups. A study by Carpenter (1964) revealed the effects of a yellow fever epidemic on the demography

Table 1.1 Probable examples of parasite-induced mortality in free-living primates

Host	Infectious agent	Type of study and summary results	References
Alouatta palliata	Yellow fever (Flaviviridae; yellow fever virus)	Various yellow fever epidemics have decimated populations of howler monkeys in Central America.	Carpenter 1964; Galindo and Srihongse 1967; Stoner 1993; James et al. 1997
A. palliata	Bot flies (*Alouattamyia baeri*)	Density of botflies per host correlated with howler mortality, and infections influenced blood chemistry and other health measures. Autopsies linked some deaths to botfly infection.	Milton 1996, see also Smith 1977
Alouatta seniculus	Unknown	Significant population losses from 1992 to 1996 (approximately 80%).	Pope 1998; Rudran and Fernandez-Duque 2003
Cercopithecus aethiops	Unknown	In a long-term field study, 14 individuals disappeared within 24 h of having been observed to be weak, listless, or suffering from outward signs of disease.	Cheney et al. 1988, D. Cheney, personal communication
Gorilla gorilla	Various, some with respiratory effects	In a long-term field study, a variety of illnesses were recorded that probably resulted in deaths.	Fossey 1983; Watts 1998
Hylobates syndactylus	Unknown pathogen	At least four individuals died of a contagious disease that produced a variety of symptoms including hair loss, dermatitis, extreme lethargy, and diarrhea.	Palombit 1992
Pan troglodytes	Diverse parasites	Individuals were documented to suffer from respiratory, intestinal, and skin diseases. In some cases these probably resulted in death.	Goodall 1986
P. troglodytes	Anthrax (*Bacillus anthracis*)	Anthrax infections resulted in the death of at least six individuals in multiple communities of chimpanzees.	Leendertz et al. 2004
P. troglodytes	Diverse illnesses	Possible illnesses include influenza and monkey pox; animals also exhibited lameness and conjunctivitis.	Boesch and Boesch-Achermann 2000
P. troglodytes and *G. gorilla*	Ebola hemorrhagic fever (Filoviridae; Ebolavirus)	Deaths due to Ebola are exacerbating detrimental effects of hunting and habitat destruction for these apes.	Formenty et al. 1999a; Boesch and Boesch-Achermann 2000; Walsh et al. 2003b; Leroy et al. 2004a
Papio anubis	Bovine tuberculosis	Effects included weight loss, lethargy, and coughing, with 35% of one troop	Tarara et al. 1985; Sapolsky and

Table 1.1 *Cont.*

Host	Infectious agent	Type of study and summary results	Reference
	(*Mycobacterium bovis*)	and 6 of 8 males in another troop dying. Infection probably was acquired from eating contaminated meat in a garbage pit.	Else1987; Sapolsky and Share 2004
Papio ursinus	Ticks (*Rhipicephalus*)	Tick infestations noted as contributing to over 50% of recorded infant deaths due to inability to suckle.	Brain and Bohrmann 1992
P. ursinus	*Yersinia* or an unknown viral infection	85% of one troop and 32% of another died, with outward signs of lethargy and hemorrhaging diarrhea.	Barrett and Henzi 1998
Theropithecus gelada	Larval stages of the tapeworm *Multiceps servalis* (possibly *Taenia/ Multiceps serialis*)	17% of adults were found to have swellings caused by the larval parasites, resulting in impaired movement and "foul suppurating masses"; at least two animals died after the swellings burst.	Dunbar 1980

of mantled howler monkeys. In 1935, prior to the epidemic, the mean group size was 18.2 individuals, with an average group sex ratio of 3.3 males to 7 females. Following the epidemic, the mean group size declined to 8.0 individuals, with an average sex ratio of 1.2 males to 4.5 females. Similar demographic shifts were documented in an epidemic in chacma baboons (*Papio ursinus*), in which all six adult males in a troop died, while only one-half of 22 females died (Barrett and Henzi 1998). These females subsequently attempted to fuse with another group. Finally, a study on savanna baboons (*Papio anubis*) by Sapolsky and Share (2004) revealed that demographic shifts resulting from epidemics can have profound, long-term consequences on behavior within groups. Following an outbreak of bovine tuberculosis that the baboons acquired from eating contaminated meat in a garbage dump, the more aggressive males in this group were more likely to succumb to infection because they were better able defend this resource, and thus were more likely to be exposed to tuberculosis through infected meat. These deaths left behind a less aggressive cohort of males. Sapolsky and Share (2004) documented that less aggressive behaviors persisted over a 10-year period, even though none of the original survivors of the outbreak remained in the group.

These examples, and additional cases provided in Table 1.1, show that parasites can generate significant impacts in natural populations of primates. Demonstrating that an animal died from parasitic infection must be done cautiously, however, because the parasite may not be the direct cause of death, or it might be impossible to identify which of several infections caused an animal to die (McCallum 1994; McCallum and

Dobson 1995). It is also important to note that sublethal effects associated with physiological impairment might increase host susceptibility to starvation or other stress, or reduce rates of growth and reproductive maturation. As a case in point, several studies have demonstrated that parasites can elevate host mortality through increased predation, even those that rarely kill their hosts directly. Thus, Temple (1987) examined levels of parasitism among small mammals that were captured by a tame hawk (*Buteo jamaicensis*) and found that hawk-captured cottontail rabbits (*Sylvilagus floridanus*) and gray squirrels (*Sciurus carolinensis*) were more likely to be parasitized by a range of endoparasites (see also Hakkarainen et al. 1998). Similarly, Hudson et al. (1992) found that predators focused selectively on red grouse (*Lagopus lagopus scoticus*) with heavy loads of caecal nematodes (*Trichostrongylus tenius*).

An issue related to parasite-induced mortality involves regulation of host populations by parasites (e.g. Scott 1987a; Hudson et al. 1998b; Tompkins et al. 2002). Previous researchers proposed that parasites regulate primate populations (Freeland 1976; Smith 1977; Milton 1996), an issue that will be discussed in greater depth in Chapter 4. Examples described above suggest that parasites can reduce population growth rates by elevating mortality or reducing fecundity. But observational studies such as these provide only indirect evidence that parasites regulate wild populations (Scott and Dobson 1989). Experimental studies are needed in which parasite loads are manipulated (preferably by removal, rather than addition, of parasitic infections!), thus providing insights into the effects of parasites on individual fitness or population growth (Tompkins and Begon 1999, 2002). Such experiments pose difficulties in long-lived, free-ranging primates, but are more feasible than might at first appear. For example, Gulland et al. (1993a) conducted studies of parasite-induced population regulation on free-ranging Soay sheep (*Ovis aries*) using a protocol involving application of anthelmitic drugs (see also Hudson et al. 1998b). This study showed that treatment of sheep for gastrointestinal nematodes significantly reduced their mortality during population crashes (Fig. 1.5). Long-term field experiments and monitoring of red grouse in the United Kingdom further revealed that host populations treated with drugs to remove nematode parasites were less likely to cycle in size over time (Hudson et al. 1998b). Importantly, similar experimental approaches could be applied to many of the long-term studies that take place in wild primate populations (Janson 2000).

To better appreciate disease risk and its evolutionary implications, we must also understand the factors that lead to a correlation between parasitism and elevated mortality rates. The pathological effects of disease are one factor, but many effects of parasites extend beyond standard views of sickness and include diverse aspects of behavior in free-living species. Thus, Kavaliers and Colwell (1995b) showed that nematode infections reduced spatial learning in mice (see also Table 3.13 in Moore 2002). In the absence of any obvious motor, visual, or motivational impairment, male mice that had been experimentally infected with the nematode *Heligmosomoides polygyrus* were less able to learn to navigate a water maze based on visual cues, as compared to control mice. Similarly, studies of *Ascaris* infections in humans have linked this parasite to depressed learning ability in school children

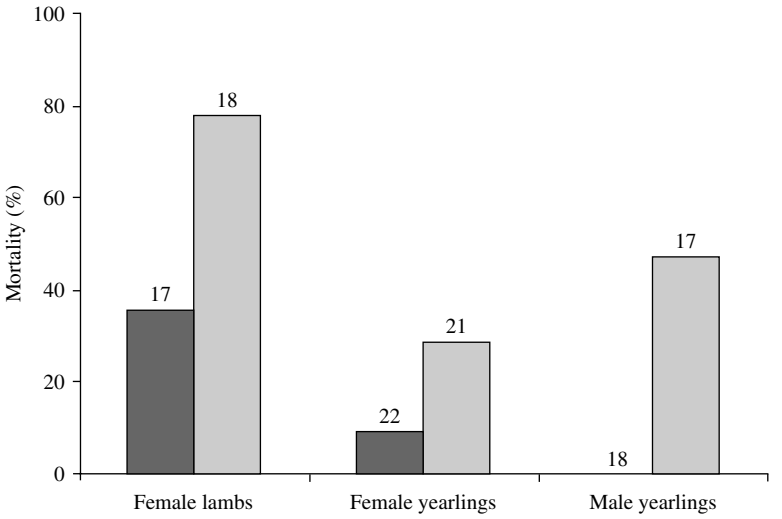


Fig. 1.5 Mortality of Soay Sheep on the Island of St. Kilda following a population crash that occurred in 1992. Dark bars show sheep that were treated orally with an antihelminthic drug several months prior to the crash, and light bars show control (untreated) sheep. Sample sizes are shown above each bar. Reprinted from F. M. D. Gullard, S. D. Albon, et al., "Parasite associated polymorphism in a cyclic ungulate population," *Proceedings of the Royal Society Series B.*, vol. 254, 7–13. Copyright (1993) by the Royal Society.

(O'Lorcain and Holland 2000). Subtle effects of parasitism, such as reduced cognition, memory loss, or learning impairment, might be among the most difficult to quantify in the wild, but should be exceptionally important in free-living animals such as primates that rely heavily on cognitive skills. For example, it would be fascinating to compare the foraging success of parasitized and un-parasitized spider monkeys that must remember the location of dispersed fruiting trees.

In summary, abundant evidence points to the existence of parasite-induced reductions in host fitness among free-living primates. These cumulative studies are important not only from the perspective of host regulation or parasite-mediated population declines, but also because they reveal that parasites can act as powerful selective agents in natural populations. Thus, host species exposed to a diverse array of parasites are expected to evolve behavioral, innate, or inducible defenses to resist or reduce the impacts of parasites and pathogens (Nunn et al. 2000; Møller et al. 2001). This prediction hinges upon demonstrating costs of infection for host survival and fecundity (in other words, demonstrating that parasites impose selection gradients at the population level). In fact, if group living and social contacts increase exposure to a variety of parasites, then highly social species should be under the greatest pressure to invest resources into anti-parasite counterstrategies. This is one of the major unexplored frontiers of studies in primate socioecology, offering great opportunities for researchers, while also providing new insights to human evolution and primate conservation.

1.5 Organizational layout of this book

This book is organized into eight chapters, moving from essential background material to a synthetic framework, and finally to applied examples in primate conservation and human health. Chapter 2 reviews the biological features of major groups of parasites and links these features to specific aspects of disease risk in primates. Chapter 2 therefore identifies parasite characteristics that are most important to understanding patterns of disease risk, including transmission strategy, host specificity, parasite life cycles, virulence, and how parasites manipulate host behavior to enhance their transmission.

Chapter 3 discusses the underlying rationale for factors that influence disease risk in primates at two levels: among individuals and across species. Throughout Chapter 3, we summarize primate behavioral and ecological traits that are essential for understanding disease risk, including dominance rank, group size and composition, dispersal, mating system, and ecological factors that correlate with these social system parameters, such as body mass, life history characters, and use of the ground versus trees for locomotion (substrate use).

Chapter 4 links host and parasite ecology by considering basic epidemiological parameters and processes, and it covers how disease patterns scale up from individuals to populations and communities. We discuss factors affecting the transmission dynamics of parasites, including the basic reproductive number R_0, the aggregation of macroparasites within populations, and frequency- versus density-dependent transmission. This chapter also considers how parasites might regulate primate populations or influence host abundance through their effects on survival and fecundity.

Chapter 5 focuses on the host's response to parasitism by considering behavioral and immunological defenses to infectious disease. In this chapter, we concentrate on the individual level by considering how primate immune systems defend against parasite infections, how animals use medicinal plants, and the avoidance of sick individuals. We also investigate the links between sexual selection and parasitism in primates, focusing in particular on mate choice.

Chapter 6 is a synthetic chapter that integrates material from the previous chapters to explore the ways in which parasites might influence primate mating and social systems. We consider how individual responses to parasitism can influence social system characteristics, and we raise the question of causality, namely, "do host traits influence patterns of parasitism, or do parasites influence patterns of sociality?" These are not mutually exclusive questions, but by considering a coevolutionary model of host and parasite traits, we can begin to address the multiple ways in which lineages of hosts and parasites interact.

Chapters 7 and 8 extend the basic framework developed in earlier chapters to applied questions in primate conservation and human health. In Chapter 7, we examine the conservation implications of parasites, including cross-species transmission, the effects of eco-tourism, and approaches to control epidemics in wildlife. We also consider the potential longer-term benefits of maintaining intact communities of hosts

and parasites. In Chapter 8, we consider how understanding infectious disease in nonhuman primates provides insights to human health. In particular, we examine the origins of human infectious diseases and their impacts in a historical context. More speculatively, we ask how behavioral counterstrategies to infectious disease in nonhuman primates pertain to understanding human behavior in the context of Darwinian medicine (Ewald 1980; Nesse and Williams 1996; Stearns 1999; Trevathan et al. 1999). We also discuss the role of wild primates in the maintenance of zoonotic pathogen and disease emergence, and we apply the concept of disease risk to investigate variation in human infections at global and regional scales.

Throughout this book, we aim to synthesize existing knowledge in ways that will lead to new questions, thus pointing the way toward future research on infectious disease and behavioral ecology in primate hosts and other animals. This goal is achieved through a "summary and synthesis" at the end of individual chapters, and with a final chapter (Chapter 9) that reviews key points in the book and identifies major questions for future research.

2

Diversity and characteristics of primate parasites

2.1 Introduction

The role of parasites in primate ecology and evolution remains vastly underappreciated relative to other factors such as predation and competition. This is not altogether surprising—imagine witnessing a brutal attack by an adult male chimpanzee against a rival male over access to females (de Waal 1986), or the spectacle of a harpy eagle swiping a capuchin monkey from its social group high in the rainforest canopy (Peres 1990b). Indeed, the thought of leopards stalking baboons on the African floodplains seems far more significant for primate survival and behavior than that of an adult female *Enterobius* (a pinworm) wriggling through the colon of squirrel monkey (Hugot 1999).

On the other hand, consider that following ingestion by primate hosts, the spiny proboscis of *Prosthernorchis* (Fig. 2.1) punches into the gut wall, with intestinal perforations in some cases resulting in depression, anorexia, and emaciation. Some might consider this example just as engrossing and consequential as the attacks described earlier. Furthermore, even though they are often hidden inside the bodies of their hosts, adult pinworms and other helminths can produce thousands of eggs in a single day, potentially spreading to large numbers of animals. In nonhuman primates, even the tiniest viruses and bacteria have caused precipitous population declines in monkey and ape populations (see Table 1.2). Collectively, these examples suggest that parasites could play a role equal to or greater than resource competition, predation, and habitat characteristics in affecting the distribution and abundance of wild primates. Exploring this possibility requires understanding the major groups and characteristic of parasites that impact primates.

Parasites and pathogens span an incredible diversity of life forms, ranging from the smallest viruses and bacteria to the larger and structurally more complex protozoa, worms, and arthropods. They are ubiquitous in natural ecosystems and comprise a major component of biodiversity, probably representing well over one-half of all living species (Price 1980; Windsor 1998). Virtually all animals harbor one or more species of parasitic organisms in their intestinal tracts, liver, blood, reproductive organs, skin, or other tissues, and some parasites have parasites of their own, leading some biologists to argue that parasites vastly outnumber all other types of species on the planet (Price 1980; Windsor 1998; Zimmer 2000).

Fig. 2.1 The thorny, retractable proboscis of the acanthocephalan *Prosthenorchis elegans*, a helminth parasite of several New World monkeys. The parasite shown here was found by B. Mueller in a female red titi monkey (*Callicebus cupreus*) at Estación Biológica Quebrada Blanco, Peru. SEM micrograph courtesy of C. Schmetz, Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany, and B. Müller, German Primate Center.

In addition to their phylogenetic diversity and pervasiveness, parasites employ an impressive array of strategies for dispersing to new hosts (Price 1980; Poulin 1998b; Poulin and Morand 2000; Bush et al. 2001). Parasite life cycles can require one, two, or more different host species for development to the adult stage. Part of these life cycles might take place outside of any host organism. Parasites that infect just a single host species are said to have *simple* or *direct life cycles*, whereas parasites that infect two or more host species to complete their development and reproduction are referred to as having *indirect life cycles* (Fig. 2.2). For parasites that use more than one host, the *definitive* or *primary host* is usually defined as the host in which sexual reproduction occurs and where the adult parasites live, and *intermediate* or *secondary* hosts harbor earlier stages of parasites. Primates commonly serve as definitive hosts for parasites, but not in all cases. For example, the protozoa that cause malaria (*Plasmodium* spp.) reproduce sexually in mosquitoes (the definitive host), with vertebrates serving as the intermediate hosts (Coatney et al. 1971; Roberts and Janovy 1999).

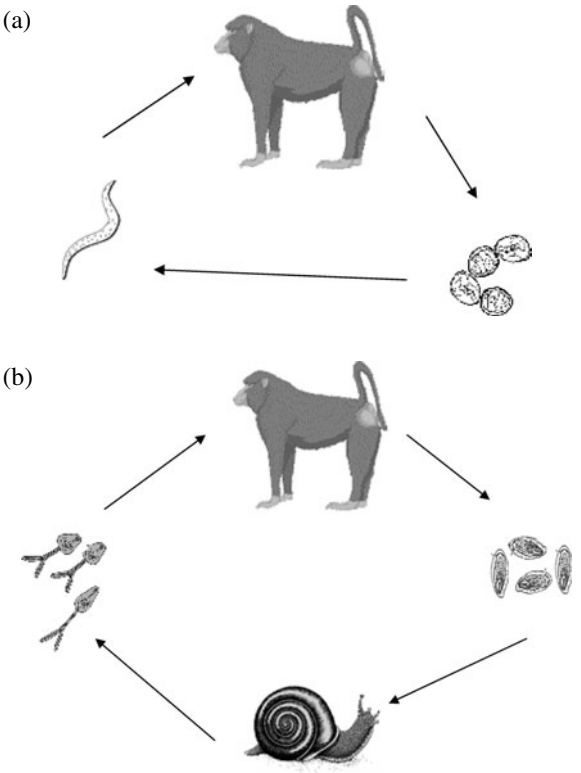


Fig. 2.2 Direct and indirect parasite life cycles. (a) Parasites with direct (monoxenic) life cycles can complete their development and reproduction using a single host species. In the example shown, adult worms in the intestinal tract shed eggs that are deposited in the perianal area (as by the pinworms *Enterobius* and *Trypanoxyuris*) or shed in feces (as occurs for *Strongyloides* nematodes). Eggs or infectious larvae are ingested by the host with food or other contaminated material, and then develop into sexually mature adult worms inside the host animal. (b) Parasites with indirect (complex, or heteroxenic) life cycles require two or more hosts to complete development and reproduction. For example, adults of the trematode *Schistosoma mansoni* live in the veins of the abdominal cavity of a vertebrate host and produce eggs that are shed into water with host feces. The eggs hatch in the water and the larvae then penetrate a snail intermediate host, where they replicate asexually before leaving the snail as free-swimming cercariae. The cercariae penetrate the skin of primates or other suitable hosts when they enter the water, and migrate to a suitable site within the host, where they reach sexual maturity to complete the cycle.

Parasites also exert a variety of effects on host fitness and abundance, in some cases altering what researchers might interpret as the outcome of predation, competitive interactions, or even host behaviors—suggesting that much of what primatologists observe in the field could depend on the presence or absence of disease-causing

Box 2.1 Studies of parasites in primates

Working knowledge of parasites reported to infect wild primates comes from a variety of studies that were conducted with different goals in mind. Many studies were motivated by improving human health and identifying sources of zoonotic infections (Nelson 1965; Nelson et al. 1965; Legesse and Erko 2004). These studies focused, for example, on yellow fever and malaria in the New World (Kumm and Laemmert 1950; Deane 1992; Lourenco de Oliveira and Deane 1995) and schistosomiasis in Africa (Nelson 1960). The explosion of research on SIV in wild primates also falls in this category (Hahn et al. 2000). This research has resulted in further sampling of primates to locate the ancestral origins of HIV lineages and to identify additional pathogens that might be transmitted to humans. Recently, surveys of primate bushmeat and humans that consume this meat have revealed the great potential for viruses to cross between nonhuman primates and humans, particularly in Africa (Peeters et al. 2002; Wolfe et al. 2004).

Parasitologists are often interested in documenting parasite diversity and systematics, and many parasitological studies have sampled primates for a variety of arthropods, helminths and protozoa. Papers of this genre often focus on details of the external morphology of the parasites, particularly characters important for taxonomic identification (Kim and Emerson 1973; Hugot 1993; Durette-Desse and Corvione 1998). Some experts on parasites and pathogens have worked closely with primatologists in the field (e.g. Stuart et al. 1993; Leendertz et al. 2004), whereas others have embraced a comparative perspective, for example in studies of phylogeny and the cospeciation of primates and their pinworm parasites (Hugot 1998, 1999).

Another important source of data on primate parasites comes from research aimed at improving the quality of imported primates for biomedical research, increasing their health in captivity, and protecting researchers from infectious agents in captive colonies (Kalter et al. 1966; Kourany and Porter 1969; Kaschula et al. 1978; Kalter and Heberling 1990). Although international protections on endangered species have reduced the capture and importation of primates, large numbers of wild-caught primates have been imported to the United States and other countries. These animals often arrived at their destinations infected with various parasites, and as an economic investment, companies were interested in identifying the sources of infection—were the animals infected in the wild, in hunters' camps, in the holding pens prior to shipping, or during transport to the final markets? Many studies that aimed to address these questions sampled primates in the wild and therefore data on natural host-parasite combinations.

More recently, a number of ecological studies focused on parasitism in primates more directly, again giving information on the presence of parasites in different hosts, along with data on prevalence and intensity of infection. Some studies investigated ecological factors that affect the sharing of parasites among primates from the same geographic areas (McGrew et al. 1989a, b). Other studies examined host characteristics associated with variation in parasitism among individual primates (Meade 1984; Müller-Graf et al. 1996, 1997). Finally, more recent studies have focused on the conservation implications of parasites in primate populations (Stoner 1996; Eilenberger 1997).

Many of the studies cited above represent papers used in a recent compilation of primate parasites in the *Global Mammal Parasite Database*, which can be found online at www.mammalparasites.org (Nunn and Altizer 2005). The version of the dataset first placed online includes 2462 lines of data, where each line captures a record of a parasite species reported from a wild primate population. These records encompass 119 primate

Box 2.1 (*Cont.*)

species and over 380 parasite species. As data on parasites of primates continues to accumulate, there is a great need for a centralized data repository for records of micro- and macro-parasites in free-living, wild caught and captive-reared primates, as this would provide researchers with an opportunity to share and access these data and to stimulate future monitoring efforts.

organisms. For field primatologists, familiarity with parasites and their distinctive pathologies often stems from witnessing infections in the animals that researchers study for other reasons (e.g. Fossey 1983; Goodall 1986; Cheney et al. 1988). Familiarity could also breed contempt for parasites when researchers contract diseases themselves in the course of performing fieldwork, or when they observe pathogen-induced population declines in their primary study species. Field primatologists are generally unaware of the incredible diversity and fascinating life histories of parasites that infect wild primates. In fact, many of these organisms remain undescribed, in part because most primate species have not been sampled exhaustively for parasites in the wild (Box 2.1).

Knowledge of parasite diversity and characteristics is crucial for understanding epidemiological patterns, effects of disease on host fitness, and host counterstrategies for avoiding parasite infection. To set the stage for a more thorough understanding of host–parasite dynamics and evolution, we begin by surveying the biological diversity of parasites that infect primates. We then review three parasite traits critical to understanding the ecology and evolution of host–parasite interactions in primates: transmission mode, host specificity, and negative effects of parasites on host fitness. Some of the most fascinating examples of parasitism in nature involve cases where infectious agents manipulate their hosts, usually with major consequences for transmission (Moore 2002; Sapolsly 2003). We therefore conclude this chapter by considering several examples of parasite-induced changes in host behavior.

2.2 Taxonomic diversity of parasites from wild primates

Six major taxonomic groups of parasites infect primates: viruses, bacteria, fungi, protozoa, helminths, and arthropods. Figure 2.3 illustrates the relative occurrence of five of these groups using a comprehensive database of parasites reported from wild primates (Nunn and Altizer 2005; Pedersen et al. 2005). For comparison, Fig. 2.3 also shows the frequency of these parasite groups in humans and domesticated animals. The most striking difference among host groups appears between humans and nonhuman primates, with the vast majority of parasites described from wild primates involving helminths, viruses, and protozoa (Pedersen et al. 2005), while the majority of disease-causing organisms in humans are represented by bacteria and

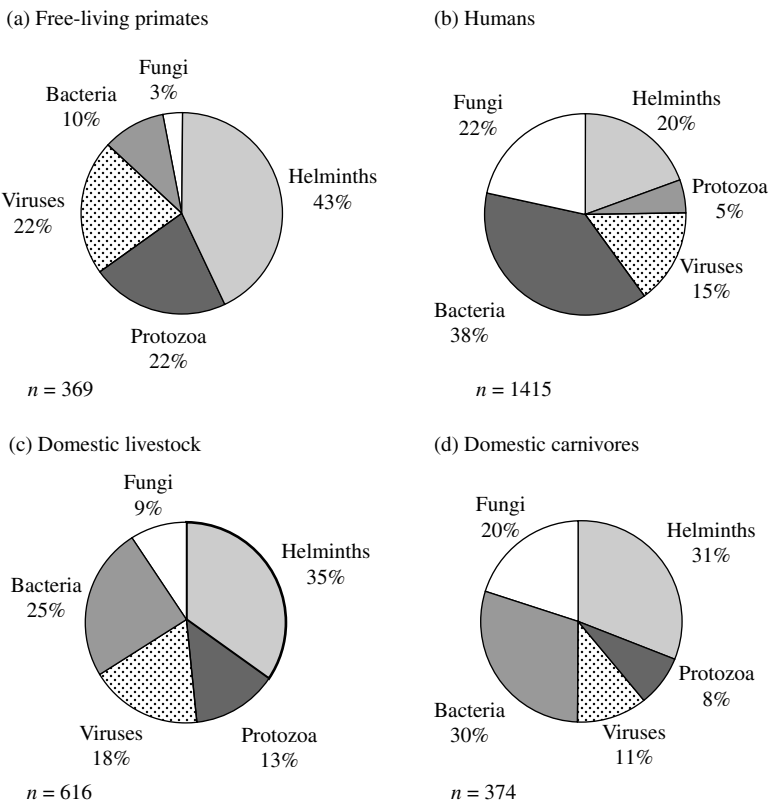


Fig. 2.3 Taxonomic distribution of five major groups of parasites from wild primates relative to those reported from humans and domesticated animals (after Pedersen et al. 2005). Sample sizes (*n*) refer to the total number of parasite species compiled for each host group. Data shown in (b)–(d) were obtained from Taylor et al. (2001) and Cleaveland et al. (2001). Arthropods are not included as comparable summary data were not available for humans or domesticated animal hosts. Reprinted from Pedersen et al. (2005) with permission from Elsevier.

fungi (Cleaveland et al. 2001; Taylor et al. 2001). Differences between pathogens reported from wild primates versus humans could reflect historical changes that allowed certain parasites to more readily colonize and spread in human populations (see Chapter 8).

Two caveats are in order when interpreting Fig. 2.3. First, some parasites are better studied than others. For example, the number of helminths in Fig. 2.3(a) might reflect that these parasites are easier to study in wild primates relative to other parasite groups. Similarly, fungi and bacteria could be underestimated among wild primates if they are more difficult to study or less interesting to biologists—or more

commonly detected in humans through more frequent use of diagnostic tests, including opportunistic or rare infections. To put this differently, *a parasite might be missing from a host species because it does not occur in that host, or because the host has not been sampled adequately for that type of parasite*. In comparative studies of parasite diversity, it is critical to control for this variation in "sampling effort," and interpret results in light of potential sampling biases (Gregory 1990; Walther et al. 1995; Nunn et al. 2003a).

Another issue for interpreting patterns of parasite diversity involves the units of analysis and categorization. Taxonomic groups shown in Fig. 2.3 are based on functional categories rather than monophyletic groups in which all members share a common ancestor. Indeed, recent molecular analyses are overturning previous taxonomic schemes for parasites and providing new insights into the evolutionary histories of major parasite groups (Prescott et al. 2001; Cox 2002; van Regenmortel and Mahy 2004). Taxonomic changes since the late 1990s resulted in major reorganization of the protozoa and viruses, for example, with a few cases described later in this chapter. Rather than phylogenic classification, for the majority of this book we adopted widely recognized functional classifications of parasites as these remain useful for considering parasite biology and effects on hosts (Clayton and Moore 1997; Cleaveland et al. 2001; Samuel et al. 2001; Williams and Barker 2001). Other functional categories used in this book include intestinal parasites, intracellular parasites, and divisions based on transmission mode or severity of infection.

Many authors separate disease-causing organisms into micro- and macroparasites (Table 2.1; Anderson and May 1991). Microparasites encompass viruses, bacteria, fungi, and protozoa, whereas macroparasites include helminths and arthropods. Although each group itself spans a tremendous diversity of organisms, some general distinctions are relevant for later chapters. One key biological difference concerns replication, with microparasites completing cycles of replication directly within infected animals, but macroparasites usually multiplying by releasing infective stages (eggs or larvae) into the environment. These infectious stages could either re-infect the same animal or infect new hosts, including one or more intermediate host species. For this reason, characteristics of the external environment tend to exert greater direct impacts on macroparasites by affecting their survival and the development of eggs, free-living stages, or the availability of intermediate hosts.

Another major distinction is that infections caused by microparasites can be epidemic in nature with episodes of high prevalence (and possibly high mortality) interrupted by periods of low prevalence (Anderson and May 1991). By comparison, macroparasites tend to cause chronic and persistent infections and are less often linked with sudden outbreaks in natural populations (Gulland 1995), although this dichotomy is not strict. A final related point is that due to the antigenic simplicity of many microparasites, infections tend to illicit short-term or lasting immunity in their vertebrate hosts, so that recovered animals resist re-infection for variable lengths of time (also see Chapter 5). By comparison, the large body size and antigenic

Table 2.1 Characteristics, examples, and biological properties of micro- and macroparasites (after Anderson and May 1991). These generalizations do not apply to all parasitic organisms within each group, but represent useful dichotomies for ecological analysis and modeling approaches described in Chapter 4

Parasite traits	Microparasites	Macroparasites
Taxonomic groups	Viruses, bacteria, protozoa, fungi,	Helminths (e.g. nematodes, cestodes, acanthocephalans), arthropods (e.g. mites, ticks, lice)
Size and reproduction	Small, unicellular, short generation times in individual hosts	Large, multicellular, longer generation times; usually no direct replication within hosts
Transmission of infective stages	Transmission via direct contact (e.g. venereal, vertical), vectors, or contaminated air/soil/water	Complex life cycles and intermediate hosts, vector transmission, or direct transmission by close or non-close contact
Effects on host immunity	Long-lasting host immunity that develops quickly, although not true for all microparasites	Antigenic diversity of parasites usually too high for host to mount effective or lasting immune response
Effects on host fitness	Disease can be acute or chronic; may have strong effects on host survival or fecundity	Effect depends on number of parasites per individual host; can affect mortality or fecundity, but usually chronic infection with sub-lethal effects
Quantification in host populations	Prevalence, seroprevalence, incidence	Prevalence, intensity, degree of aggregation in individual hosts

complexity of most macroparasites make adaptive immunity less effective; thus, animals that recover typically remain susceptible to later re-infection. Additional differences between micro- and macroparasites are discussed in Chapter 4, specifically as they apply to understanding population dynamics of parasites and their impacts on host populations.

2.2.1 Viruses

Viruses are structurally and biologically the simplest group of microparasites and consist of two major parts—a protein coat and genetic material (Fig. 2.4). Having no cell wall or membranes, and lacking cytoplasm and organelles, viruses cannot replicate outside of living host cells and are therefore obligate intracellular parasites. Receptor molecules that aid in recognizing surface proteins on host cell membranes cover the virus outer jacket (Prescott et al. 2001). Once viruses invade a host cell,

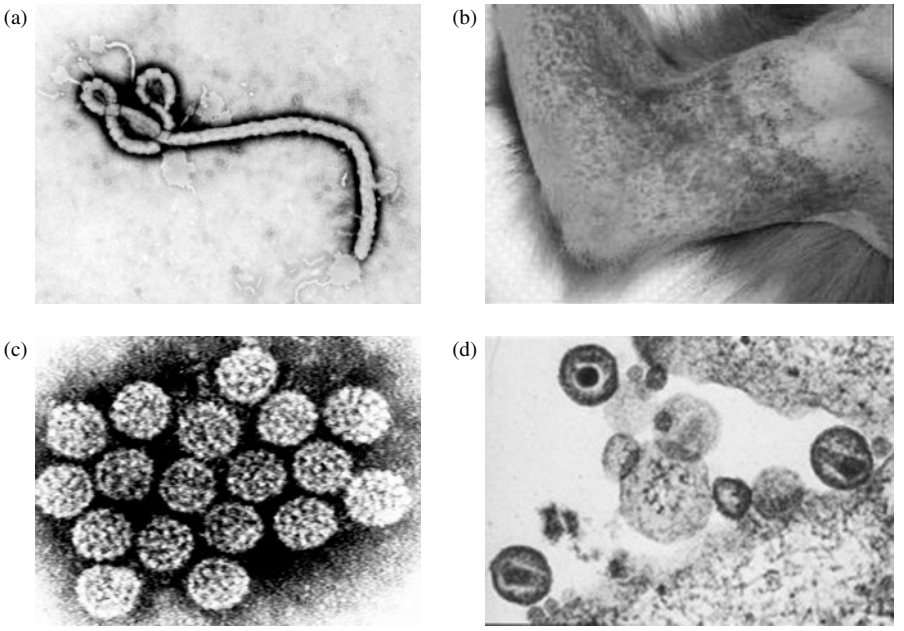


Fig. 2.4 Viruses reported from free-living primates. (a) Transmission electron micrograph of Ebola virus, an RNA virus in the family Filoviridae (Reproduced from Public Health Image Library 2004. Image credit: CDC/C. Goldsmith). (b) Severe rash on the right arm of a rhesus monkey nine days after infection by Ebola virus (Reproduced from Geisbert et al. 2003 with permission from Elsevier). (c) Electron micrograph of papillomavirus virus particles, DNA viruses in the family Papillomaviridae (Micrograph courtesy of Severia Campo, University of Glasgow). (d) Micrograph of simian immunodeficiency virus (SIV), an RNA virus in the family Retroviridae. Micrograph courtesy of R. J. Munn, University of California, Davis (CNPRC 2004).

they hijack the cell's machinery to produce new viral proteins and genetic material. The genetic material of viruses can be either RNA (usually single-stranded) or DNA (usually double-stranded). Relative to DNA viruses, RNA viruses tend to have smaller genomes and are characterized by much higher mutation rates, in part because RNA replication lacks repair and proof-reading mechanisms (Drake 1991; Holmes 2003). Biological differences between these two viral groups can have important implications for rates of evolution and patterns of host specificity in primates (Pedersen et al. 2005).

Because they are so small and are difficult to identify without high-powered microscopy or sophisticated molecular techniques, many viruses are detected via serology by collecting and testing host blood for the presence of *antibodies* that recognize viral surface proteins (called *antigens*; Chapter 5). However, patterns of

prevalence based on serological evidence for antibodies do not necessarily reflect current infections because animals can retain antibodies for many years after recovering from viral infections, including antibodies generated from sub-clinical infections. More recently, methods based on polymerase chain reaction (PCR) have been used to detect viruses, with the advantage of requiring minimal host material and non-invasive sampling. For example, fecal samples have provided evidence of simian immunodeficiency virus (SIV) infections in wild chimpanzees and sooty mangabeys sampled in the field (Ling et al. 2004; Nerrienet et al. 2005).

Analyses of viral nucleotide sequences are providing insights into viral evolutionary history and phylogenetic relationships within and among lineages (Murphy et al. 1995; van Regenmortel and Mahy 2004, see the *International Committee on the Taxonomy of Viruses* online database for current virus classifications). As of 2000, the ICTV recognized 1550 viruses, organized into 63 families and three major orders (Fauquet and Mayo 2001). Yet relative to other parasite groups, the current resolution of virus taxonomy remains poor, and future studies should reveal whether viral isolates currently classified as the same virus are in fact comprised of phylogenetically distinct units or "host races".

A large number of viruses have been isolated from wild primates (Nunn et al. 2003a; Pedersen et al. 2005), including representatives from 17 different viral families (Fig. 2.4). Some more commonly known DNA viruses include those in the families *Poxviridae* (monkeypox virus), *Herpesviridae* (*Simplexvirus* and *Varicellovirus*) and *Papovaviridae* (*Papillomavirus*). Among humans and other primates, RNA viruses include several widely recognized groups in the families *Flaviridae* (yellow fever virus and dengue fever virus), *Ortho* and *Paramyxoviridae* (influenza and measles viruses), and *Retroviridae* (SIV) and simian foamy virus (SFV). Most of these viruses fall into two major categories: vector-borne generalist pathogens (usually RNA viruses) capable of infecting hosts from multiple orders, and directly transmitted viruses with greater levels of host specificity, including sexually transmitted diseases (STDs, Pedersen et al. 2005).

Viruses are currently the only pathogen group in wild primates where sexual transmission is known to be relatively common, although most viruses with sexual transmission can also be spread vertically and by close nonsexual contact. Relative to viruses transmitted by close contact, those transmitted by biting arthropods tend to be reported as infecting hosts from multiple orders, and these tend to be dominated by RNA viruses (Fig. 2.5). It is important to note, however, that the current taxonomic resolution of some RNA viruses might be limited by their rapid evolution, which could pose challenges for scientists in terms of the phylogenetic organization of this group, delineating taxonomic boundaries, and determining levels of host specificity.

Viruses increasingly are recognized as playing important ecological roles in natural populations and have generated severe disease epidemics in wildlife, including in African wild dogs, seals, and lions (Gascoyne et al. 1993; Roelke-Parker et al. 1996; Funk et al. 2001). Among primates, wild ape populations in Africa have been

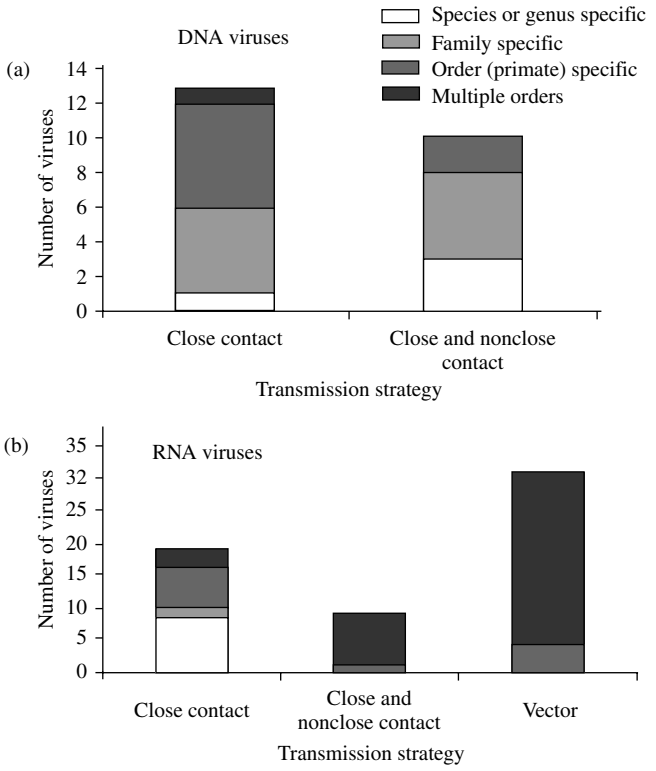


Fig. 2.5 Viruses from free-living primates. Bars show of relative levels of host specificity (i.e. whether a virus was recorded as specific at the level of host species, genus, family, or higher levels) in relation to major transmission strategies of (a) DNA viruses ($N = 23$) and (b) RNA viruses ($N = 59$). Shading represents host specificity according to whether viruses were restricted to a single host species or genus, or to hosts in a common family, order, or multiple orders. Because some parasites could be transmitted by more than one strategy, frequencies of parasites with both single and combined strategies are shown. Figure provided by A. B. Pedersen, data are from Pedersen et al. (2005).

decimated by Ebola hemorrhagic fever (Walsh et al. 2003b; Leroy et al. 2004a, see Chapter 7). In addition, viruses from nonhuman primates have received increasing attention for the risks they pose to human health, including SIV, SFV, and herpesvirus B (Brown 1997; Wolfe et al. 1998, 2004; Hahn et al. 2000). At least 27 viruses have been reported to infect both wild primates and humans (Pedersen et al. 2005), and the vast majority of these are classified as emerging threats in human populations (reviewed in Chapter 8). Finally, it is exciting to note that molecular analyses are providing new evidence for virus-host coevolution and cospeciation (Holmes 2003), as recently evidenced by a study showing a long history of

cospeciation of SFVs across 44 species of Old World monkeys and apes (Switzer et al. 2005).

2.2.2 Bacteria

Bacteria are unicellular prokaryotes with genetic material unbound in the cytoplasm. They can be identified by a variety of criteria, including cell shape and patterns of cell aggregation or grouping, Gram-stain reaction, and motility or the presence of flagella or pilli (Prescott et al. 2001; Fig. 2.6). Many bacteria are characterized by a rigid cell wall (comprised of sugars and amino acids chains) in addition to a plasma membrane. Asexual reproduction is the major mode of bacterial replication, although genetic material can be shared or transferred via plasmids, by viruses, or through DNA uptake from the environment. Among their other interesting biological properties, some bacteria are well known for producing resistant spores during unfavorable conditions, and spores from bacteria such as *Bacillus anthracis* can remain dormant and viable for up to 50 years or longer when buried in the soil (Dragon and Rennie 1995). Bacteria are also recognized for their ability to grow on

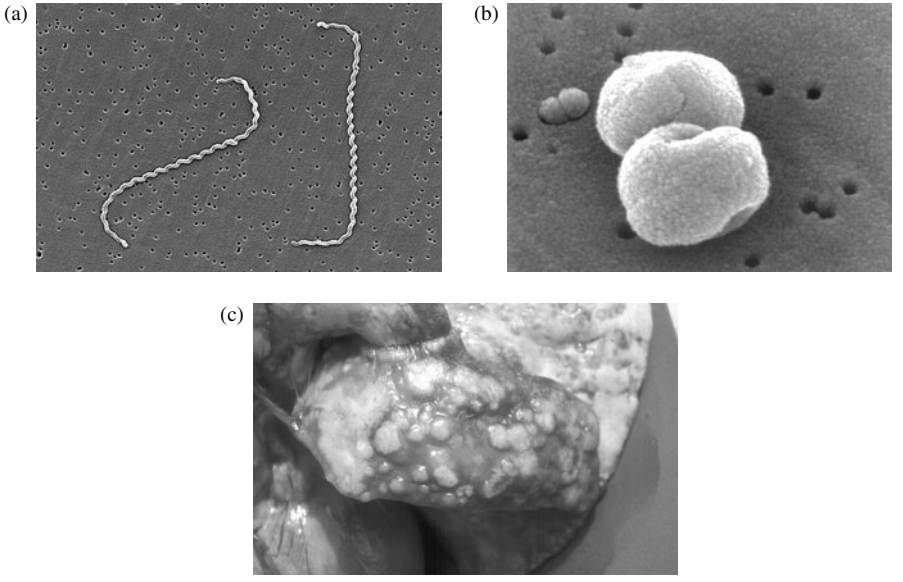


Fig. 2.6 Bacteria reported from free-living primates. (a) Scanning electron micrograph of *Leptospira interrogans* (Reproduced from Public Health Image Library 2004. Image credit: CDC/Rob Weyant). (b) Scanning electron micrograph of *Streptococcus pneumoniae* (Reproduced from Public Health Image Library 2004. Image credit: CDC/Dr Richard Facklam). (c) Lungs of a chacma baboon (*Papio ursinus*) showing tuberculous lesions caused by infection with the bacterium *Mycobacterium bovis*. Image courtesy of Dr D. Keet, Veterinary Investigation Center, Kruger National Park.

novel substrates or thrive in extreme environments, such as anaerobic bacteria that grow in the absence of oxygen, either facultatively or obligately (Prescott et al. 2001).

In human populations, bacterial pathogens have caused some of the most devastating and widely known historical epidemics, including the "black death" (caused by the bacterium *Yersinia pestis* which can lead to bubonic, pneumonic, or septicemic plague), cholera (caused by *Vibrio cholerae)*, tuberculosis (caused by *Mycobacterium tuberculosis*), and typhoid fever (caused by *Salmonella typhi*). Bacteria are also well known as agents that can cause human STDs such as syphilis, gonorrhea, and chlamydia (caused by *Treponema pertenue, Neisseria gonorrhoeae*, and *Chlamydia trachomatis*, respectively). Although antibiotic drugs have been powerful in combating many bacterial infections, bacterial diseases in human populations continue to cause epidemics or are re-emerging, in part because some bacteria have evolved resistance to the majority of available antibiotics (Palumbi 2001).

A major challenge to investigating bacteria as pathogens is that many are commensal and even aid in proper digestion, but in some circumstances these same bacteria can cause disease. In humans, for example, some of the normal bacterial flora (e.g. *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae*) are also known to cause disease following weakness or injury, or when these pathogens infect atypical organ systems (Levin 1996). Other bacteria can live outside a host but cause infections opportunistically by invading wounds or sores, including soil-dwelling bacteria like *Clostridium tetani*, the causative agent of tetanus.

In light of their importance as human pathogens, it is somewhat surprising that relatively few bacteria have been reported from free-living primate populations (Fig. 2.3). Furthermore, most current examples of bacteria reported to cause disease in nonhuman primates include those from the genera *Borrelia, Mycobacterium, Salmonella, Shigella, Streptococcus*, and *Leptospira* (e.g. Fig. 2.6), with the majority of these species also reported to infect humans (Taylor et al. 2001; Pedersen et al. 2005). In fact, a recent study found that 31% of the bacteria species reported from wild primates have been classified as emerging diseases in humans (Pedersen et al. 2005). This observation points to the need for additional comprehensive studies to determine the occurrence of bacteria in wildlife populations and their role as causative agents of primate disease.

2.2.3 Fungi

Fungal infections are important in affecting the health of humans and domesticated animals, but fungi represent the least commonly reported pathogen group from wild primates (Fig. 2.3), possibly because other groups of parasites are easier to study or fewer biologists are interested in fungal infections in primates. Many fungi live as free-living saprophytes that feed on dead or decaying material. Fungi differ from other parasite groups in their possession of a rigid cell wall made of chitin. Fungi

also express distinctive growth forms, including reproductive spores and elongated vegetative hyphae that can, at times, grow straight through host cells. Other fungi replicate by fission or yeast-like budding.

Like bacteria, fungi are ubiquitous in the environment and can cause opportunistic infections in compromised hosts. The majority of pathogenic fungi infecting vertebrate animals are from the phyla Ascomycota or Basidiomycota, and these typically infect the lungs by airborne inhalation, or the skin following contact with spores. Many human fungal infections (also called mycoses) are caused by species that commonly feed on decaying material (such as those in the genera *Acremonium, Aspergillus*, and *Rhizopus*), with human cases representing secondary opportunistic infections. Other fungi are more commonly known as disease-causing agents, such as *Trichophyton* and *Microsporum* that can infect the skin, hair, and nails of humans and other animals. Examples of fungi reported to infect wild primates include *Histoplasma capsulatum*, which causes a respiratory disease and is spread by contact with bird or bat feces, *Cryptococcus*, another causative agent of lung disease spread by contact with bird droppings or contaminated soil, and *Candida*, which are yeast that can infect the mouth, throat, and genital region and in some cases cause severe systemic infections (Fig. 2.7; see Al-Doory 1969; Naiff et al. 1996; Legesse and Erko 2004). Finally, *Pneumocystis carinii* is a fungal pathogen that was formerly classified with the protozoa. This fungus opportunistically infects the lungs of several mammal species (including humans) and has been reported to infect some wild macaques (*Macaca fuscata* and *M. fascicularis*) at relatively high frequency (Fujita et al. 1996).

2.2.4 Protozoa

Protozoa are the second most diverse group of parasites reported from wild primates in terms of total number of species (Fig. 2.3). Most protozoa are free-living, but parasitic representatives of these unicellular eukaryotes are incredibly diverse and inhabit a wide variety of host organs and tissues, including red blood cells, muscles, nervous tissue, intestines, the mouth, and genitalia (Bush et al. 2001). New molecular tools are greatly altering our understanding of protozoan diversity and phylogenetic relationships (Bush et al. 2001; Cox 2002). Since the late 1990s, protozoa have been reorganized into 13 phyla, with seven of these capturing important parasitic genera (Cox 2002). Some groups of protozoa, such as those in phylum Sporozoa (formerly referred to as Apicomplexa, including all species of *Plasmodium* and *Cryptosporidium*) are intracellular parasites, whereas others, such as the Euglenozoa (including *Leishmania* and *Trypanosoma*), are extracellular (Fig. 2.8). Some parasitic protozoa are highly specific to single host species or genera, but others, such as those causing toxoplasmosis and trypanosomiasis, have a wide host range (Su 2003), and reservoir hosts can serve as sources of infection for humans or vulnerable wildlife species.

Although many protozoa have direct life cycles and do not require intermediate hosts, dispersal via biting arthropods represents the dominant transmission strategy

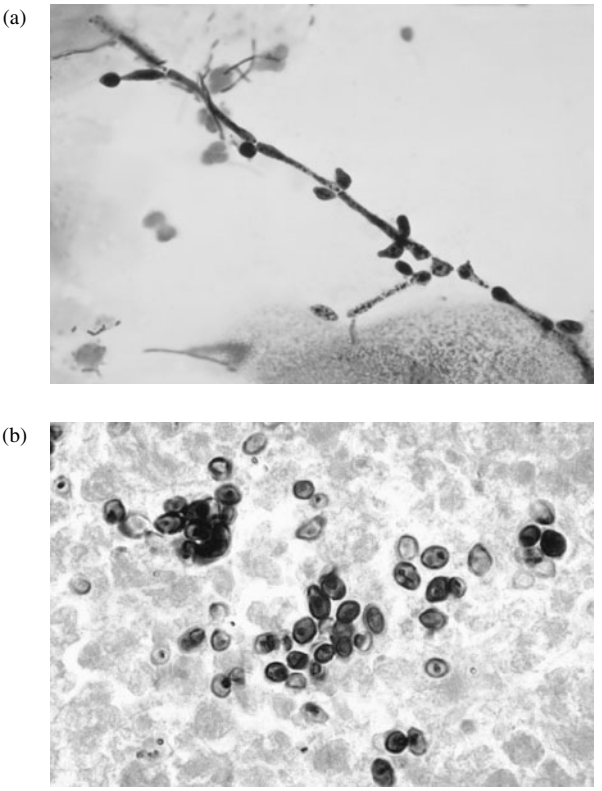


Fig. 2.7 Two examples of fungi reported to infect free-living primates. (a) Photomicrograph of *Candida albicans*. (b) Photomicrograph of *Histoplasma capsulatum*. Both images reproduced from Public Health Image Library, 2004, Image credits CDC/Dr Stuart Brown and CDC/Dr Edwin P. Ewing, Jr.

among protozoa infecting primates (Pedersen et al. 2005). Important examples of vector-borne protozoa in primates include more than 20 species of *Plasmodium* (Garnham 1966; Deane et al. 1969; Coatney et al. 1971; Davies et al. 1991; see Box 8.1), and over ten species of *Trypanosoma* and *Leishmania* (Lainson et al. 1989). In many cases, these blood-borne parasites complete critical stages of their life cycles within infected arthropods and are transmitted to vertebrates through the saliva or feces of biting insects. Other protozoa that infect primates, such as *Giardia* and *Entamoeba* (Freeland 1979; Stuart et al. 1998; Rothman and Bowman 2003), are intestinal parasites spread when animals ingest spores or cysts resistant to harsh environmental conditions. Finally, a few protozoa, such as those in the genus *Sarcocystis*, can inhabit primates as intermediate hosts by encysting in muscle tissue, with carnivores representing the definitive host (McConnell et al. 1974).

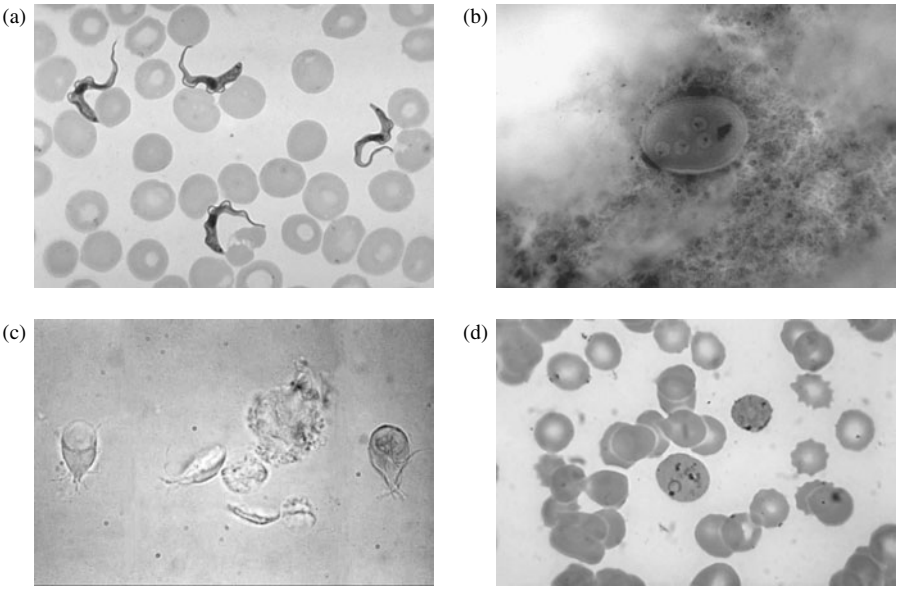


Fig. 2.8 Protozoan parasites reported from free-living primates. (a) *Trypanosoma* parasites in a blood smear from a human patient with African trypanosomiasis (Reproduced from Public Health Image Library 2004. Image credit: CDC/Dr Myron G. Schultz). (b) *Entamoeba coli* cyst (Reproduced from Public Health Image Library 2004. Image credit: CDC/Dr George R. Healy). (c) *Giardia lamblia* trophozoites in the small intestine of an infected human host (Reproduced from Public Health Image Library 2004. Image credit: CDC/Dr Mae Melvin). (d) *Plasmodium vivax* ring stage parasites in a human blood smear (Reproduced from Public Health Image Library 2004. Image credit: CDC/Dr Mae Melvin).

2.2.5 Helminths

Helminths are parasitic worms that typically reside within their hosts. Collectively, helminths are the most commonly reported and taxonomically diverse group of parasites in wild primates (Fig. 2.3 and 2.9). The major groups of parasitic helminths include (1) roundworms in the phylum Nematoda, (2) flatworms (cestodes and digenean trematodes) in the phylum Platyhelminthes, and (3) thorny-headed worms in the phylum Acanthocephala. Some helminths exhibit extremely complicated life cycles, residing in different host species for different developmental stages, whereas other helminths can develop to maturity within a single host (see Fig. 2.2). Animals that serve as secondary hosts but where no parasite development occurs are called *paratenic* hosts, and these hosts can bridge important ecological or trophic gaps (Bush et al. 2001). Some helminths are capable of producing resting or encysted stages that can persist in the environment outside of any living organism, and larval worms of certain taxonomic groups can enter a phase called *hypobiosis*, arresting as

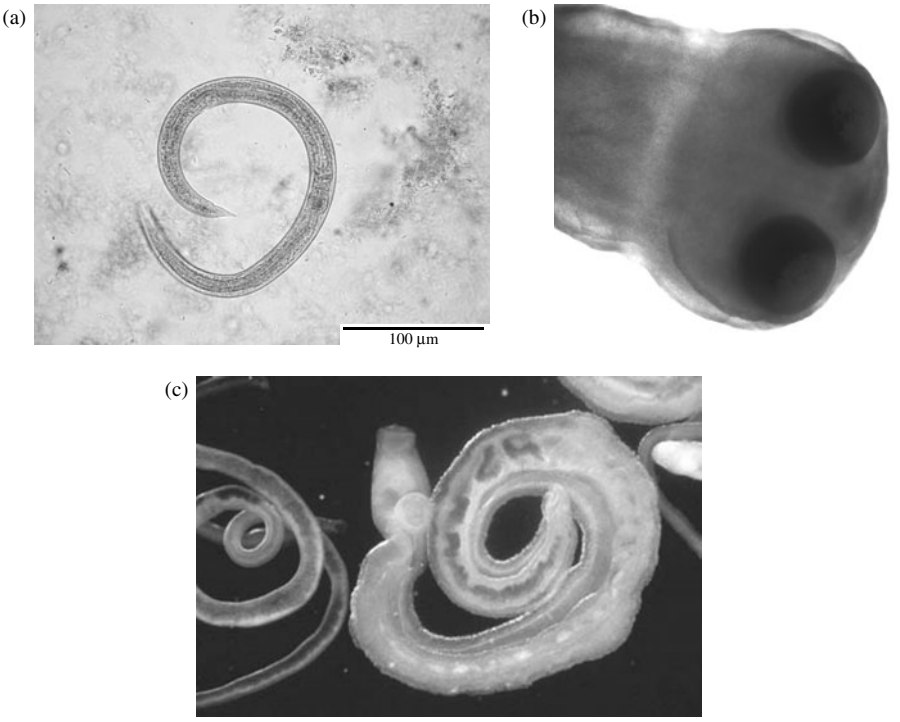


Fig. 2.9 Examples of primate helminths from several major taxonomic categories: nematodes (roundworms), cestodes (tapeworms), and trematodes (flukes). (a) Larval nematode from a red titi monkey (*Callicebus cupreus*, courtesy of B. Müller, German Primate Center). (b) Scolex of the cestode *Taenia saginata* (Micrograph courtesy of Brian Byrd, Department of Tropical Medicine, Tulane University). (c) Adult stage of the trematode *Schistosoma haematobium* (Reproduced from WHO/TDR 2004. Image credit: WHO/TDR/Stammers).

immature stages inside the definitive host when climatic conditions outside the host are too harsh to allow effective transmission (Roberts and Janovy 1999).

2.2.5.1 Nematodes

Nematodes are by far the most diverse group of parasitic worms (Fig. 2.9(a)), both across all vertebrates (Orihel and Seibold 1972; Bush et al. 2001; Vitone et al. 2004) and among primates (Nunn et al. 2003a; Vitone et al. 2004). Many books are devoted to exploring the fascinating diversity of nematodes (e.g. Maggenti 1981; Anderson 1992; Lee 2002), and their varied life histories make it difficult to draw indisputable generalizations about this group of organisms.

Parasitic nematodes exhibit a range of direct and indirect transmission strategies. At the level of individual hosts, some species of nematodes invade by penetrating the skin and others are ingested as eggs or encysted larvae (Orihel and Seibold 1972).

Pinworm eggs (including those from the genus *Enterobius*) are small enough that they can actually become airborne (Bush et al. 2001), although transmission of this parasite is probably usually accomplished via direct contact. Larval stages of filarial nematodes, common among wild primates, spread to their definitive hosts through biting arthropods, including mosquitoes (e.g. *Brugia malayi* and *B. pahangi*), black flies (*Dipetalonema* and *Dirofilaria*), and horseflies (*Loa loa*, see Laing et al. 1960; Orihel and Seibold 1972; Sousa et al. 1974; Mak et al. 1982).

Unlike most other helminths, parasitic nematodes generally lack "holdfast" structures for maintaining contact with the host, and instead live within host tissues or move through the gut. Some nematodes, however, have developed firm attachments to hosts, including hookworms (*Ancylostoma* and *Necator*), threadworms (*Strongyloides*), and whipworms (*Trichuris*). Another group of nematodes, the pinworms, show evidence for patterns of co-speciation with their hosts, including primates (Brooks and Glen 1982; Harvey and Keymer 1991; Hugot 1998, 1999).

2.2.5.2 Cestodes

Tapeworms, or cestodes, are parasitic flatworms that inhabit the intestinal tracts of vertebrate animals. Adult cestodes lack a gut, and instead absorb nutrients through the surfaces of their bodies while attached to the host with a scolex, or head-like structure that is often equipped with a combination of suckers and/or hooks (Fig. 2.9(b)). Adult cestodes have segmented bodies with proglottids, or egg-filled reproductive segments at their posterior end, and these gravid segments can be expelled with the feces of the host. Several species of cestodes are common in primates, including *Bertiella, Anoplocephala*, and *Hymenolepis* (Ghandour et al. 1995; Ashford et al. 1996; Stuart et al. 1998). Cestodes typically have complex life cycles, with infections in definitive hosts acquired through ingestion of intermediate hosts such as insects and vertebrate prey, although a few species (including *Hymenolepis nana*) can complete their life cycles without an intermediate host. Immature stages of tapeworms called cystercerci can encyst in various organs of the body, including the brain, liver, and lungs (Roberts and Janovy 1999). Dunbar (1980) provided a possible example of this in gelada baboons (*Theropithecus gelada*), in which larval stages of *Taenia* (= *Multiceps*) *serialis* caused painful swellings and even death in a significant number of individuals.

2.2.5.3 Trematodes

Trematodes, commonly called flukes, are another major group within the flatworms (Fig. 2.9(c)). The digenean trematodes are slug-shaped parasites that have two suckers on their bodies in the adult stage. All species exhibit multi-host life cycles, with intermediate stages in as many as three host species; some trematodes also have free-living stages (Bush et al. 2001). These complex life cycles are commonly linked to the feeding strategy or lifestyle of their definitive hosts, which frequently involve contact with molluscan or crustacean intermediate hosts.

As compared to nematodes and cestodes, fewer trematode species are reported to infect primates, but several prominent examples can be found (Kuntz 1972). Liver flukes such as *Fasciola* (tentatively reported in Madagascar, Hogg 2002) and *Dicrocelium* have been documented in African monkeys and apes (Myers and Kuntz 1968; Landsoud-Soukate et al. 1995). Liver flukes are typically recognized as parasites of sheep, cattle, and humans and are known to cause massive mortality and morbidity in domesticated animals (Bush et al. 2001; Pybus 2001). Schistosomes are probably the parasitic trematodes most familiar to readers, as members of this group also cause serious disease in humans (schistosomiasis). These parasites spread to their definitive primate hosts through contact with water in which intermediate stages (called *cercariae*) have been released. Parasite eggs are shed in feces or urine of the definitive host, and snails or other aquatic invertebrates become infected by an early developmental stage of the parasite (Bush et al. 2001). An estimated 200 million humans suffer from schistosomiasis in Africa and Asia (Crompton 1999), and infections have been reported from African primates, particularly species that come into contact with water (e.g. *Papio* and *Cercopithecus aethiops*: Else et al. 1982; McGrew et al. 1989a; Ghandour et al. 1995; Müller-Graf et al. 1997; Munene et al. 1998).

2.2.5.4 Acanthocephalans

The aptly-named thorny-headed worms (acanthocephalans, see Fig. 2.1) are rarely reported in wild primate populations, although they are well known as dangerous parasites in captive primates (Schmidt 1972). Acanthocephalans typically are transmitted through ingestion of insect, crustacean, or other arthropod intermediate hosts (Bush et al. 2001). Like cestodes and some nematodes, they possess a holdfast mechanism that anchors them to the gut of the definitive host (Fig. 2.1). This thorny proboscis is invaginated in many species into a receptacle in the worm's body, and following ingestion by a definitive host, the worm attaches to the gut wall by forcibly everting the proboscis. In comparison to the other groups of helminths, the acanthocephalans are a relatively less diverse group overall, and only a few species have been documented in wild primates (Kuntz and Myers 1966; Appleton and Boinski 1991; Stuart et al. 1998).

2.2.5.5 Other "wormy" organisms

For completeness and clarification, leeches also attack monkeys (Bywater and Mann 1960; Fox and Ediger 1970; Pryor et al. 1970). They are not commonly grouped with other parasitic worms, nor are they commonly recognized as parasites due to their short-term associations with their hosts.

2.2.6 Arthropods

A large number of arthropods, even those that are not directly parasitic themselves, are key players in the transmission cycles of a variety of infectious diseases (Fig. 2.10). Thus, many blood-feeding arthropods (including mosquitoes, flies, ticks, and fleas) operate as vectors that transmit viruses, protozoa, or filarial worms among

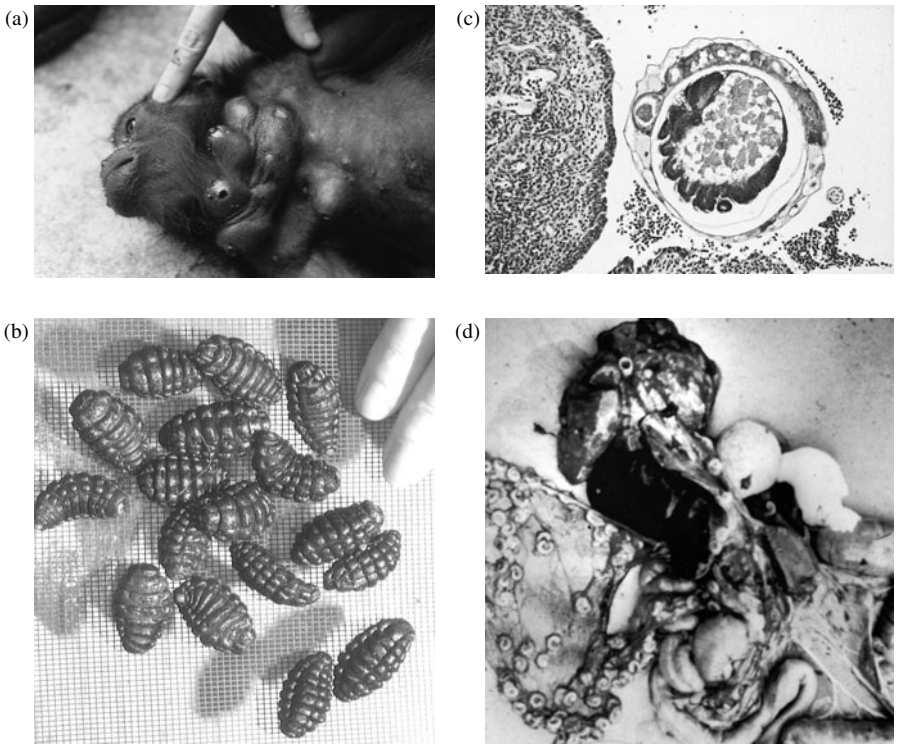


Fig. 2.10 Examples of arthropod parasites reported from free-living primates. (a) Mantled howler monkey, *Alouatta palliata*, with bot fly (*Alouattamyia baeri*) infection on neck (Photo courtesy of K. Milton and D. Murowski, see also Milton 1996). (b) Howler bot fly larvae, third instar (Photo courtesy of K. Milton and D. Murowski). (c) Lung mite (*Pneumonyssus simicola*) within a bronchiolar structure of a captive-bred primate, shown as the darkly stained object in the center of the image (Courtesy of K. Mätz-Rensing, German Primate Center). (d) Pentastomid larvae (*Armillifer armillatus*) appear as small c-shaped bodies (in the lower left portion of the image) on the peritoneum and mesentery of an African monkey. Reprinted from Reeder, M. M. and P. E. S. Palmer, 2000, The Imaging of Tropical Diseases, with kind permission of Springer Science and Business Media.

vertebrate animals. Other arthropods serve as intermediate hosts in the life cycles of parasitic flatworms, nematodes, and acanthocephalans. However, despite the fact that arthropods are ubiquitous among primates and influence their behavior and fitness (Dudley and Milton 1990; Milton 1996), surprisingly few ecological studies or field surveys have sampled arthropods parasitizing primates (e.g. only 11% of 415 species of parasites reported to infect free-living primates were arthropods, Nunn et al. 2003a; Pedersen et al. 2005).

Among arthropods that can parasitize primates and other animals during at least one stage of their life cycles, two classes dominate: Chelicerata (ticks and mites) and Insecta (bot flies, lice, and fleas; for example, McConnell et al. 1974; Brain and Bohrmann 1992; Milton 1996; Stuart et al. 1998). The majority of parasitic arthropods are ectoparasites that occur on skin, hair, and other body surfaces and feed on blood or keratinous material. These ectoparasites often have highly specialized holdfast mechanisms, such as those used to remain attached to host hairs. Ectoparasites reported from primates include several genera of ticks, sucking lice (e.g. *Pedicinus*, Kuntz et al. 1968), biting lice (e.g. *Trichodectes*, Fiennes 1972b) and fleas (*Ctenocephalides*, Myers and Kuntz 1965). Some of these ectoparasites live on the same host animals for most or all of their entire lives, whereas others have free-living stages or frequently move among hosts. Thus, larvae of the howler botfly live and feed in warbles under the skin, leading to highly visible lumps, particularly around the neck, throat, chest, and stomach (Fig. 2.10.(a) and (b)). In addition to direct harm caused to the host, they provide an opportunity for other infections (Milton 1996). Botfly larvae exit the host just before pupation and free-flying adults probably search for suitable oviposition sites near places visited by the host animals.

Not all parasitic arthropods are ectoparasites. Another group called lung mites (Fig. 2.10.(c)) include respiratory parasites of baboons, macaques, and other Old World monkeys. These mites live and reproduce in the lungs (e.g. *Pneumonyssus*) or nasal passages (e.g. *Rhinophaga*) and are transmitted by close contact (Innes et al. 1954; Kim and Kalter 1975). *Pneumonyssus simicola* is the most commonly reported lung mite, with nearly 100% incidence in rhesus monkeys that are captured and brought into captivity (Innes et al. 1954; Abbott and Majeed 1984). Most infections are asymptomatic, but heavy infestations of these mites can produce lung lesions, pulmonary disease, impede host mobility, and in severe cases result in host death (Kuntz and Myers 1966; Kim and Kalter 1975).

Pentastomids (commonly called tongue worms) are another endoparasitic arthropod, with at least one species reported to infect primates (*Armillifer armillatus* in baboons and possibly galagos, Fig. 2.10(d); Kuntz and Myers 1966; Durden et al. 1985). Although their phylogenetic identity is uncertain, their parasitic life cycle resembles those of cestodes and other trophically transmitted helminths by including one or more intermediate hosts, with snakes as the most common definitive host. Thus, in terms of their life cycles, pentastomids could be grouped with helminths, but phylogenetically they are probably more closely related to arthropods. Primates could serve as intermediate hosts, but unless the infection occurs in small-bodied primates subject to predation by snakes or other reptiles, primates are likely to be dead-end hosts for this parasite (Durden et al. 1985; Bush et al. 2001).

2.3 Strategies for parasite transmission

Parasites exhibit an impressive variety of transmission strategies, with a major dichotomy between those that require close contact between animals versus parasites

Table 2.2 Major parasite transmission strategies, activities leading to transmission, and their potential interactions with host traits. Examples of primate parasites that share each major transmission strategy are provided in the right hand column. It is important to note that many parasites can be transmitted by multiple routes and not all transmission modes are indicated for each example provided below

Transmission strategy	Activities leading to transmission	Host traits important to transmission	Examples from wild primates
Close contact—Sexual	Copulation and mating behaviors	Mating promiscuity, sexual selection	Papillomaviruses, herpesviruses, SIV, and STLV
Close contact—Non-sexual	Biting, scratching, grooming, touching, huddling	High local density or aggregation, affiliative and aggressive contacts	Influenza virus, Varicellovirus, *Pneumonyssus*, *Trichomonas*
Close contact—Vertical	Parent–offspring interactions	Gestation length, birth rate, parental care	Cytomegalovirus, Hepatitis G virus, STLV
Non-close contact—Environmental	Fomites, contaminated soil, water, or food	Diet, habitat use, geographic range, territoriality, climate	*Toxoplasma*, *Isospora*, *Strongyloides*, *Leptospira*
Vector-borne	Biting arthropod vectors	Habitat use, climate, latitude, geographic range	*Trypanosoma*, *Plasmodium*, Dengue fever virus, Yellow fever virus
Complex life cycle/ Intermediate host	Ingestion of intermediate hosts, contact with active stages	Diet, habitat use, geographic range	*Mansonella*, *Filariopsis, Taenia*, *Schistosoma*

for which transmission is decoupled from host contact (Table 2.2). In terms of infections spread through close contact, some contagious parasites spread when primates huddle, mate, groom, or fight; examples include bovine tuberculosis (*Mycobacterium bovis*, Keet et al. 2000), SIV, and other retroviruses (some of which might also be transmitted vertically; Galat Luong et al. 1994; Jolly et al. 1996; Blewett et al. 2000; Parrish et al. 2004), and pinworms (Hugot 1999). Vector-borne parasites, such as the causative agent of malaria (*Plasmodium*, Garnham 1966; Coatney et al. 1971), are transmitted by biting arthropods. Other parasites are transmitted when hosts feed on leaves or insect prey, with parasites moving through food webs via predation or incidental ingestion of intermediate hosts (e.g. acanthocephalans: Tantalean et al. 1990; Appleton and Boinski 1991; Kawabata and Nishida 1991; Rea and Irwin 1994; Choisy et al. 2003). Parasites that require multiple host species face the challenge of finding the next host in the cycle. Some parasites species meet this challenge by producing large numbers of immobile infectious stages, whereas others produce free-living larval stages that actively seek hosts (Bush et al. 2001).

Another way parasites might increase their probability of successful dispersal to a new host is to manipulate host behavior in ways that facilitate transmission, an issue discussed in Section 2.6.

As might be expected, different taxonomic groups of parasites appear to rely on different strategies for transmission among primate hosts (Fig. 2.11). Among viruses infecting wild primates, transmission by close (or combined close and non-close) contact is most common (Fig. 2.11 (a)). A variety of STDs have been reported from nonhuman primates, and virtually all of these examples are viruses (Nunn and Altizer 2004; see Chapter 3). Vector transmission, on the other hand, is more commonly observed among protozoa than other parasite groups (Fig. 2.11 (b)), and also widespread among viruses. Helminths are the only group in which transmission through intermediate hosts is common (Fig. 2.11 (c)). Extreme variation in transmission is also evident within parasite groups. Some nematodes, for example, spread through contact with contaminated soil or infected individuals (e.g. pinworms, whipworms, hookworms, and threadworms), others reach new hosts via blood-feeding vectors (filarial nematodes), and yet others make use of complex life cycles involving intermediate hosts (some lungworms and spiruroid nematodes). Importantly, a large number of parasites appear to exhibit multiple transmission strategies, as indicated by the combined category "close and non-close" in Fig. 2.11. For example, many viral STDs can be transmitted vertically and by close non-sexual contact, and

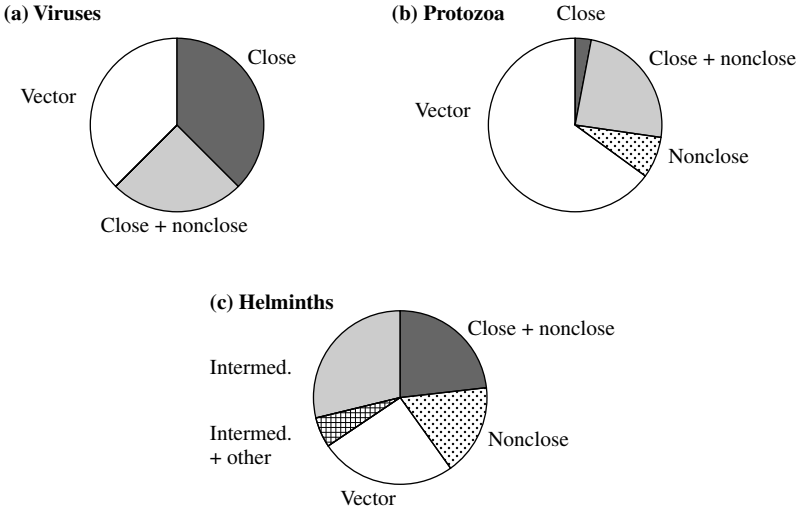


Fig. 2.11 Transmission strategies represented by primate parasites from three groups: (a) viruses (n = 81), (b) protozoa (n = 80), and (c) helminths (n = 157). Close contact includes close nonsexual contact in addition to vertical and sexual transmission (although these latter two modes are represented only by viruses). Because some parasites could be transmitted by more than one strategy, frequencies of parasites with both single and combined strategies are shown (from Pedersen et al. 2005, with permission of Elsevier).

many protozoa and helminths transmitted by close contact can also be transmitted by non-close contact.

Transmission strategy is fundamentally important to parasite ecology and evolution for at least two reasons. First, opportunities and limitations on parasite transmission govern the degree of damage they cause to their hosts. In particular, parasites that depend on host mobility, longevity, mating, or reproduction for their own transmission should be relatively more benign than parasites for which transmission is decoupled from host fitness (Ewald 1983, 1994a). Second, transmission strategies interact with host behavior and life history to determine parasite dynamics in wild animal populations (Table 2.2). The establishment of an STD, for example, depends on sexual contacts and the longevity of infected adults (Smith and Dobson 1992; Thrall et al. 1998). Increased sociality and greater host population density are predicted to increase the spread of parasites transmitted by close contact (Thrall and Antonovics 1997), whereas parasites spread by biting vectors or exposure to contaminated soil or water should be more sensitive to changes in environmental conditions.

In practice, determining major routes of parasite transmission in natural systems can be difficult and usually requires detailed monitoring and verification by experimental manipulation. This is often more difficult for large, cryptic, or endangered mammals, such as many primates, and the sheer number of parasite species makes complete understanding of all transmission modes a daunting task. Hence, information on the transmission modes of many primate parasites must often be obtained from similar infections in closely related host species that have been studied in greater depth. Epidemiological clues can also be derived from spatial or demographic clusters of high disease risk. Thus, large numbers of parasites near water sources point to patterns of water-borne transmission, or could indicate that transmission requires vectors that breed near water sources. Demographic patterns can also provide important clues to transmission mode. Among nonhuman primates, for example, STDs should be found in sexually active adults, with exceptions presumably due to vertical transmission from infected mothers to offspring, or in maturing juveniles as they become experienced sexually. Strikingly higher disease prevalence among adults relative to immature animals could therefore point to sexual activity as an important transmission route (Nunn and Altizer 2004).

2.4 Host specificity and "multi-host" parasites

Host specificity refers to the spectrum of host species that a parasite can exploit at a particular stage of its life cycle. Parasites are often assumed to be under selection for specialization on commonly infected host species (Berenbaum 1996; McPeek 1996; Combes and Theron 2000), in part because the machinery required for invasion, growth, and transmission might vary from one host species to another (Price 1980; Whitlock 1996). In contrast to this viewpoint, an increasing number of empirical studies and review papers point to the commonness of generalist, or *multi-host*, parasites. In fact, over 60% of human micro- and macroparasites, and 80% of those reported to infect domesticated animals, are capable of infecting more than one host

species (Cleaveland et al. 2001; Taylor et al. 2001; Woolhouse et al. 2001). Understanding the distribution and population biology of these multi-host pathogens is important for wildlife conservation and human health (Murray et al. 1999; Daszak et al. 2000). Adding host species to existing host–parasite systems can have major consequences for disease spread and evolution (Frank 1993; Woolhouse et al. 2001; Antonovics et al. 2002; Gandon 2002, 2004; Holt et al. 2003).

Understanding the determinants of host specificity among parasites in natural populations remains challenging (Poulin 1992; Adamson and Caira 1994; Kennedy and Bush 1994), but the ability to infect multiple hosts should be influenced by at least two key variables. First, host specificity should be determined by the ability of parasites to disperse among multiple host species (Woolhouse et al. 2001; Johnson et al. 2002). Thus, transmission strategies that provide opportunities to encounter new hosts, such as transmission by biting arthropods or through contaminated soil or water, could increase the range of hosts that a parasite can infect (Woolhouse et al. 2001). Second, greater genetic variability and more rapid generation times might allow certain pathogens to readily exploit new host species. For example, parasites with high antigenic variation or high mutation rates should have an increased ability to recognize host proteins or evade host immune defenses relative to those with slower mutation rates or less genetic variability (Bitter 1998; Simon et al. 1998; Cleaveland et al. 2001; Woolhouse et al. 2001).

An important concept related to these processes involves the distinction between phylogenetic and ecological components of host specificity (Bush et al. 2001). A parasite might inhabit a range of hosts because they are closely related and therefore require more similar "machinery" for parasite invasion or replication, thus leading to the prediction that increased phylogenetic relatedness leads to greater overlap of parasite communities (Perlman and Jaenike 2003). Alternatively, two host species might share the same parasites because the hosts have similar ecological characteristics, such as common diets, habitat types, or geographic ranges, thus exposing them to a common pool of infectious organisms. For example, terrestrial vervet monkeys might share a virus with congeneric arboreal guenons (classified in the genus *Cercopithecus*) due to their phylogenetic similarity, but vervets might also share parasite species in common with baboons and bovids that use the same habitats and consume the same resources. Some recent studies have pointed to ecological similarity and geographic proximity as more important than phylogenetic distance in explaining patterns of host use among parasites within the same clade (Roy 2001). Investigating this issue is complicated, however, by the fact that closely related hosts often tend to share a variety of ecological traits through "phylogenetic niche conservatism" (Harvey and Pagel 1991) and may also live in close spatial proximity, confounding these two processes. It is important to remember that many parasites documented in primates are also found in other mammals, and even some non-mammals. Thus, expanding the taxonomic scope beyond primates could help in evaluating the relative roles of ecology and phylogeny for host sharing by parasites.

Being a generalist would seem to be advantageous for parasites and other organisms and, as noted, is common among parasites studied to date (Cleaveland et al.

2001). An important question therefore arises for specialist parasites: what factors lead a parasite toward increased host specificity? This question is particularly relevant given that specialization might be accompanied by increased risk of extinction, with specialization linking the fate of the parasite to just one or a few host species (Poulin 1998a). Using the same arguments from above involving parasite dispersal, specialization is common among parasites transmitted by close contact, such as sexual contact or grooming (see Lockhart et al. 1996). Parasites with narrower host ranges are also more common among more slowly evolving parasites with longer generation times or lower mutation rates (Price 1980; Morand et al. 1996; Whitlock 1996; Gupta et al. 1998).

These arguments could explain why a recent comparative study of parasites from wild primates found that levels of host specificity were highest among helminth parasites and lowest among viruses (Fig. 2.12, Pedersen et al. 2005). The higher mutation rates and shorter generation times of viruses, as compared to the other groups of parasites, might allow them to rapidly adapt to a larger number of niches. In fact, nearly half of all primate viruses reported in the literature were extreme generalists capable of infecting hosts from multiple orders; virtually all of these were RNA viruses, which have higher mutation rates than DNA viruses (see Fig. 2.5; Drake 1991; Domingo and Holland 1997; Holmes 2003). By comparison, approximately one-half of the helminths reported from primates were recorded as species-specific (Fig. 2.12). Helminths have longer generation times than most microparasites

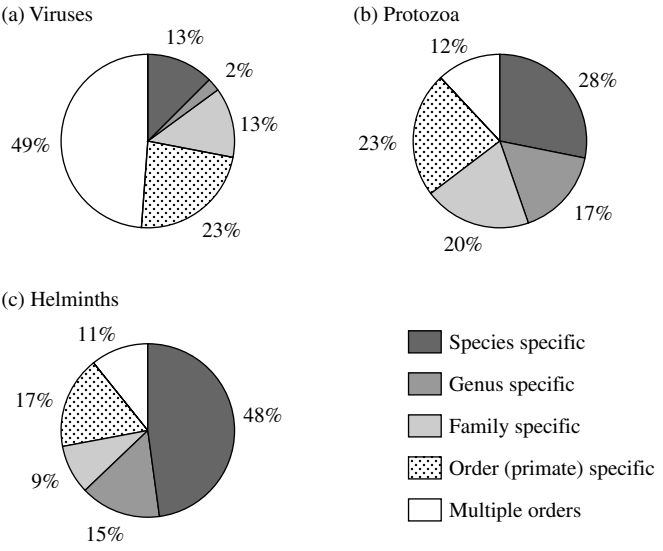


Fig. 2.12 Levels of host specificity among primate parasites from three major taxonomic groups. For viruses and protozoa, $N = 82$; for helminths, $N = 163$ parasite species (from Pedersen et al. 2005, with permission of Elsevier).

(Anderson and May 1991), and their relatively more complex life history strategies could limit their ability to infect or adapt to new host species.

Placing specificity in the context of parasite life cycle stage is critical, as many parasites differ in their specificity toward definitive and intermediate hosts. For example, *Schistosoma japonicum* is found in a wide variety of mammalian hosts (and hence shows relatively low specificity), but the range of molluscan intermediate hosts is relatively more narrow, in some areas restricted to particular subspecies of intermediate hosts (Bush et al. 2001). Similarly, blood-feeding insects encounter a range of parasites from vertebrate animals, but only a few species of insects can successfully transmit particular parasites (Lehane 1991). Human malaria caused by *Plasmodium falciparum* is transmitted by only a few mosquito species in the genus *Anopheles*, and factors affecting the ability of mosquitoes to permit parasite development have been studied as potential control measures against this devastating disease (Shahabuddin et al. 1998).

Host specificity represents an axis of variation crucial to understanding patterns of disease risk because many primates acquire parasites not just from conspecifics, but also from heterospecific hosts. Sharing of parasites among multiple host species will be most readily achieved in the case of generalist parasites, although it is also possible that a specialist parasite could shift to sympatric hosts (Antonovics et al. 2002; Jensen et al. 2002). As noted above, host sharing or shifting should occur most commonly among closely related hosts, although there have been several documented exceptions to this prediction in primates, including probable shifts of host-specific pinworms between primates and squirrels (Hugot 1999).

Finally, it is important to note that patterns of host specificity derived from published host–parasite combinations could reflect a number of limitations and biases. First and foremost, any comprehensive list of parasites from wild primates is likely to be incomplete, in large part because many of the host species have not been sampled adequately for parasites in the wild. Similarly, published records of parasites might be biased toward pathogens of greatest concern to humans. Thus, one explanation for a high proportion of multi-host parasites among viruses (Cleaveland et al. 2001) is that scientists have focused their studies on viruses with zoonotic potential, which are by definition capable of crossing among multiple host species. The goals of scientific studies addressing other pathogen groups might also produce misleading patterns. Thus, nematologists might be most interested in collecting and describing new helminth species, leading to large numbers of relatively host-specific parasites reported in this group. With that in mind, it seems likely that patterns reported from natural systems could change with increased understanding of the parasites that infect wild primates.

2.5 Virulence: negative effects of parasites on their hosts

In the ecological literature, parasite effects on host fitness fall under the umbrella of "virulence evolution," where virulence has been defined as the negative effects of

parasites on host fitness and therefore includes components of both host survival and reproduction. Parasites vary in the type and degree of damage they cause to their hosts, and they can cause a range of lethal and sublethal effects, including increased sterility. At one extreme, Ebola virus and anthrax have led to deaths in natural populations of African apes in recent years (Formenty et al. 1999a; Walsh et al. 2003b). At the other end of the spectrum, some nematodes can be found in all individuals of a social group with almost no apparent effects on their hosts (e.g. Ashford et al. 1990; Stuart et al. 1990).

The pathology produced by a parasite further depends on the host species affected, and this is especially true when dealing with host-specific parasites or strains that are occasionally found outside the natural host. Thus, SIV has little pathogenic effect on its natural hosts, which include African apes and monkeys (Norley et al. 1999), but a strain of SIV obtained from sooty mangabeys kills Asian macaques when artificially exposed in captivity. Similarly, Herpes B (simian herpesvirus) is relatively benign in its natural primate host (usually macaques and other monkeys) but can cause fatal infections in humans, while human herpes (caused by herpes simplex viruses HSV-1 and 2) can be fatal to nonhuman primates exposed in captivity (Brown 1997). HIV/AIDS is perhaps the best-known example of a wild nonhuman primate virus that was benign in naturally SIV-infected primate hosts, but highly virulent in humans (Hahn et al. 2000). Unusually low levels of allelic variation documented at several MHC Class I loci among three subspecies of chimpanzees (*Pan troglodytes troglodytes, P. t. schweinfurthii, P. t. verus*) could provide evidence that SIV was not always so benign in African primates: de Groot et al. (2002) suggested that an ancient and highly virulent SIV-like viral pandemic caused an apparent selective sweep in this primate lineage.

Parasites can negatively impact hosts through a variety of mechanisms, including physical damage caused by penetration of skin or intestinal walls, or lysing of erythrocytes or other host cells. Parasite replication or growth can also deplete essential nutrients, and some pathogens produce specific toxins or virulence factors that induce diarrhea, vomiting, or even death (see Table 2.4 in Bush et al. 2001). These damaging effects of parasites on their hosts are thought to be an unavoidable outcome of parasite reproduction, with the end result being detrimental to both hosts and parasites. Yet a large body of theory developed over the past two decades predicts that selection driven by host or pathogen biology can increase virulence (Levin and Pimentel 1981; Ewald 1983, 1994a; Herre 1993, 1994; Antia et al. 1994; Ebert 1994; Antia and Lipsitch 1997; Day 2001).

Until the 1980s, the received wisdom stated that disease-causing agents should evolve to have mild effects, and that virulent diseases that kill hosts quickly have not yet adapted to their hosts. To the degree that disease-induced mortality reduces this infectious period, parasites will themselves suffer from shortening the lifespans of their hosts. Therefore, if parasite transmission, virulence, and host recovery are free to vary independently, then parasite fitness should be maximized by low host recovery and low virulence, as this will maximize the duration over which infected hosts can transmit the pathogen (Anderson and May 1982; Frank 1996; Levin

1996). Because both hosts and parasites should benefit from decreased virulence, this framework predicts that pathogens should evolve to become benign.

This former view was challenged in recent decades because transmission rates, virulence, and host defenses are biologically linked by within-host replication of the parasite and therefore will not evolve independently of one another (Anderson and May 1991; Lenski and May 1994). For example, it is likely that parasite transmission to new hosts requires extensive within-host replication, leading to a positive relationship between transmission probability and replication (Fig. 2.13(a)). Greater parasite replication will also damage host tissues and deplete host resources, leading to a positive relationship between replication and virulence (Fig. 2.13(b)). Although the exact shape of these curves can vary, superimposing the processes of transmission and virulence suggests that parasite fitness will be optimized at intermediate rates of within-host replication, and hence by intermediate virulence (Fig. 2.13(c)). In other words, parasites that are too benign are less likely to be transmitted to new hosts (e.g. if these infections are cleared by the immune system before transmission, Antia et al. 1994), and parasites that are too virulent will kill their hosts before new transmission occurs. Therefore, the conventional wisdom that parasites evolve to become benign has been replaced by an "enlightened theory" that parasites will evolve to intermediate levels of virulence based on the relationship between

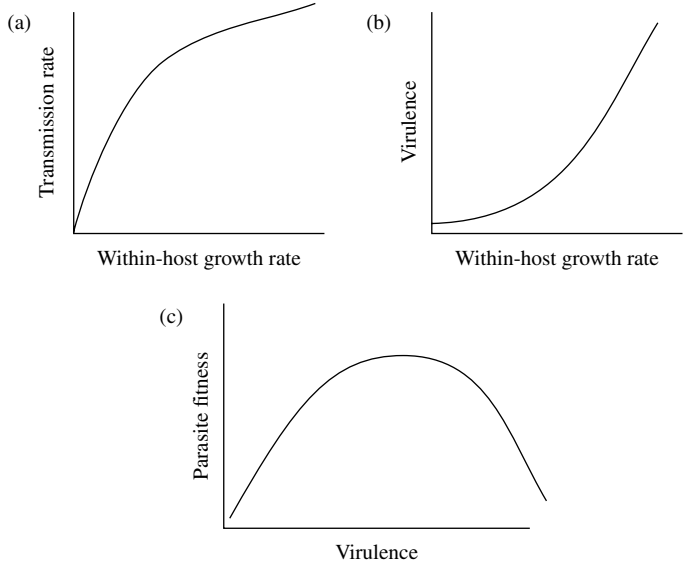


Fig. 2.13 Proposed relationship between within-host parasite replication and (a) transmission, (b) virulence, and (c) total pathogen fitness. This relationship underlies the trade-off theory of pathogen virulence, whereby total pathogen fitness is maximized at intermediate virulence.

virulence and the transmission biology of the pathogen (also referred to as the tradeoff hypothesis).

Selection on pathogen virulence will be complicated by at least three additional factors. First, potential competition among different parasite strains within hosts can select for increasingly virulent parasites through a mechanism analogous to the tragedy of the commons (Hardin 1968; de Roode et al. 2005). Thus, when multiple strains infect the same host individual, more virulent strains that replicate the fastest (and hence do the most damage) should be at a competitive advantage over less virulent strains, even if this leads to host death (Van Baalen and Sabelis 1995; Frank 1996; Ebert 1999; Read et al. 2002). In this competition, all parasites strains will die if their host dies. However, the less virulent strains should experience a disadvantage because prior to host death, more virulent strains might compete better for host resources and hence should achieve greater transmission or produce more dispersal stages. Infections consisting of genetically different strains of the same pathogen are common, indicating that conditions favoring increased competition for limited host resources are also common (Read and Taylor 2001).

Second, the routes by which parasites are transmitted will affect the optimal degree of parasite virulence. Thus, parasites that depend heavily on host mobility, survival, or reproductive activity (including mating) for their transmission should evolve to cause less damage to their hosts. At one extreme are vertically transmitted parasites, whose fitness might be so closely tied to the reproductive output of infected females that any disease-induced reductions in host survival or reproduction could drive the parasites themselves extinct (Lipsitch et al. 1995a). At the opposite extreme are parasites transmitted by biting arthropods or contaminated soil or water, where transmission is relatively independent of host activity and host mortality might represent a much lower cost in terms of lost transmission events (Ewald 1994a). In general, greater opportunities for horizontal transmission (either with or without host-to-host contact) should be associated with higher levels of pathogen virulence (Ewald 1983, 1994a; Herre 1993, 1995; Fenner and Fantini 1999).

Third, although most models of virulence evolution assume that parasites lower host survival, virulence could also be expressed in the form of reduced host fecundity. In this case, the costs of virulence to parasites in terms of a shorter duration of infectiousness become irrelevant, and pathogens that sterilize their hosts might continue to be transmitted over relatively long time intervals. One modelling study showed that when virulence is expressed as host sterility rather than mortality, selection should favor parasites with maximum virulence that essentially sterilize their hosts to increase their own transmission (O'Keefe and Antonovics 2002), even if this leads to host extinction. Negative effects on host fecundity have been reported for a wide range of parasites including many STDs (Lockhart et al. 1996), which tend to be less virulent in the mortality sense (potentially due to limited transmission opportunities), but more virulent in terms of their effects on host fecundity.

The issue of virulence will arise again in later chapters. In Chapter 4, effects of parasites on host fitness form a vital component of epidemiological models, with overriding effects on pathogen invasion, persistence, and impacts on host abundance.

In Chapter 5, we consider how hosts themselves are under selection to minimize infection and disease-induced mortality through behavioral and immune responses; these host responses can also influence pathogen virulence (Ebert and Hamilton 1996; Imhoof and Schmid-Hempel 1998; Mackinnon et al. 2002). The spatial distribution of hosts has also been suggested to influence the evolution of virulence, with increasing spatial structure favoring reductions in virulence (Boots and Sasaki 1999; O'Keefe and Antonovics 2002; Boots et al. 2004). This effect could be important in primate societies in which animals form social groups within populations, an issue we discuss in Chapter 6. Finally, conditions that influence parasites to become more or less benign are increasingly important for managing disease risks to wild animals, a topic covered in Chapter 7, with highly virulent infectious diseases causing dramatic declines in some wildlife populations (Walsh et al. 2003b; Leendertz et al. 2004; Leroy et al. 2004a). Tests of evolutionary and ecological determinants of pathogen virulence are urgently needed from natural populations, especially those that show variation in host and parasite biology.

2.6 Parasite transmission and manipulation of host behavior

Some of the most fascinating examples of parasitism in nature involve cases where infectious agents manipulate their hosts, usually with major consequences for transmission and ultimately host–pathogen dynamics (Dobson 1988; Moore 2002; Sapolsly 2003). In extreme cases, the behavior and morphology of a manipulated host can be changed so radically that even trained systematists have incorrectly identified parasitized individuals as new species (Moore 1995). One well known example of host manipulation involves the trematode *Leucochloridium paradoxum* (Fig. 2.14). This parasite infects birds as the definitive host, and in their snail intermediate host, sporocysts of this parasite migrate to the tentacles and pulsate, dramatically increasing their size, brightness, and apparency to bird predators (Wickler 1968). Although this example serves as a classic story of parasite manipulation, Moore (2002) notes that, surprisingly, no studies provided quantitative evidence that the parasite increases predation on infected snails. In another example involving mammals, the fluke *Dicrocoelium dendriticum* infects sheep as the definitive hosts, with an intermediate stage in ants (Manga-Gonzalez et al. 2001). In this case, the parasite induces infected ants to climb to the top of a blade of grass, where they are more likely to be incidentally ingested by foraging sheep.

Examples of parasite-induced changes in invertebrate behavior are common among intermediate hosts of parasites with complex life cycles. Thus, every acanthocephalan species studied to date can alter the behavior of at least one of its hosts, usually mollusks, crustaceans, or insects that serve as prey to the definitive host (Moore 2002). For other parasites, mammals serve as intermediate hosts, such as occurs when rodents infected with the protozoan *Toxoplasma gondii* increase their exploratory behavior and become less fearful in the presence of cat odors (Berdoy et al. 2000), potentially increasing their chances of consumption by a carnivore

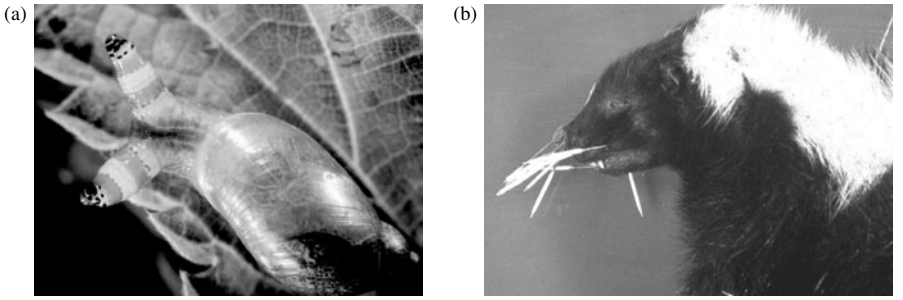


Fig. 2.14 Examples of parasite-induced changes in host behavior (or appearance) that affect the probability of transmission to other hosts. (a) A freshwater snail (*Succinea* sp.) parasitized by the digenean trematode *Leucochloridium*. Sporocysts of the parasite containing cercariae develop in the host's eye stalks and are ingested when a definitive host (a bird) eats the snail. The sporocysts are brightly colored (green and yellow) and pulsate continually, making the snails more visible to avian predators. Photo credit: R. Mannesmann and C. Fuchs, Bielefeld University. (b) A skunk infected with rabies showing evidence of a porcupine attack—a common occurrence among rabid carnivores in North America that show increased aggression and disorientation. Image courtesy of G. Wobeser, University of Saskatchewan. Reprinted from "Essentials of Disease in Wild Animals, Wobeser, G. A., Copyright (2005) with permission from Blackwell Publishing.

definitive host. Directly transmitted microparasites can also manipulate host behavior in ways that increase their transmission. Rabies transmission occurs when saliva from an infected animal enters a susceptible host, usually through a bite wound. After uptake into the peripheral nerves and transportation to the central nervous system, cerebral infection leads to a number of host behavioral changes, including wandering behavior and increased aggression (Baer 1991, Fig. 2.14).

It has been suggested that STDs would benefit from changing host sexual behavior in ways that increase mating frequency, the attractiveness of infected hosts, or rates of partner exchange (Møller 1993; Lockhart et al. 1996; Knell 1999). Indirect support for this hypothesis comes from the observation that a large number of STDs, including those infecting humans and livestock, are more likely to induce host sterility than related non-STDs (Lockhart et al. 1996). Such an effect should enhance their transmission if infected females are sterile, cycle repeatedly, and therefore mate more often (Nunn et al. 2001; Nunn and Altizer 2004). In another striking example, a sexually transmitted fungal infection altered the mating preferences of its insect host (Møller 1993). In this case, male flies preferred females with larger abdomens, in part because female abdomen size may be an indicator of overall fecundity. The contact-transmitted fungus alters the appearance of infected flies to make them appear as large females, so that dead infected flies of either sex have bloated abdomens. Møller (1993) found that healthy male flies preferred to mate with dead infected partners over healthy females, and presumably fungal conidia were transferred to males upon contact with the cadavers.

2.6.1 Causes and consequences of altered behavior

Considering the effects of parasitism on host behavior in an ecological framework can help scientists understand the consequences for parasite transmission and identify general conditions under which host manipulation by parasites might occur (Poulin 1994). In this regard, Dawkins (1982) provides a compelling argument for considering how hosts serve as "extended phenotypes" of parasite genes. Physiological or behavioral changes in the host may facilitate parasite transmission, selecting for parasite genes that cause these changes in the host. Thus, a sexually transmitted parasite may benefit from increasing the attractiveness of infected males to potential mates, which also benefits the male—although these benefits must be considered against the potential loss of fecundity in mates that he infects (Knell 1999; Boots and Knell 2002).

Dobson (1988) used an epidemiological framework to investigate the effects of parasite manipulation of intermediate hosts for parasites with complex life cycles, insect vectors of blood-borne protozoa, directly-transmitted microparasites, and worms with free-living stages outside of the host. Parasite-induced changes in host behavior made it easier for parasites to invade a susceptible host population by increasing the frequency of contact events (i.e. net transmission rate) leading to new infections (Dobson 1988). Furthermore, selection for parasites that manipulate their hosts is expected to be strongest when this alters a limiting step or makes unusually rare events leading to parasite transmission more common; thus, host manipulation by indirectly transmitted parasites may be adaptations to exploit host populations that are fragmented into smaller groups.

In some cases, it is difficult to separate manipulation by parasites from host behavioral defenses (Moore 2002). For example, infection of mammalian hosts by *Plasmodium* tends to make animals lethargic, which could facilitate attack by mosquitoes (the vector of malaria and the host in which the protozoan reproduces sexually). Is lethargy an adaptive host defense to fight the parasite immunologically, or a case of parasite manipulation (Moore 1995)? Other behavioral changes induced by parasites are less equivocal. For example, rabies is known to increase aggressive behavior, makes swallowing difficult, and is propagated in saliva—all factors that likely increase both contact rates and per contact probability of transmission of this viral pathogen (Fig. 2.14(b); Baer 1991).

2.6.2 Manipulation of primate hosts

Primates serve as hosts to some parasites that are known to manipulate the behavior of other (non-primate) hosts. For example, encysted stages of tapeworms in the genus *Echinoccus* have been suggested to increase the likelihood of predation on their intermediate mammalian hosts, possibly by inducing chest pain and thereby limiting responsiveness to predators (Moore 2002). This parasite has been found in baboons (Myers and Kuntz 1965). Similarly, *Eimeria* has been documented in the slow loris, *Nycticebus coucang* (Colley and Mullin 1972), and mice infected with a

congeneric protozoan (*Eimeria vermiformis*) were shown to fail more often at avoiding cat (predator) odors in a Y-maze, as compared to uninfected mice. Finally, *Toxoplasma gondii*, the parasite that has been shown to evoke fearlessness in rats and mice (Berdoy et al. 2000), has been recovered from both New and Old World monkeys (e.g. McConnell et al. 1974; Stuart et al. 1998). Remarkably, *Toxoplasma* infections in humans (likely arising from consumption of contaminated meat or contact with infected house cats) has been implicated in a variety of personality changes, delayed reaction times, and greater risk of schizophrenia (see Chapter 8).

It also seems likely that parasites could manipulate intermediate hosts to increase the likelihood of transmission to wild primates, or they might affect the behavior of arthropod vectors that spread parasites from host-to-host (Moore 2002), thereby impacting patterns of parasitism in primate host populations. As a case in point, tsetse flies infected with trypanosomes have been shown to probe mammalian hosts more frequently and feed more often, which results from parasite manipulation of insect neurons that receive information from the digestive tract (Jenni et al. 1980). Similarly, a recent study found that children harboring the infectious stages of *P. falciparum* were more attractive to mosquitoes (Lacroix et al. 2005). Although little evidence exists for the effects of parasites on primate behavior in the wild, such effects are plausible and would undoubtedly influence parasite transmission. Hence, this should remain an area for future research, particularly when primatologists investigating host behavior have the opportunity to simultaneously assess the health status of animals being studied.

2.7 Summary and synthesis

Because primates are one of the best-studied groups of mammals and harbor a diverse array of parasites, they represent a valuable system for investigating patterns of infection in natural populations and the effects of parasites on hosts. In this chapter, we defined and illustrated key parasite traits that are necessary for understanding interactions between hosts and parasites, including taxonomic identity, transmission mode, host specificity, and virulence. These traits are expected to have substantial impacts on host-parasite dynamics, host behavioral and immune defenses, and population viability.

One surprising result to emerge from recent studies of pathogen characteristics in primates and other mammals is that the overwhelming majority of parasites can infect hosts from multiple genera, families, or orders. Increasingly, the lines between risks to human health and wildlife conservation are blurred by the awareness that emerging pathogens in humans and wildlife are those that can cross species barriers—particularly viruses that can infect humans, wildlife, and domesticated animals (e.g. West Nile Virus, SARS, Ebola, and avian influenza). Understanding factors that drive outbreaks of these multi-host parasites, including how their transmission strategies interact with the environment and host ecology, could benefit conservation efforts and limit the damaging effects of human activities that trigger disease outbreaks (Chapter 7).

Major questions remain about the evolutionary relationships among extant parasites. Although this information is important to understanding parasite diversity, in this chapter we focused on describing major functional groups of parasites and highlighting characteristics expected to influence their spread and impact on animal populations. Many of the groups we described are not monophyletic, and this summary barely scratches the surface of the myriad dimensions of parasite diversity. Interested readers may wish to consult other, more comprehensive sources for information on parasite diversity and biological traits.

3

Primate socioecology and disease risk: predictions and rationale

3.1 Introduction

The previous chapter reviewed the incredible diversity of parasites found in primates and highlighted some of the ways that parasites are transmitted from host-to-host. This chapter addresses a different question: how do primate behaviors, life history, and ecology influence disease risk? To illustrate the links between primate traits and disease risk, we begin by describing three hypothetical examples that aim to capture how infections might spread through primate populations.

First, consider a male ring-tailed lemur (*Lemur catta*, Fig. 3.1) from Madagascar. Males of this species move between social groups upon reaching maturity, leaving

Fig. 3.1 A male ringtailed lemur at the Duke University Primate Center using his antebrachial (carpal) glands to mark a sapling. Photo by C. Nunn.

Fig. 3.2 Two ringtailed lemurs at the Duke University Primate Center performing allogrooming, with a juvenile about to join in. Ringtailed lemurs use their mouths to groom the fur of other individuals and pairs of individuals often perform the grooming activities simultaneously. Photo by C. Nunn.

their natal group to search for breeding opportunities in other groups (Jones 1983; Pereira and Weiss 1991). The grooming network of juvenile males within their natal ranges includes their mothers and other juveniles (Kappeler 1993; Nakamichi and Koyama 1997). Ring-tailed lemurs groom each other with their mouths (allogrooming, Jolly 1966; Fig. 3.2), an activity that provides hygienic benefits but also facilitates parasite transmission through contact with infectious stages caught in the fur or from saliva left by previous grooming partners. Close proximity during grooming could also facilitate the spread of respiratory pathogens. In socially structured primates like these lemurs, contact within groups provides a network for the spread of pathogens, and male dispersal to new groups serves as a conduit for among-group parasite transmission. Thus, patterns of group fidelity and host dispersal are central to understanding the establishment and spread of directly transmitted parasites (Freeland 1979).

As a second example, consider a female mantled howler monkey (*Alouatta palliata*) living in Costa Rica (Fig. 3.3). Howler monkeys are exposed to an incredible array of vector-borne parasites, such as *Plasmodium brasilianum* (a relative of the human malaria parasite) and flaviviruses such as those that cause yellow fever (Galindo and Srihongse 1967; Stuart et al. 1998). These monkeys also suffer from arthropod parasites, including a species of botfly (*Alouattamyia baeri*, see Fig. 2.10) that specializes on howler monkeys and can contribute toward mortality (Milton 1996). As a result, female reproductive success in mantled howler monkeys is probably tightly linked to avoiding flies, mosquitoes, and other blood-feeding arthropods. How can female monkeys avoid such parasites? Viewing arthropods as micropredators (see Chapter 1), one behavioral defense is to use predator-avoidance

Fig. 3.3 Mantled howling monkey from Costa Rica. Image courtesy of K. Glander, Duke University.

tactics, such as living in a group (Hamilton 1971; Janson 1992), to lessen the individual risk of being attacked by an arthropod (the "encounter-dilution" effect, Mooring and Hart 1992). Females in larger groups therefore can reduce risk from vector-borne diseases, but this strategy could come at the cost of increased prevalence of socially transmitted infections in these larger groups. At smaller spatial and temporal scales, females actively defend themselves by using specific arthropod-avoidance behaviors such as slapping at insects to shoo them away. But these behavioral defenses can be energetically costly (Dudley and Milton 1990) and might take away from time spent resting, foraging, or socializing. Thus, living in social groups and actively avoiding mobile arthropods represent key behavioral mechanisms used by primates to limit their risk of contracting a vector-borne disease, but these behaviors are themselves associated with energetic or opportunity costs and greater risk of acquiring other pathogens.

Finally, consider an adult female bonobo (*Pan paniscus*, Fig. 3.4). In many ways, bonobos are similar to chimpanzees (*P. troglodytes*), but bonobos display extremely promiscuous behavior (Wrangham 1993). A female bonobo typically mates with several males and may also rub genitals with other females in the community (Manson et al. 1997). The bonobos' promiscuous hetero- and homosexual behaviors should provide a highly efficient network for the spread of sexually transmitted diseases (STDs). Surprisingly little is known about STDs in bonobos (Van Brussel et al. 1998), but data are available on probable STDs in other apes (Eberle 1992; Verschoor et al. 1998; Gao et al. 1999; Santiago et al. 2002) and monkeys (Lockhart et al. 1996). Because the transmission of STDs should be tightly linked to host mating contacts, bonobos should harbor a variety of STDs that could play an important role in their reproductive success and conservation. Alternatively, the

Fig. 3.4 Bonobos grooming, with infant in background. Photographed by F. White, University of Oregon.

extreme promiscuity of bonobos might have followed from the evolution of effective behavioral and immune defenses in this host species, or other factors that caused the loss of STDs in wild bonobo populations.

These examples reveal some of the many links between parasite transmission and host behavior and ecology. Obviously even simple questions become complicated when the same activities—such as grooming or clustering in groups—lower the risk of certain parasite types but increase exposure to others. To make progress in identifying the links between parasites and primate socioecology, we need a conceptual framework that identifies the primary host traits that influence disease risk for parasites with different transmission modes. For example, lemur social groups probably serve as metapopulations for directly transmitted parasites, but what about parasites that use invertebrates as intermediate hosts or vectors, in which host population sub-structuring might pose less of a barrier to pathogen spread? In the example of howler monkeys, how are the benefits of living in a larger group to reduce risks of biting fly attacks balanced against the costs of acquiring infectious diseases spread through social contact? Do bonobos possess effective behavioral defenses to STDs, such as choosing healthy mates and post-copulatory genital grooming (Hart et al. 1987; Nunn 2003)? If so, do these behavioral defenses influence the characteristics of STDs, such as the expression of outward signs of infection (Knell 1999)?

A comprehensive framework for studying disease risk is needed to elucidate mechanisms underlying patterns of parasitism and to identify particular host defenses to infectious disease. To develop such a framework, we must first identify

Box 3.1 Chapter outline (specific hypotheses are summarized in Table 3.1)

Background concepts
- Encounter and infection probability (Section 3.2.1)
- Formulating hypotheses at individual and comparative levels (3.2.2)

Host traits and disease risk
- Body mass, life history, and individual age (3.3.1)
- Host population size and density (3.3.2)
- Social organization, group size, and dominance rank (3.3.3)
- Reproduction, mating behavior, and sex differences in parasitism (3.3.4)
- Ranging patterns, substrate use, and diet (3.3.5)
- Environmental factors and seasonality (3.3.6)

Synthesis and conclusions (3.4)

the combinations of host and parasite traits that impact disease risk. The goal of this chapter is to identify these traits, their interactions with parasite characteristics, and the evidence for each trait as influencing disease risk. Later chapters build on this framework with more sophisticated theoretical approaches. Because this chapter might be consulted at later stages, we provide an outline of the major classes of host traits examined in this chapter (Box 3.1) and a table that summarizes the key predictions (Table 3.1). Before moving on to consider these traits on a case-by-case basis, we review background concepts related to the occurrence of particular host–parasite combinations and the levels at which different traits may operate.

3.2 Background concepts

3.2.1 Encounter and infection probability

What factors explain variation in the diversity and types of parasites found in different primate species? The reproductive fitness of any parasite depends on its ability to successfully infect and replicate within an individual host and to disperse to other hosts. We can therefore think about whether or not parasites occur in a given host as depending on two major factors—encounter between hosts and parasites, and successful infection following encounter.

3.2.1.1 Encounter probability

The probability that a host encounters a parasite depends on whether hosts and parasites co-occur in space and time. Encounter rates therefore depend on habitat preferences of hosts and parasites, and on host density, social contact, diet, and habitat use. For example, Davies et al. (1991) proposed that differences in malaria infection rates among species of Amazonian primates were related to differences in

Table 3.1 Hypothesized host traits and ecological factors that affect disease risk in primates

Variable	Prediction	Evidence from primates
Body mass, life history, and individual age	Positive associations are expected between disease risk and body mass,[3] longevity,[3] and individual age.[1]	Positive effects of body mass on parasite diversity and prevalence have been found across species, but this pattern often disappears after controlling for phylogeny (Table 3.2 and Box 3.2). Comparative studies of longevity and individual age have produced mixed results (Table 3.2).
Population size	Larger population size facilitates parasite invasion, leading to increased parasite species richness and prevalence.[2,3]	Available evidence points to the importance of population size (especially for effects on parasite diversity), although few studies have investigated this variable directly while controlling for other host traits.
Population density	Parasite diversity and prevalence are expected to increase with population density.[2,3]	Cross-species data support this prediction for a variety of pathogens, but studies within species have produced fewer definitive results.
Group size	The presence of directly transmitted parasites should increase with group size, but could decrease at the population level if sub-structuring increases isolation among groups.[2,3]	Analysis of patterns within species provides evidence for this prediction, whereas results from cross-species studies are less conclusive. Mixed patterns are also found in the case of vector-borne diseases and mobile arthropods, possibly due to differences in vector behavior.
Social rank	Positive associations are expected between dominance rank and encounter with parasites, but predictions based on compatibility are less clear-cut (Table 3.3).[1]	Mixed (Table 3.4), possibly because multiple mechanisms impact the links between social dominance and exposure and susceptibility to parasites.
Reproductive status	Prevalence or intensity should increase during gestation and lactation and during the mating season for males and females.[1]	Available evidence fails to support this hypothesis in females: parasitism tends to be reduced during pregnancy and lactation. Few studies have investigated the effect of mating season.
Mating promiscuity	Increased promiscuity leads to increased STD prevalence and diversity.[1,3]	Supported in studies of white blood cell counts, and qualitatively based on primate species from which STDs have been reported (Table 3.5).
Sex differences	Prevalence in males is expected to be greater than in females,[1] possibly varying according to sex differences in stress and exposure to parasites.[2,3] STDs are an exception, with prevalence expected to be higher in females.[1]	Mixed results for non-STDs, but prevalence is higher among females for STDs (Table 3.6).

Range use	Larger ranging area should increase parasite species richness, but more intensive use of a home range may increase prevalence or intensity via opportunities for re-infection.[1,2,3]	Patterns vary according to the type of parasite examined.
Range overlap, dispersal, and territoriality	Parasite diversity is expected to increase with increasing range overlap, higher rates of dispersal, and the frequency of aggressive contacts during territorial behavior, particularly in species with well-developed canines.[1,2,3]	Results are inconclusive due to lack of study.
Geographic range size and overlap	Parasite richness should increase with geographic range size and greater overlap with other species (host sympatry).[3]	Geographic range size and sympatry emerge as predictors of parasite diversity in primates.
Terrestrial substrate use	Increased use of terrestrial substrates, or a mixture of terrestrial and arboreal substrates, could expose animals to more parasites.[1,2,3]	Explicit tests of these hypotheses have found no support in cross-species comparisons, but patterns may be found in tests focused on specific parasites that are found mainly on terrestrial substrates.
Diet	Parasite species richness, prevalence, and intensity are predicted to increase with greater insectivory, folivory, or omnivory, and with specific feeding and drinking behaviors.[1,2,3]	Little evidence for an effect of diet, although some analyses of folivory produced significant results. Tests of parasites within transmission modes are needed, especially involving intermediate hosts.
Environmental factors and seasonality of rainfall and temperature	Increased rainfall and warmer temperatures should increase parasite diversity, prevalence, and intensity, although rainfall may also wash away parasites.[2,3] Risk is expected to vary with seasonal changes in rainfall and temperature, but not always the same patterns for different parasite species.[1]	Conflicting results, but a general trend exists for wetter habitat or seasons to result in increased disease risk.

[1] operates at individual level. [2] operates across populations. [3] operates across species.

encounter rates with mosquitoes that carry *Plasmodium*. The authors found that larger-bodied monkeys living in larger aggregations exhibited higher prevalence of malaria, presumably by attracting more mosquitoes (Davies et al. 1991). Sleeping behaviors could also account for variation in malaria infections, with primates that sleep in enclosed tree-holes exhibiting lower prevalence than animals that sleep in the open (Heymann 1995; Nunn and Heymann 2005, see Chapter 5). As another example of differences in encounter probability, Müller-Graf et al. (1997) studied schistosome infections in baboons and found higher levels of infection in the troop with the greatest contact with humans. Thus, both host characteristics and environmental parameters can influence encounters with parasites, resulting in variation in disease risk within and across species.

3.2.1.2 Infection probability

Even when hosts and parasites come into contact, infection requires that the host is susceptible to the parasite in question, including compatibility between host and parasite genotypes, and that environmental conditions are conducive to infection (Combes 2000, 2001). Some novel host–parasite combinations can result in successful infection because naïve hosts present few immunological obstacles to "new" parasites, most likely due to historical lack of selection for host defenses to these parasites. In other cases, parasites might be unable to infect novel hosts because they lack the ability to adhere to or invade host membranes and cells, or because they fail to avoid host immune responses or other anti-parasite defenses (Mescas and Strass 1996; Finlay and Falcow 1997). The effectiveness of host immune defenses further depends on reproductive hormones, stress levels, age, and diet (Solomon 1969; Lloyd 1995; Sheldon and Verhulst 1996; Nunn 2002a). Hosts might also actively remove parasites following exposure using behavioral counterstrategies, such as grooming or ingestion of medicinal plants. Thus, a range of interactions at the level of individual hosts and parasites, many of which are addressed in detail in Chapter 5, will determine whether host–parasite encounters result in successful infections.

3.2.2 Formulating hypotheses at individual and comparative levels

Questions concerning disease risk can be addressed at two main levels. The first level involves patterns of disease risk among individual hosts (individual variation). Within a social group or population, why are some hosts more likely to be parasitized than others? The key issue involves individual traits, such as age, sex, or dominance rank that influence patterns of individual disease risk. The second level examines factors that generate variation in disease risk among populations or species (comparative patterns). Do ecological, life history, habitat, or social features of some populations or species increase the success of parasite establishment? This comparative approach is essential for understanding broad patterns of primate social evolution (Clutton-Brock and Harvey 1977; Lee 1999; Nunn and Barton 2001), and it also plays a vital role in identifying factors important for the conservation of threatened species (Purvis et al.

2000; Cardillo et al. 2004; Fisher and Owens 2004). In many cases, cross-species comparison requires that the investigator identify surrogate measures for the variables of interest, for example by using relative testes mass as a proxy for levels of mating promiscuity (Nunn et al. 2000; Nunn 2002a), based on previous comparative findings that testes are larger in species in which females have multiple mates (Harcourt et al. 1981, 1995). Comparing disease risk across species also requires information on primate phylogeny to account for the non-independence of species data points (Box 3.2; Harvey and Pagel 1991; Nunn and Barton 2001), and methods to control for the fact that some host species are well studied whereas others are poorly known (Gregory 1990; Walther et al. 1995; Nunn et al. 2003a).

3.3 Host traits and disease risk

In the sections that follow, factors that influence disease risk are organized into six broad categories: (1) host body mass, life history, and age, (2) population characteristics involving host density and population size, (3) social organization, group size, and individual differences in dominance rank, (4) reproduction and mating behavior, (5) diet and habitat use, and (6) environmental factors, including habitat characteristics and seasonality (see Box 3.1). Most hypotheses within each category are derived from theoretical models and empirical data. Although we organized the following discussion around host traits, it is also essential to remember that the influence of a particular host trait on disease risk depends on parasite characteristics, including transmission strategies. When appropriate, we address processes governing disease risk among individuals within species, as well as among species using a comparative approach. Table 3.1 provides an overview of the main variables and their predicted effects on disease risk; some details on the parasite transmission strategies that are relevant to that prediction are given in the table, with further details in the text. This table also provides a summary of support based on available evidence.

3.3.1 Body mass, life history, and individual age

Hosts have been described as "island habitats" for their parasites, with the rationale being that larger-bodied animals offer larger habitat patches that can support larger parasite populations, and they provide more niches for parasite colonization (Kuris et al. 1980; Poulin 1995; Gregory et al. 1996; Poulin and Morand 2004). Larger-bodied hosts have greater energy requirements and could therefore be exposed to more parasites through increased resource intake. Moreover, large animals represent more apparent targets for vectors that carry parasites, perhaps by emitting increased levels of chemical attractants (e.g. mosquitoes are attracted to humans with greater mass or surface area, Port et al. 1980; Davies et al. 1991).

It is now well established that primate life history traits show strong scaling relationships with body mass, so that larger bodied primates tend to live longer,

Box 3.2 Phylogenetic comparative methods and patterns of infection across species

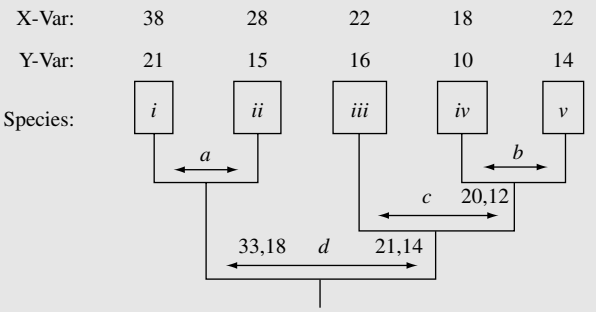
Comparative studies investigate broad patterns of evolution by using trait measures for different species in an analysis (Clutton-Brock and Harvey 1984). In primates, these studies might examine what factors best account for the number of males in primate groups (Andelman 1986; Mitani et al. 1996a; Nunn 1999), allometric scaling of behavioral and morphological characteristics (Martin et al. 1985; Nunn and Barton 2000; Smith and Cheverud 2002), or differences in life history traits across species (Harvey and Clutton-Brock 1985; Ross and Jones 1999). In recent years, comparative biologists have developed phylogeny-based methods to account for the fact that closely related species might not represent independent data points, and to control for variation shared through common descent (Felsenstein 1985; Harvey and Pagel 1991; Garland et al. 1992; Martins 1996). One commonly used method, based on "phylogenetically independent contrasts," is shown in the Figure 3.5. These methods provide a means to examine correlated evolutionary change in traits and therefore deal with the possibility that species data points are not independent of one another. Nunn and Barton (2001) review these methods in the context of comparative studies of primate adaptation and allometry.

Except in the case of purely vertically transmitted parasites, infectious diseases are probably not shared through common descent in the way that brain size, diet, or life history traits are shared. The question therefore arises as to whether controlling for host phylogeny is necessary when investigating comparative patterns of parasite richness, prevalence, and intensity of infection. In support of using these methods, a parasite community is to some extent a characteristic of a host species, and it can be maintained as a community over time through transmission among host individuals across overlapping generations. Moreover, the community itself and the prevalence of particular parasite species will be determined by a combination of host traits that are shared through descent, and environmental factors that are often more similar among closely related species. Finally, from a statistical perspective, if phylogenetic propinquity between two species is associated with more similar trait values, then data points in a comparative analysis will violate the statistical assumption of independence, regardless of the mechanisms that underlie similarity in trait values. Collectively, these factors suggest that cross-species comparisons of parasite richness and abundance will require methods to control for phylogeny.

Several researchers have revolutionized parasitology by incorporating host phylogeny into comparative tests of the factors that influence parasitism (e.g. Poulin 1995; Morand and Harvey 2000; Sorci et al. 2003), and this has been followed by comparative research in primates (Nunn et al. 2003a, 2004, 2005; Vitone et al. 2004). But a more nuanced view suggests that before incorporating host phylogeny, researchers should test whether measures of parasitism are in fact more similar among more closely related host species (i.e. whether they show "phylogenetic signal," Abouheif 1999; Freckleton et al. 2002; Blomberg et al. 2003). If traits are unassociated with phylogeny, some researchers advocate using standard statistical tests based on species values rather than phylogeny-based methods (Abouheif 1999). In comparative studies of primate parasites, we found evidence for phylogenetic signal in measures of parasite richness (after controlling for sampling effort, Nunn et al. 2003a) and prevalence (Nunn and Heymann 2005). Other analyses showed that white blood cell counts were more similar among closely related primates (Nunn 2002a).

Comparing phylogenetic and non-phylogenetic results can reveal the presence of confounding variables (Nunn and Barton 2000, 2001). For example, several analyses of primate parasite datasets showed that host body mass was a significant predictor of parasite species richness in non-phylogenetic tests, but this effect disappeared once phylogeny was taken into account (Nunn et al. 2003a; Vitone et al. 2004). Similar effects of phylogeny on analyses of body mass have been shown in other mammals and birds (Poulin 1995). These differences in phylogenetic and non-phylogenetic analyses raise the possibility of alternative

Box 3.2 (*cont.*)



	a	*b*	*c*	*d*
ΔX	10	4	2	12
ΔY	6	4	4	4

Fig. 3.5 Calculation of phylogenetically independent contrasts. Independent contrasts are calculated as differences between species values or higher nodes. In this diagram, species are indicated by Latin numbers and contrasts between species sets are labeled with lower case letters. The values of two traits to be compared are indicated by *X* and *Y*. In this example, a pair of contrasts can be calculated as the difference between species i and ii: $\Delta X = 38-28 = 10$, and $\Delta Y = 21-15 = 6$, with other contract calculated as shown. Ancestral states at higher nodes can be reconstructed, and contrasts calculated at these branching points as well. These contrasts are independent of one another and as species differences, they represent evolutionary change since two species last shared a common ancestor. Thus, a contrasts plot (such as Fig 3.6 and other figures in this volume) can be interpreted as evolutionary change in *X* in relation to evolutionary change in *Y*. See Nunn and Barton (2001) for further details.

explanations for patterns of parasite diversity (Nunn and Barton 2000, 2001). For example, body mass is a surrogate variable that covers a large number of potential mechanisms that might increase disease risk or parasite diversity, such as niches for parasite colonization and increased energy needs of large-bodied hosts (Nunn et al. 2003a). Greater body mass is also correlated with greater host defenses or immunity, with larger-bodied primates and carnivores exhibiting higher leukocyte counts (Nunn et al. 2000, 2003b; Nunn 2002a) and larger spleens (Nunn 2002b). Similarly, larger bodied species are often more dimorphic in body mass (Mitani et al. 1996b; Smith and Cheverud 2002), and competition among males might make these individuals more susceptible to parasites through the immunosuppressive effects of testosterone. And from an epidemiological view, body mass is correlated negatively with population density in mammals (Damuth 1981), even though both variables are usually hypothesized to be positively associated with parasitism, suggesting conflicting associations (see Nunn et al. 2003a for discussion of these and other issues). Thus, differences between phylogenetic and non-phylogenetic tests—when such differences exist—can often point to biologically relevant factors for investigation in future studies.

reproduce later in life, and have lower average birth rates (Harvey and Clutton-Brock 1985; Ross and Jones 1999). Among individuals, older individuals should harbor greater parasite diversity because they encounter more parasite species and are exposed to a larger number of infectious stages throughout their lifetimes (Pacala and Dobson 1988; Bell and Burt 1991). This principle is perhaps most obvious for STDs, where prevalence should be higher in sexually active adults than in younger, sexually naïve animals (Nunn and Altizer 2004). Mathematical models further predict that host life history traits should interact with key epidemiological processes because high host mortality will limit parasite establishment (Chapter 4 and Anderson and May 1979; Thrall et al. 1993a; De Leo and Dobson 1996; Altizer and Augustine 1997). Thus, across species, those taxa in which hosts have longer lifespans should encounter more parasites. These effects of age and life history mainly involve encounter probabilities, but age-related effects on infection probability can also be important. Thus, for many species, individual immune defenses are weakest at the beginning and end of life (Lloyd 1995), with the latter association possibly leading to increased parasite susceptibility among older animals or species with slower life histories (Morand and Harvey 2000).

Based on these considerations, a positive association should exist between measures of disease risk and body mass, and between disease risk and age or longevity, both at the individual and species levels (Table 3.1). Separating the correlated effects of age and body mass is challenging but crucial for explaining comparative and within-species patterns, as is controlling for other variables frequently correlated with these two variables, including dominance rank, sex, age at first reproduction, interbirth interval, population density, and habitat use. In what follows, we present evidence bearing on these predictions from primates and other mammals.

3.3.1.1 Body mass

In a phylogenetic comparative study of white blood cell counts in primates, body mass was positively correlated with neutrophil counts (Fig. 3.6), suggesting that larger-bodied species experience greater disease risk. In cross-species comparisons of primates and other mammals, body mass also correlated positively with parasite species richness and prevalence of infection, but mainly in tests that did not control for host phylogeny (Table 3.2). For example, in a cross-species comparative study of Amazonian primates, Davies et al. (1991) showed that malaria infection rates increased with (sleeping) group size and body mass, possibly because larger-bodied primates emit more cues used by mosquitoes to locate hosts. The effect of body mass on malaria prevalence became non-significant once phylogeny was taken into account, possibly because group size is a better estimate of the area over which a group is spread, as compared to mean body mass of individual hosts in that species (Nunn and Heymann 2005). Another recent study of mammals found that the

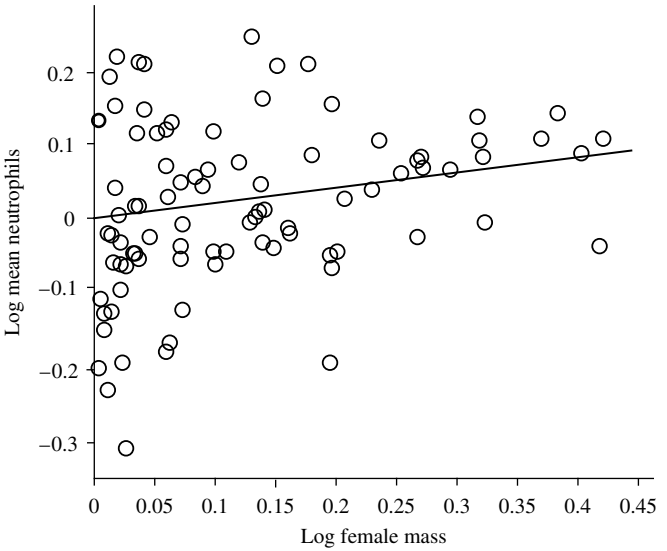


Fig. 3.6 Primate body mass and neutrophil counts. Plot shows phylogenetically independent contrasts, with data taken from Nunn (2002). Neutrophils are part of innate immunity as described in Section 5.2.1.1. The association between these two variables was statistically significant (see Nunn, 2002).

prevalence of infection increased with body mass, and that sex differences in prevalence were correlated with sexual dimorphism and male-biased mortality (Moore and Wilson 2002).

Within single host species, few field studies have focused directly on links between body mass and parasitism. In chacma baboons (*Papio ursinus*), Pettifer (1984) used body mass as a proxy variable for age and suggested that prevalence and intensity increased with age for several helminth species (Table 3.2). In non-primates, Halvorsen (1986) found that larger-bodied male reindeer were more likely to harbor intestinal parasites (results were non-significant for females). However, body mass was again used as a proxy variable for dominance rank, thus emphasizing the need to control for multiple, potentially confounding variables when testing predictions involving age and body mass.

3.3.1.2 Effects of age

Within host species, age effects on infection probability have been examined in a number of field studies (Table 3.2). In yellow baboons (*Papio cynocephalus*), for example, Hausfater and Watson (1976) found that adult males shed more eggs of intestinal parasites than subadult males, and another study of baboons found higher levels of schistosome infections in adult than immature animals (Miller 1960).

Table 3.2 Effects of body mass or age on parasitism

Host	Parasites examined	Effect of age or body mass	Reference
Across species (Neotropical primates)	*Plasmodium* (prevalence)	Body mass: positive association, but this result became non-significant after controlling for phylogeny.	Davies et al. 1991; Nunn and Heymann 2005
Across species (69 anthropoid primates)	Helminth species richness	Body mass: positive association, but this result became non-significant after controlling for phylogeny.	Vitone et al. 2004
Across species (101 anthropoid primates)	Total parasite species richness	Body mass and longevity: mass became non-significant in most tests when controlling for phylogeny, and longevity results were sensitive to inclusion of outliers.	Nunn et al. 2003a
Papio ursinus	Eight helminth species	Body mass: trends for parasite prevalence and abundance to increase with age for several parasites, but statistical tests were not provided.	Pettifer 1984
Papio cynocephalus	Intestinal parasites	Age: adult males shed more parasites than subadults.	Hausfater and Watson 1976
Alouatta seniculus	Nits and lice	Age: no significant differences among age classes in ectoparasite loads.	Sanchez-Villagra et al. 1998
Papio anubis	Lice nits	Age: nits were more likely to be found on immature animals.	Eley et al. 1989
Papio anubis	Five helminth species	Age: prevalence and intensity of infection with *Strongyloides* was greater in younger animals.	Müller-Graf et al. 1996
Papio anubis	*Schistosoma mansoni*	Age: marginally significant result indicating higher prevalence in younger animals.	Müller-Graf et al. 1997
Alouatta palliata	Intestinal parasites	Age: no prevalence differences among age classes except in the case of *Controrchis biliophilus*, which increased with age.	Stuart et al. 1998
Papio anubis	*Schistosoma mansoni*	Age: older males were more likely to be infected, but females showed no consistent age-related pattern.	Miller 1960
Cercopithecus ascanius	*Hepatocystis kochi*	Age: adults have higher prevalence than immatures (not tested statistically).	Haddow 1951
Papio cynocephalus and *Cercopithecus aethiops*	Intestinal parasites	Age: most parasites show a trend to increase with age, with opposite trend for the nematode *Strongyloides*.	Meade 1984
Theropithecus gelada	Larval stage of the cestode *Multiceps serialis* (possibly *Taenia/ Multiceps serialis*)	Age: prevalence in adults is an order of magnitude higher than in infants, juveniles, and subadults.	Ohsawa 1979; Dunbar 1980

All subadults in these populations probably were low ranking, potentially confounding the effect of age with that of dominance rank.

Other studies found no significant effect of age on disease risk, or even patterns opposite to predictions. For example, Sanchez-Villagra et al. (1998) found no age-related differences in ectoparasite loads in red howler monkeys, and a study of mantled howlers found no differences among age classes in infection with intestinal helminths (Stuart et al. 1998). Among baboons, younger animals showed greater prevalence and intensity of infection with both endoparasitic worms and ectoparasites. Thus, Eley et al. (1989) reported that juvenile baboons exhibited greater infestation with lice nits (eggs). For five classes of helminths analyzed in olive baboon feces at Gombe, only one parasite showed an association with age, with prevalence and intensity of the nematode *Strongyloides* found to be significantly higher in younger animals (Müller-Graf et al. 1996). In another study, the prevalence of *Schistosoma mansoni* was again higher in younger baboons, with results approaching significance ($p = 0.051$, Müller-Graf et al. 1997). The authors suggested that this pattern was probably caused by differences in encounters with parasites, as younger baboons contact water more frequently than adults. Meade (1984) found that rates of infection with *Strongyloides* were highest in baboon and vervet infants, possibly because this nematode is transmitted vertically to infants from their mothers, and partial immunity then develops and persists into adulthood.

Fewer comparative studies have examined associations between parasitism and life history traits across species of primates or other mammals. Among anthropoid primates, Nunn et al. (2003a) found a positive effect of host longevity (measured as maximum life expectancy) on the diversity of protozoan parasites, but these results were driven by several outliers. Arneberg (2002) found no effect of longevity in his study of 45 species of mammals. In a comparative study of 23 mammals, however, Morand and Harvey (2000) found a *negative* association between longevity and helminth species richness after controlling for basal metabolic rate, body mass, and sampling effort, suggesting that parasites could be an important factor that reduces host longevity.

3.3.2 Host population size and density

Jared Diamond, in his (1997) book *Guns, Germs and Steel*, highlighted three factors that "launched the crowd of infectious diseases" in human populations. These included a more sedentary lifestyle (resulting from agriculture), increased world trade, and perhaps most importantly, the growth of urban centers associated with densely packed human populations (see also McNeill 1977; Anderson and May 1991). Indeed, a large number of epidemiological models, supported by data from several empirical studies, point to strong links between host density or population size and the spread of directly transmitted parasites, not just in humans, but across a wide array of host species (Chapter 4 and Anderson and May 1979; Arneberg 2002; Swinton et al. 2002). A broad range of mathematical models suggest that total host abundance is probably the major factor affecting transmission between host individuals

for many parasite species (Anderson and May 1991). Total host abundance in this case refers to population size over an area where uniform contacts are likely to occur, and a key assumption in these models is that host populations are well-mixed, meaning that all individuals have an equal probability of contacting other individuals in the population—an assumption that is addressed in Chapter 4.

Hosts living at high density or with large populations and frequent intraspecific contacts should accumulate more parasite species (reviewed in Morand 2000; Roberts et al. 2002; Poulin and Morand 2004), but the predicted positive relationship between host abundance and pathogen fitness is subject to two caveats. First, this relationship probably applies best to directly-transmitted contagious parasites for which host contact rates increase with population size or density (Getz and Pickering 1983), and will be less important for vector-borne parasites and STDs where transmission is decoupled from host population density (Thrall et al. 1993a, 1998; Thrall and Antonovics 1997). An additional complicating factor involves identifying the natural unit or spatial scale at which population density or abundance affects disease transmission (Swinton et al. 2002). Thus, metapopulation models have shown that certain pathogens can persist even in low density host populations, provided that spatial heterogeneities and host dispersal generates sufficient opportunities for disease transmission (Hess 1996; Keeling 1999b).

3.3.2.1 Evidence for effects of population density or size

Few studies of disease risk within species of wild primates have examined the role of host population size directly. In a comparison of muriquis (*Brachyteles arachnoides*) in different habitats, Stuart et al. (1993) found that animals from the largest population exhibited the highest prevalence and species richness of intestinal parasites. The authors described their result as "unexpected" because this population also exhibited the lowest local density. However, this observed pattern highlights the importance of understanding the spatial scale at which host contacts and parasite transmission occur. In this case, total population size might have affected parasite establishment more so than local density. Other explanations are also possible, including the use of medicinal plants in the population with fewer parasites (Strier 1992, 1993).

Empirical studies of mammals have investigated the importance of local population density in explaining patterns of parasitism through time (Dobson and Meagher 1996b), across populations (Stuart et al. 1990; Stoner 1996), and across species (Arneberg et al. 1998). Several studies of primates attributed differences in levels of infection to variation in host population density. For example, Chapman et al. (2005a) found that prevalence of *Trichuris* increased with increasing host density in two species of colobines during population changes associated with logging. Similarly, Stuart et al. (1990) found higher prevalence of intestinal parasites in mantled howler monkeys at La Pacifica relative to less dense populations in Santa Rosa (both sites are in Costa Rica). On the other hand, a later study (Stoner 1996) compared prevalence at La Pacifica with a population of mantled howlers at La Selva,

Costa Rica, and found that prevalence was higher in the low-density population, with 100% of the individuals at La Selva harboring two or more parasite species based on fecal samples. These conclusions must be interpreted cautiously because comparison of only two populations makes it difficult to rule out the effects of other variables (e.g. McGrew et al. 1989a; Garland and Adolph 1994; Stuart and Strier 1995). For example, at La Selva, howler monkey populations probably experienced a moister environment, and other habitat variables might have contributed to differences between these populations (see Stoner 1996).

A comparative study also tested the importance of population density in explaining patterns of parasite species richness in anthropoid primates. In this study, Nunn et al. (2003a) controlled for other factors, including host life history, diet, and geographic range size. Population density emerged as the most consistent host trait that influenced overall parasite diversity (Fig. 3.7). Density also correlated positively with the diversity of viruses, protozoa, and helminths tested separately. In subsequent analyses, significant results were obtained when using an estimate of population size, measured as density multiplied by geographic range size. Studies by Arneberg and colleagues found similar relationships between population density and the diversity of helminths across a wider range of mammals (Arneberg et al. 1998, 2002).

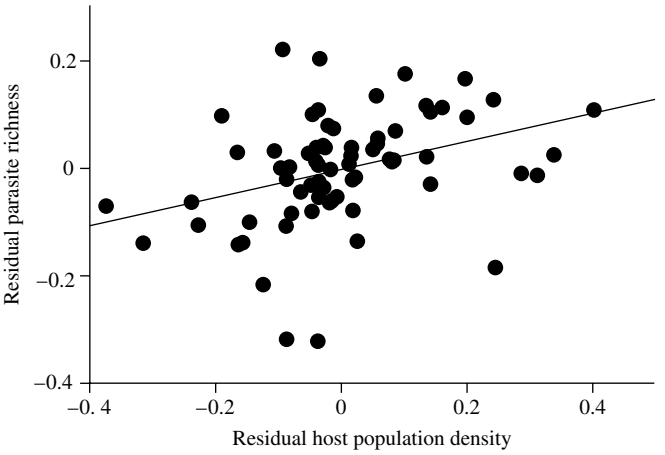


Fig. 3.7 Relationship between population density and overall parasite species richness in primates. Plots show the relationship between host population density (after controlling for body mass by taking residuals) and the size of the parasite community (after controlling for sampling effort by taking residuals). Similar results were obtained when sampling effort was controlled in three ways, with results here shown using Web of Science citation counts. Data points represent independent contrasts (as described in Box 3.2). From Nunn et al. 2003: Comparative tests of parasite species richness in primates. *American Naturalist* **162**:597–614. Copyright 2003 by The University of Chicago Press.

In their study of 23 non-primate mammals, however, Morand and Harvey (2000) found no effect of density on helminth species richness. Another study investigated the relative effects of population size and density in fish and found that total population size, but not density, explained species richness and abundance of directly transmitted parasites (Bagge et al. 2004). Future comparative research could investigate patterns among parasites grouped by transmission strategy, focusing especially on directly transmitted parasites, and could also use independently derived estimates of total population size to better assess the independent effects of density, geographic range size and overall population size on levels of parasitism.

3.3.3 Social organization, group size, and dominance rank

Social interactions form the network of contacts through which many parasites spread (Anderson and May 1979, 1991). If close proximity or contact among host individuals increases parasite transmission, then greater degrees of host sociality or gregariousness should translate to higher parasite prevalence, intensity, and diversity (Møller et al. 1993; Altizer et al. 2003b). Highly social host species are therefore predicted to suffer greater exposure to parasites (Brown and Brown 1986; Møller et al. 2001), experience increased selection for immune defenses, and evolve behavioral defenses against parasites (Chapter 5, 6, and Freeland 1979; Loehle 1995). Population density is the key socioecological variable incorporated into standard epidemiological models (Chapter 4 and Anderson and May 1979), but group size is a major component of social organization that is widely viewed as increasing disease risk in primates (Freeland 1976; Davies et al. 1991; Tutin 2000) and other animals (see Møller et al. 1993; Côté and Poulin 1995; Krause and Ruxton 2002). More recently, however, it has been proposed that by subdividing populations into smaller groups, social organization could actually reduce disease risk. We examine these alternative scenarios and then review empirical evidence for effects of group size on disease risk in primates.

Several processes indicate that group size should *increase* with the risk of infection by directly transmitted parasites. First, group size represents a measure of local population density, specifically the density of hosts in their typical social environments. Second, the number of contacts among hosts may be greater in larger groups, for example through sharing of food or grooming interactions (Dunbar 1991). Third, social groups represent natural habitat patches for parasites, linked through dispersal events, which diminishes the importance of overall population size for disease spread relative to local group size (McCallum and Dobson 2002). Finally, the size and composition of social groups affect other aspects of social systems, such as mating system and the existence of dominance hierarchies (Kappeler and van Schaik 2002).

In contrast to the usual prediction that group size correlates positively with disease risk, several authors have argued that sociality should *reduce* the risk of acquiring

directly transmitted parasites (Watve and Jog 1997; Wilson et al. 2003). These conclusions are based on theoretical models showing that increased clustering reduces disease risk if dispersal among groups is low (Fig. 3.8). As individuals become more tightly clumped into relatively permanent groups, infections could be effectively "quarantined" into patches, and parasites are therefore less likely to establish in these structured metapopulations (Hess 1996). However, although population sub-structuring could reduce the spread of disease at the population level, as compared to panmictic mixing, once clumping occurs disease risk might still be expected to increase in larger groups.

Finally, vector-borne diseases could be *positively or negatively* influenced by group size, with effects depending on vector behavior and biology. Thus, mobile parasites that actively search for hosts, such as flying arthropods, could be preferentially attracted to larger groups, perhaps through greater emission of cues used by arthropods to locate hosts (Davies et al. 1991; Nunn and Heymann 2005). Alternatively, living in a larger group could help animals avoid flying vectors; if the probability of locating a group does not increase proportionally with group size or lead to higher biting rates by individual insects, individual infection risk should be lower in larger groups. Mooring and Hart (1992) refer to this process as the

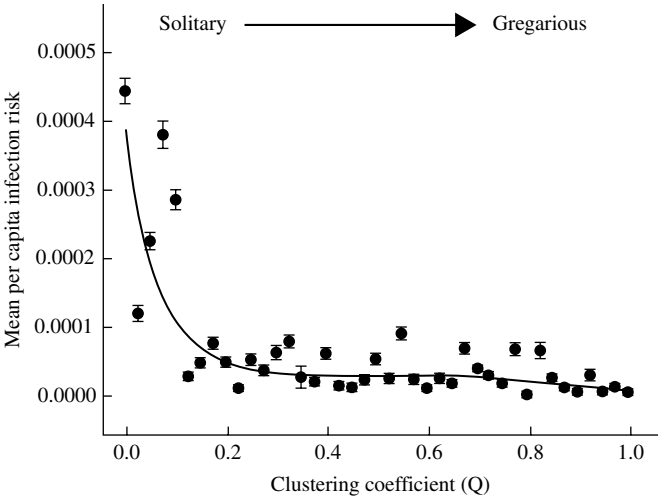


Fig. 3.8 Host clustering and sociality may reduce disease risk by subdividing the population and reducing parasite spread. This plot, from Wilson et al. 2003, shows how increased clustering (Q) decreases per capita infection risk in a simulation study. At $Q = 0$, reproduction occurs at random to any site within the population, and at $Q = 1$, all reproduction is local, which is equivalent to a highly structured host population in which individuals live in permanent groups. Line represents the best-fit exponential function. From Wilson, K., R. Knell, M. Boots, and J. Koch-Osborne (2003). Group living and investment in immune defence: An interspecific analysis. *Journal of Animal Ecology*, 72, 133–143. Permission granted by Blackwell publishing.

encounter-dilution effect, suggesting that feeding characteristics of flying insects can exert different effects on the grouping behavior of animals. Thus, host grouping could reduce attacks by blood-sucking flies because such micro-predators typically are satiated after one or two blood meals, whereas warble flies can deposit eggs on multiple animals, with grouping providing fewer benefits to individual hosts (Mooring and Hart 1992; Hart 1994).

In summary, a variety of mechanisms are likely to play a role in generating correlations between group size and disease risk, with contact among individuals, contact among groups, parasite transmission mode, and vector behavior paramount among these factors.

3.3.3.1 Empirical evidence for an effect of group size: contagious parasites

Empirical tests of the link between group size and infection with directly transmitted parasites have produced mixed results (Krause and Ruxton 2002). Multiple field studies of mammals support this hypothesis (Kunz 1976; Freeland 1979; Hoogland 1979; Wilkinson 1985; Brown and Brown 1986; Shields and Crook 1987; Hoogland 1995). On the other hand, some field studies of non-primate mammals failed to find a significant association between group size and parasite risk (e.g. Arnold and Lichtenstein 1993), and probably many other non-significant results remain unpublished. In an attempt to synthesize the results of many field tests, a study spanning insects, birds, and mammals showed that links between group size and parasitism depend on parasite transmission mode (Côté and Poulin 1995). The authors classified parasites into two categories: those spread directly from host-to-host or through intervening substrates (contagious parasites), and parasites that actively search for hosts in water or air (mobile parasites). Using meta-analysis techniques, Côté and Poulin (1995) found a positive association between group size and parasitism for contagious parasites.

Several field studies of primates have tested for an effect of group size on patterns of parasitism. In a classic study, Freeland (1979) found an association between group size and the number of intestinal protozoan species in mangabeys (*Cercocebus albigena*) at Kibale. Similarly, McGrew et al. (1989a) found a positive trend between nematode infections and group size in baboons at Gombe ($n = 3$ groups). However, comparative studies in primates have so far revealed few links between social group size and disease risk. Examples include tests of parasite species richness using data on protozoa, helminths, and viruses (Nunn et al. 2003a), and studies of immune system parameters involving relative spleen size (Nunn 2002b) and white blood cell counts (Nunn et al. 2000; Nunn 2002a; Semple et al. 2002). Two studies of helminth species richness in anthropoid primates showed limited support for an effect of group size in primates, but these results became non-significant once phylogeny was taken into account (Nunn et al. 2003a; Vitone et al. 2004). Research on parasite richness in primates has generally focused on taxonomic groups of parasites without regard to transmission mode; thus, future studies should investigate patterns of species richness and prevalence more directly within transmission mode categories, particularly among socially transmitted parasites.

3.3.3.2 Empirical evidence for an effect of group size: vector-borne parasites

In their meta-analysis, Côté and Poulin (1995) found that the intensity of infection with mobile parasites, such as biting flies, showed a negative association with host group size, indicating that animals can lower their individual risk of infection by living in larger groups (e.g. Rutberg 1987; Ralley et al. 1993). Analyses of primate vectors and vector-borne diseases have produced some different patterns. Thus, in a comparative study of 25 species of New World primates, Davies et al. (1991) found that malaria prevalence increased with group size. This result was confirmed in a phylogenetic comparative study based on an updated dataset with the same clade of primates (Nunn and Heymann 2005; Fig. 3.9). Because arthropod vectors spread malaria, these results contradict predictions that group size reduces prevalence and individual infection risk from mobile parasites, possibly because larger groups attract more flying insects.

In contrast, Freeland (1977) argued that the risk of mosquito attacks best explained the timing of polyspecific associations in primates at Kibale, to the exclusion of alternative explanations involving predation and activity levels (see Fig. 1.3). To measure rates of biting fly attacks, Freeland (1977) used data on mosquito activity at Kibale and another field site in Uganda. He found that the hourly occurrence of polyspecific associations correlated positively with mosquito activity levels (see Fig. 1.3), but polyspecific associations were unrelated to rates of eagle attacks (although the sample size of predator attacks was small, with only 18 observed attempts over a nine-month period). The idea that associations among multiple host

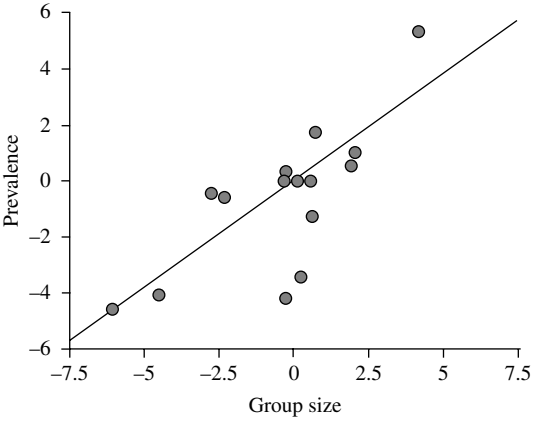


Fig. 3.9 Malaria prevalence in Neotropical primates in relation to group size. Plots show phylogenetically independent contrasts. Evolutionary transitions in group size are positively correlated with transitions in malaria prevalence ($t = 4.25$, $p < 0.001$). Results remained significant when using two different phylogenies and three sets of branch lengths, and when transitions to sleeping in closed microhabitats were excluded (see Chapter 5). Data from Nunn and Heymann (2005).

species can lower the risk of infection from vector-borne diseases is consistent with the outcome of one recent modeling study that showed how vulnerable hosts might be protected from pathogen-driven extinction by the presence of alternative host species (Rudolf and Antonovics 2005). Surprisingly, however, Freeland's conclusions have not been investigated in follow-up studies, and most researchers have focused on other ecological factors as drivers of polyspecific associations, such as foraging or predation benefits (Waser 1987).

3.3.3.3 Social status and individual disease risk

Among individuals, variation in social rank could influence patterns of parasitism. In terms of encounter probabilities, higher status or rank might come at the cost of greater parasitism, as dominant individuals often experience increased mating opportunities and more frequent aggressive interactions. Similarly, socially dominant hosts that forage without restriction could ingest more parasites, just as dominant males that mate with a greater number of partners should be exposed to more STDs (see Chapter 5; Graves and Duvall 1995; Thrall et al. 2000). Thus, in general we expect that encounter probabilities will lead to higher infection rates in more dominant individuals. One possible exception could occur when lower-ranking hosts are forced to use lower quality habitats that might contain more parasites.

Infection probabilities following encounters with parasites produce less clear-cut predictions (Table 3.3). In some cases, more dominant males may suffer to a greater extent from the immunosuppressive effects of testosterone and other hormones, especially in unstable dominance hierarchies (Folstad and Karter 1992; Dixson 1998; Bercovitch and Ziegler 2002). Alternatively, stress in low ranking animals could increase disease risk through modulation of immune defenses (Lloyd 1995; Cohen 1999). Stressful effects of hormones, such as cortisol, may depend on dominance rank and opportunities for kin support (Abbott et al. 2003). Finally, higher dominance rank could improve access to resources that boost overall condition and immunocompetence, leading to better anti-parasite defenses among higher-ranking individuals and therefore lower prevalence of infection.

Thus, as summarized in Table 3.3, higher-ranking individuals should be exposed to a greater number and diversity of parasites, and following exposure, infection probability could augment or offset the encounter probability. Consistent with these diverse expectations, conflicting or ambiguous empirical patterns have been documented in primates (Table 3.4). In their study of yellow baboons, for example, Hausfater and Watson (1976) found that higher-ranking animals expressed increased output of helminth eggs, with the effect more pronounced in males than in females. This result was supported in a later study of the same population using larger sample sizes (Meade 1984). More recent studies of olive baboons, however, found no association between social rank and measures of intestinal helminth infection (Müller-Graf et al. 1996b). Other studies showed that lower-ranking individuals experienced increased disease risk, measured as parasite intensity and impacts on host fitness, including an experimental study of male long-tailed macaques

Table 3.3 Dominance rank and disease risk: roles of encounter and infection probabilities

Variable or effect	Association between higher rank and parasitism
Encounter probability: socially dominant individuals are expected to contact more parasites through better access to food, water, and other resources.	Positive
Encounter probability: dominant individuals may experience increased social and mating contact and therefore are more likely to be exposed to parasites.	Positive
Infection probability: dominant individuals may experience immunosuppressive effects of testosterone and stress.	Positive
Infection probability: improved access to resources may strengthen immune function.	Negative

Table 3.4 Social status and parasitism in primates

Host	Parasite(s)	Rank class with greater parasitism	Notes	Reference
Papio cynocephalus	Two nematode genera	High	Higher-ranking individuals shed more eggs, with effects more pronounced in males than females.	Hausfater and Watson 1976; Meade 1984
Papio anubis	Six groups of helminths	No effect	No association for multiple measures of parasitism, and in males and females.	Müller-Graf et al. 1996
Cercopithecus aethiops	Unknown	Low	Lower-ranking individuals were more likely to die from exposure to infectious disease.	Cheney et al. 1988
Papio anubis	Lice nits, possibly *Pedicinus hamadryas*	Low	Among adults, nits were found more often on females from low-ranking families.	Eley et al. 1989

(*Macaca fascicularis*) Cohen et al. 1997; Cohen 1999). In the wild, Cheney et al. (1988) found that parasites have a more devastating effect on lower-ranking vervet monkeys (*Cercopithecus aethiops*). Similarly, lice nits were found more commonly on female olive baboons from lower-ranking families (Eley et al. 1989).

An interesting complication is that parasitism could influence social dominance (rather than vice versa), so that heavily parasitized hosts should also be less able to achieve high dominance rank. Such an effect was suggested for the debilitating effects of cestode infections in geladas (*Theropithcus gelada*) (Ohsawa 1979). Discerning the direction of cause-and-effect for parasitism and social rank requires experimental manipulations to demonstrate costs of parasitism in terms of failure to achieve high rank. Thus, Freeland (1981b) found that male mice experimentally infected with the nematode *Heligmosomoides polygyrus* failed to become dominant, but only at the highest inoculation levels (250 larvae per host). Similar results were obtained in an independent experiment using the nematode *Trichinella spiralis* (Rau 1983).

In summary, the uncertain association between social rank and disease risk in primates probably reflects multiple mechanisms by which social dominance affects exposure and susceptibility to parasites, combined with the fact that we lack a firm understanding of how parasitism could influence dominance rank itself. Future studies that attempt to separate the effects of encounter and infection probabilities, as well as measures of host stress, are needed to reconcile the diverse results in Table 3.4.

3.3.4 Reproduction, mating behavior, and sex differences

3.3.4.1 Reproductive status and breeding effort

Reproduction is a costly activity, and breeding season stress could reduce immune system responsiveness, particularly when resources are limited (Sheldon and Verhulst 1996; Klein and Nelson 1999). Increased reproductive effort in several bird species has been shown to correlate with higher parasite burdens and lower antibody production and cell-mediated immunity (Hillgarth and Wingfield 1997; Duckworth et al. 2001; Moreno et al. 2001; Møller and Petrie 2002). In primates, males might experience stress from testosterone and mating displays, and among primate species without male parental care, females could exhibit breeding season stress from pregnancy, lactation, and energy devoted to offspring care. Thus, Festa-Bianchet (1989) showed that lactating bighorn sheep (*Ovis canadensis*) had higher levels of lungworm infection than non-lactating ewes (see also O'Sullivan and Donald 1970). Ewes that raised sons, which are probably more costly to produce than daughters due to extreme sexual dimorphism, had higher levels of infection than those raising daughters (Festa-Bianchet 1989). Pregnant females might also be at greater risk of acquiring parasites during the period of parturition, as mammals have been shown to lower their own immunity during gestation and birth (Lloyd 1983). This probably reduces harm to the fetus, but could also increase the susceptibility of females to infection during or immediately following pregnancy (Cattadori et al. 2005).

Few studies have examined parasitism relative to host reproductive activity in primates, but the limited evidence fails to support the prediction that parasite risk increases during gestation or lactation. Yellow baboon females at Amboseli that

were lactating or not cycling (and thus possibly pregnant) shed fewer worm eggs than females showing estrous cycles (Hausfater and Watson 1976), although a later study found higher parasite levels among pregnant females in the same population (Meade 1984). Similarly, Müller-Graf et al. (1996, 1997) found that reproductive status was unrelated to the prevalence of intestinal parasites and schistosome infections in female baboons at Gombe, although lactating females showed higher intensity of infection with *Trichuris* sp. Interestingly, pregnant females exhibited the lowest level of infection. Among female howler monkeys, those with dependent offspring had fewer botfly larvae than females without infants, at least toward the end of the dry season (Smith 1977). Patterns that are opposite to predictions might be caused by greater investment in behavioral and immune defenses among reproductive females, or by negative effects of infection on female reproduction. Further field and experimental research on parasite risk among lactating and cycling females could shed more light on these questions, and on the more general effect of mating season on patterns of parasitism.

3.3.4.2 Mating promiscuity

Sexual contact provides an effective means for parasite transmission, as revealed by the remarkable diversity of STDs in humans (Holmes et al. 1999). Risks of acquiring STDs should be higher in animals with promiscuous mating systems (Loehle 1995; Lockhart et al. 1996; Heymann 1999; Nunn et al. 2000) or in populations with higher variance in male mating success (i.e. mating skew; Thrall et al. 2000). The latter effect arises because a few individuals with large numbers of mating partners can serve as loci ("super-spreaders") for infections to spread through populations (see Chapter 4 and Anderson 1999). Finally, STDs may be more common relative to other infectious diseases in species living solitarily at low density, as mating is one of the few times in which social contact occurs (Smith and Dobson 1992; Thrall et al. 1998).

Is STD risk greater in species characterized by promiscuous mating contact? Although more than 20% of primate species have been classified as monogamous (C. Nunn, unpublished comparative database), the vast majority of reported STDs have been documented in non-monogamous primate species (Table 3.5 and Nunn and Altizer 2004). However, this apparent pattern could also reflect sampling bias if researchers tend to search for STDs in more promiscuous primate species.

Nunn and colleagues (2000, 2002a) conducted comparative tests across a diverse assemblage of primates to assess whether baseline leukocyte counts were associated with mating promiscuity. Consistent with predictions, primate lineages characterized as being more promiscuous exhibited higher leukocyte counts in phylogenetic comparative tests (see Fig. 1.2). These results were upheld when using different measures of promiscuity, after controlling for additional variables, and when limiting the analysis to adult females or males only. More recently, a similar pattern was obtained using an independent dataset on primate leukocyte counts (Anderson et al. 2004) and in an analysis of carnivores (Nunn et al. 2003b). In Chapter 5, we consider the mechanisms that might underlie this pattern.

Table 3.5 Sexually transmitted parasites documented in wild primates

Genus[1]	Parasite(s) exhibiting probable sexual transmission[2]	Mating system
Alouatta palliata	STLV	Polygynandrous
Ateles fusciceps	STLV	Polygynandrous
Callithrix jacchus	*Brucella arbortus*	Variable: Polyandrous, Polygynous, Monogamous
Cebus capucinus	STLV	Polygynous or Polyandrous
Cercocebus (3)	SIV, STLV	Polygynandrous
Cercopithecus (10)	SIV, STLV, SFV Papillomavirus	Polygynandrous or Polygynous
Colobus guereza	SIV, STLV	Polygynandrous or Polygynous
Erythrocebus patas	SIV, STLV	Generally Polygynous
Gorilla gorilla	STLV, Alphaherpesvirus	Polygynous
Hylobates (1–2)	STLV, Hepatitis B	Monogamous
Macaca (10+)	STLV, Herpes B	Polygynandrous
Mandrillus (2)	SIV, STLV	Polygynandrous or Polygynous
Miopithecus talapoin	SIV, STLV	Polygynandrous
Pan troglodytes	SIV, STLV, SFV, Hepatitis B, Papillomavirus, Ebola	Polygynandrous
Papio (2+)	SIV, STLV, *Mycoplasma, Brucella*, Herpes, Papillomavirus, Cytomegalovirus	Polygynandrous
Pongo pygmaeus	STLV, Hepatitis B	Polygynandrous/Dispersed
Presbytis (2)	STLV	Polygynous or Polygynandrous
Procolobus verus	SIV	Polygynandrous
Theropithecus gelada	STLV	Polygynandrous/Polygynous

[1] Numbers after genera indicate number of species in which one or more of the parasites listed has been documented. Data from the *Global Mammal Parasite Database* (Nunn and Altizer 2005).

[2] Most studies have not tested experimentally for sexual transmission. Parasites were coded as having a sexual component to their transmission based on the known biology of the pathogen, data from captive studies, or information from closely related host species (as described in Pedersen et al. 2005). It is important to note that many primate viruses recorded as sexually transmitted could also spread by other routes, including close non-sexual contact and vertical transmission.

In addition to mating promiscuity, other behavioral and morphological traits probably influence STD risk in primates. Species with complex genitalia, especially the "spines" found on the penises of some species (Fig. 3.10), could damage the genitalia of mating partners, thus increasing risk of disease transmission. The duration of intromission during mating obviously influences the duration of genital contact, with a longer period of copulation increasing the probability of STD transfer. Remarkable variation in the duration of intromission exists in primates (Dixson 1998; Dixson and Anderson 2004). Chimpanzees exhibit extremely short copulations, lasting on an average only 7 s and involving only 8.8 pelvic thrusts (Tutin and McGinnis 1981). By comparison, orangutans have been reported to copulate for over 45 min (Nadler 1977), and lesser galagos (*Galago moholi*) were observed to mount for up to 53 min (Pullen et al. 2000). STD risk might also be greater in primate species that have multiple

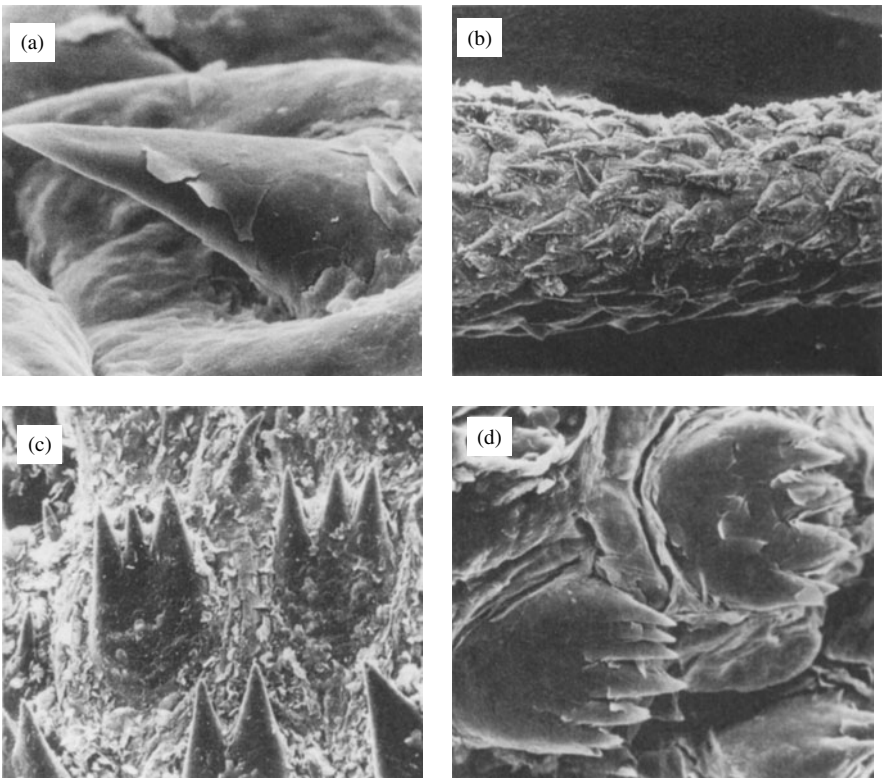


Fig. 3.10 Examples of penile spines found in primates. Images show scanning electron micrographs from (a) *Callithrix jacchus*, (b) *Galagoids demidoff*, (c) *Galago (Otolemur) garnetti*, and (d) *Microcebus murinus*. See Dixson (1998) for further details on morphological classifications of these spines in primates. Images provided by A. Dixson, Conservation and Research for Endangered Species at the Zoological Society of San Diego.

intromissions prior to ejaculation (Dewsbury and Pierce 1989; Dixson 1998), because this could increase the risk of micro-injury (abrasions, cuts) to the genitals and the total contact time for each copulation. Finally aggressive interactions among males that are competing for access to females could lead to the spread of disease (Tutin 2000).

3.3.4.3 Sex differences in disease risk

Three main factors can cause patterns of infection to differ between males and females (Zuk and McKean 1996; Combes 2001). First, body size dimorphism should require that males consume more resources, thus exposing them to more infectious stages of parasites. Their larger nutritional requirements could also make males more susceptible to infections (Barrett and Henzi 1998). Second, males and females are likely to differ in their exposure to directly transmitted parasites due to sex differences in social relationships, variation in access to mates, and differences in diet or habitat (Meade 1984; Nunn and Altizer 2004). Finally, sex differences in hormones could account for

differences in parasitism, including effects of pregnancy on immune defenses (Solomon 1969; Alexander and Stimson 1988), or through the immunosuppressive effects of testosterone in males (Folstad and Karter 1992; Zuk and McKean 1996).

Studies covering a wide range of host species have demonstrated a sex difference in parasitism, with most studies finding higher prevalence or intensity of infection among males (Zuk and McKean 1996; Combes 2001). A recent comparative study by Moore and Wilson (2002) showed that across mammals (including data from four primate species), males exhibited higher prevalence than females (Fig. 3.11). On the other hand, studies focusing on ectoparasites and intestinal helminths in wild primates have failed to show consistent sex differences in prevalence (Table 3.6). Among primate studies that documented a significant sex difference, some authors

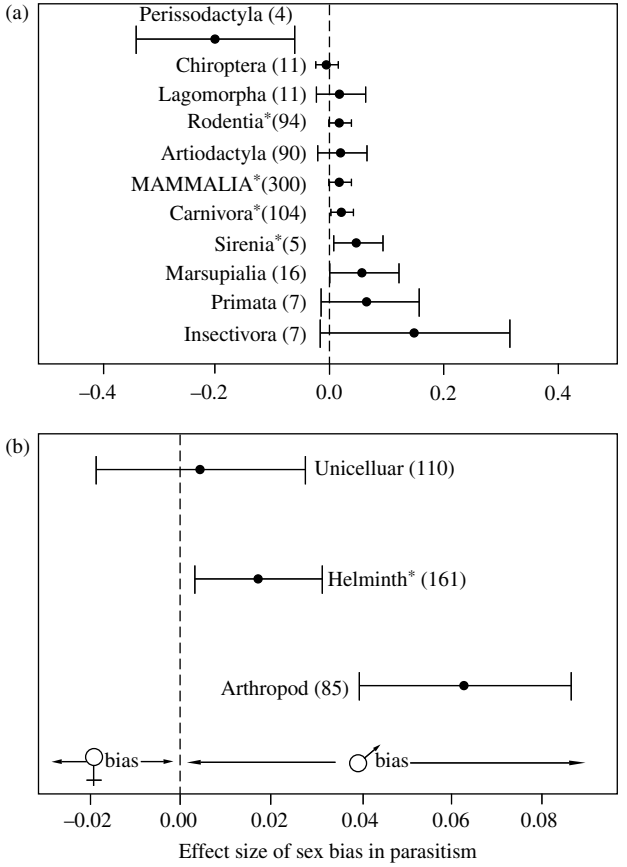


Fig. 3.11 Sex bias in parasitism in relation to (A) mammalian host orders and (B) parasite taxa. Plots show effect sizes and 95% confidence intervals. An asterisk denotes statistical significance at the 5% level, and numbers in parentheses indicate the number of studies. Reprinted with permission from S. L. Moore and K. Wilson, Science 297, pp. 2015–2018. Copyright (2002) AAAS.

Table 3.6. Parasitism in relation to sex

Host	Parasite(s)	Sex bias	Notes	Reference
Papio cynocephalus	Two nematode genera, *Trichuris* and *Trichostrongylus*	F	Higher abundance of eggs	Hausfater and Watson 1976
Alouatta palliata	Howler bot fly (*Alouattamyia baeri*)	—	Examined both prevalence and intensity	Milton 1996
Alouatta seniculus	Unknown epidemic	F	Females reported to be more affected by epidemic than males†	Pope 1998
Papio anubis	Multiple helminths and protozoa	F	Higher intensity of *Streptopharagus* sp. infections	Müller-Graf et al. 1996
Papio anubis	*Schistosoma mansoni*	M	Higher intensity of infection and trend for prevalence*	Müller-Graf et al. 1997
Alouatta seniculus	Nits and lice	—	No sex difference in ectoparasite loads†	Sanchez-Villagra et al. 1998
Alouatta palliata	Intestinal parasites	—	No sex differences in prevalence	Stuart et al. 1990; Stuart et al. 1998
Alouatta palliata	Nematode and trematode eggs	—	No sex differences in prevalence or intensity of infection	Stoner 1993, 1996
Papio ursinus	Eight helminths identified to level species	M	Higher prevelance of *Physaloptera caucasica*†	Pettifer 1984
Alouatta palliata	*Dermatobia hominis*	—	No sex differences†	Smith 1977
Papio cynocephalus	Eight intestinal parasites	—	No significant differences	Meade 1984
Macaca fuscata	Multiple	M	Males were more likely to die from infectious diseases; semi-free-ranging population	Fedigan and Zohar 1997
Comparative study of STDs	SIV and STLV	F	Prevalence significantly higher in females	Nunn and Altizer 2004

†: statistical results not provided
*: Müller-Graf et al. (1997) used a significance level of $\alpha = 0.01$, with $p = 0.041$ for sex differences in intensity of infection with *Schistosoma mansoni*. The p-value for sex differences in prevalence was 0.081.

reported higher prevalence in females (e.g. Hausfater and Watson 1976; Pope 1998), whereas others reported higher prevalence in males (Müller-Graf et al. 1997). At least one study of primates provided evidence supporting the importance of encounter with parasites in the environment. In this study, Müller-Graf (1997) found that males more frequently contacted water containing infectious stages of *Schistosoma mansoni*, resulting in higher prevalence of this parasite among males

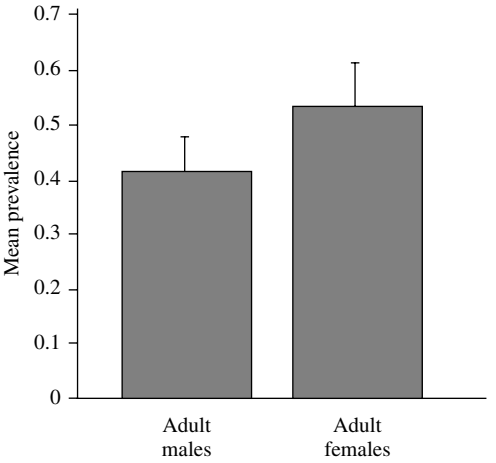


Fig. 3.12 Sex differences in the prevalence of STDs. Bars represent mean prevalence of STDs in males and females, +1 SE, based on 19 estimates of STD prevalence in adults from 8 Old World primates. The difference in prevalence was statistically significant (matched pairs test, $t_{18} = 2.49$, $P = 011$, one-tailed). From Nunn and Altizer (2004), printed with permission of Cambridge University Press.

than females. In another study, Pettifer (1984) suggested that physiological differences between the sexes accounted for a higher prevalence of *Physaloptera caucasica* in males, although the author also noted that it could be due to sex differences in consumption of the arthropod intermediate hosts. In terms of STDs, a recent comparative test showed that prevalence was higher among females (Fig. 3.12, Nunn and Altizer 2004), as predicted by individual-based models showing increased biases in prevalence toward females as sexual selection increases (Thrall et al. 2000).

Thus, few consistent patterns in relation to sex have been documented in primates (Table 3.6, see also Solomon 1969), potentially because multiple factors operate in different directions. Comparative approaches are likely to offer the strongest tests of the factors that influence patterns of parasitism among the sexes (Moore and Wilson 2002), but to obtain sufficient sample sizes, such tests will require additional field studies that collect parasite data from individually recognizable males and females (e.g. Müller-Graf et al. 1996, 1997). Future studies should investigate additional host and parasite traits that drive patterns in unexpected directions. Encounter probabilities in particular are under-explored. For example, if females are more likely to seek protein by consuming insects, while larger-bodied males eat leaves, this could increase female exposure to parasites transmitted via intermediate hosts.

3.3.5 Ranging behavior, substrate use, and diet

3.3.5.1 Range use

Animals that inhabit larger areas, utilize a greater variety of habitats, or travel longer distances per day should encounter a greater variety of parasite species (Mohr and

Stumpf 1964; Nunn et al. 2003a). Alternatively, animals restricted to smaller areas could experience continual re-infection with parasites that accumulate in the habitat, particularly infectious stages of intestinal parasites that are shed in feces (Freeland 1976, 1980; Hausfater and Meade 1982; Stoner 1996). Thus, hosts with wide geographic ranges should harbor a greater diversity of many types of parasites, whereas hosts that defend a stable home range should experience more intense infections by parasites that accumulate in the environment (Freeland 1976).

Primate field researchers typically report three measures of ranging behavior: home range size, day journey length, and a variable derived from these two measures known as the "defensibility index" or D-index (Mitani and Rodman 1979). Home range size refers to the area covered by a group of primates, usually throughout the year. Within this range, a smaller area might actually be defended (Cheney 1987). Day journey length refers to the distance that a group (or individual) travels in a day, based on following the animals throughout their active period. Finally, the D-index measures the intensity of range use and is calculated by examining day journey length relative to the size of the home range, based on the assumption of a circular home range. Mitani and Rodman (1979) found that the D-index correlated positively with qualitative measures of territoriality across species of primates (see also Lowen and Dunbar 1994), indicating that animals were more likely to defend areas that are regularly utilized. The probability of re-infection with parasite infectious stages that build up and persist in the environment should correlate positively with this measure of range use intensity.

Few field or comparative studies of primates examined the effect of range use on parasitism. In their comparative studies of parasite species richness in primates, Nunn et al. (2003a) found that day range length correlated positively with the number of virus species reported in different primate hosts. Counter to predictions, however, a negative association between home range size and parasite species richness arose for some analyses (C. Nunn, unpublished data) and the D-index was positively correlated with helminth species richness (Nunn and Dokey, in review). Even fewer studies examined patterns within species, although a study of California meadow mice (*Microtus californicus*) found that mice with larger home ranges harbored more intense chigger infections (Mohr and Stumpf 1964).

Finally, use of specific parts of a home range could affect disease risk. Hausfater and Meade (1982) proposed that a troop of baboons at Amboseli altered their use of sleeping groves in response to infectious stages of parasites that accumulate in the soil below sleeping trees. Similarly, animals might modify ranging behavior to avoid fetid water sources, fecal contaminated soil, or other habitats that expose them to parasites (see Chapter 5).

3.3.5.2 Range overlap, territoriality, and dispersal

Increased contact between social groups should improve the ability of parasites to spread and establish in primate populations (Freeland 1976, 1979; Loehle 1995; Watve and Jog 1997; Wilson et al. 2003). Between-group contact might occur indirectly when group ranges coincide, as this provides a means for parasites to

spread through contact with water or soil contaminated by other groups, or even through contact with dead animals from neighboring groups (Walsh et al. in review). The extent of range overlap varies greatly among primate species (Cheney 1987), and general predictions are that most measures of disease risk will increase with range overlap. Thus, a recent study of gorillas in the Kahuzi-Biega National Park found that home range overlap influenced the infection rate of individual gorilla hosts based on fecal samples of gut parasites (Eilenberger 1997). However, a preliminary comparative study of parasite richness in relation to primate home range overlap produced no significant results (Nunn and Dokey, in review). Future studies could investigate patterns of range overlap and parasitism to a greater extent in wild populations.

Animals dispersing from infected groups represents another route for parasites to spread through populations. This possibility was discussed by Freeland (1976), who suggested that animals might undergo a period of "social ostracism" before being allowed to enter a new group (see also Tutin 2000). Host dispersal should affect the spread of STDs, since this class of parasites requires intimate contact, and therefore host movement between groups should increase the establishment of STDs in a population (Thrall et al. 2000). For non-STDs, Freeland (1979) found that different groups of baboons (*P. anubis*) harbor more similar protozoa than do rainforest monkeys, and he suggested that this can be explained by the observation that individuals transfer between groups more commonly in baboons. As further testimony to this possibility, Barrett and Henzi (1998) noted that an unidentified pathogen was introduced to a new troop of baboons through transfer of an infected animal, and a disease similar to yaws was also likely to have spread through inter-troop transfer among baboons at Gombe (A. Collins, personal communication).

Finally, territoriality will likely reduce contact among neighboring groups, but in some cases it could also lead to aggressive interactions during territorial encounters, resulting in the spread of disease between groups (Loehle 1995). Many viruses are spread through territorial interactions in free-living carnivores, including rabies in foxes (White et al. 1995) and FeLV in feral cats (Pontier et al. 1998). Risks of pathogen transfer via aggressive contacts should increase in primate species with long canines that can pierce the skin and increase contact with blood or saliva (Tutin 2000). In a semi-free-ranging population of mandrills (*Mandrillus sphinx*), for example, SIV and STLV probably spread through biting associated with male intra-sexual competition (Nerrienet et al. 1998). Thus, patterns of disease risk with directly transmitted parasites should covary with canine size and quantitative measures of territoriality in comparative tests.

3.3.5.3 Geographic range size

All else equal, host species with larger geographic ranges—defined as the range of the species as a whole—should encounter more varied habitats and thus a wider diversity of parasites (Dritschilo et al. 1975; Price and Clancy 1983; Gregory 1990; Poulin and Morand 2004). Similarly, host species with larger geographic ranges are expected to overlap with a greater number of other host species, increasing the

possibility of cross-species transmission events among sympatric hosts (Ezenwa 2003; Nunn et al. 2004). Parasites spread through fecal contamination of the environment, for example, could readily infect multiple host species in the same habitat, a situation that may be common for nonhuman primates with ranges that overlap with humans and domesticated animals (Chapter 7 and Nizeyi et al. 1999; Wallis and Lee 1999; Graczyk et al. 2001). Direct contact among different primate species also occurs when primates of different species form aggregations known as polyspecific associations, possibly for avoiding arthropod parasites (Freeland 1977) and other benefits (Waser 1987).

A number of parasite surveys in overlapping primate populations revealed shared parasite communities that could reflect the effects of overlapping geographic ranges (Meade 1984; McGrew et al. 1989a, b; Bakarr et al. 1991). For example, Landsoud-Soukate et al. (1995) compared patterns of prevalence in sympatric chimpanzees and gorillas in Lope Reserve, Gabon. They found that gorillas exhibited higher levels of parasitism with a variety of protozoa and helminths, as compared to chimpanzees, but six of the parasites (one may be commensal) occurred in both species of apes.

From a comparative perspective, Nunn et al. (2003a, 2004) found that geographic range size correlated with the richness of viruses and protozoa across anthropoid primates. Moreover, two measures of geographic range overlap among primate hosts explained additional variation in the diversity of generalist and specialist viruses, even after controlling for the correlated effect of geographic range size (Nunn et al. 2004). Host ranging variables should be explored in greater depth when more information becomes available on the global distribution of parasites in humans, domesticated species, and other mammals.

3.3.5.4 Terrestrial substrate use

Animals often defecate, cough, vomit, bleed, or urinate on the ground or low-lying substrates, and in so doing, they can disperse infective stages of parasites. Thus, it is reasonable to expect that terrestrial primates experience greater disease risk than arboreal primates (Nunn et al. 2000). Based on similar reasoning, Minette (1966) proposed that the general absence of *Leptospira* infections in New World monkeys reflects the more arboreal lifestyles of this group of primates, since this parasite is spread through contact with contaminated soil and water. Dunn (1968) even proposed that records of infection with trematodes and *Leptospira* could provide a useful proxy for the degree of arboreality for primate species whose behavior has not yet been studied!

Although this hypothesis is appealing, phylogenetically controlled cross-species studies thus far have generated no support for the role of substrate use as a factor that influences disease risk. Terrestriality failed to explain variation in leukocyte counts and spleen size after controlling for body mass (Nunn et al. 2000; Nunn 2002a,b); in fact, if any pattern is present, relative spleen size actually *declined* with increasing use of terrestrial substrates, in a direction opposite to predictions. The percentage of time terrestrial also showed no relationship with parasite species richness for three

major groups of parasites (protozoa, viruses, and helminths), and similar results were obtained for categorical measures of terrestriality (arboreal, mixed, and terrestrial, Nunn et al. 2003a).

Several factors could explain a lack of association between disease risk and terrestriality. First, the basic assumption underlying the hypothesis, namely that arboreal species are protected from contaminated substrates, might be incorrect. Thus, Freeland (1980) found that mangabeys commonly defecated on branches used for arboreal locomotion, providing a means for intestinal parasites to spread even in an arboreal environment. Second, hypotheses concerning substrate use might be better tested using data on parasites that are known to have a strong environmental component to their transmission, such as contact with infectious stages in water. For example, *Schistosoma* have been reported mainly in ground-dwelling monkeys (e.g. *Papio anubis, P. hamadryas, P. papio, and Cercopithecus aethiops*; Else et al. 1982; McGrew et al. 1989a; Ghandour et al. 1995; Müller-Graf et al. 1997; Munene et al. 1998). This association makes sense because transmission of *Schistosoma* requires contact with a molluscan intermediate host—conditions that are less available in arboreal habitats

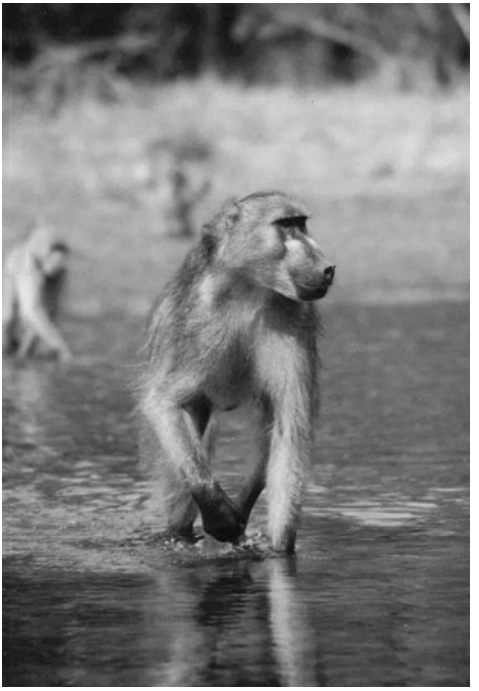


Fig. 3.13 Male chacma baboon walking through water at a research site in Botswana. Contact with slow moving or standing water could expose animals to intermediate stages of the trematode *Schistosoma mansoni* and parasitic worms, protozoa, viruses, and bacteria transmitted through water contaminated with animal feces or human sewage. Photo by D. Kitchen, The Ohio State University.

(e.g. Fig. 3.13). Finally, a commonly overlooked alternative hypothesis is that animals using *both* terrestrial and arboreal substrates might be exposed to more parasite species than those that specialize on only one of these substrate categories (Dunn 1968; Altmann 1974; Nunn et al. 2003a). These factors could be explored in future studies that compare populations or species that vary in their degree of arboreality.

3.3.5.5 Diet

Primates and other animals unintentionally ingest parasites by consuming contaminated food and water. Leaf-eating (folivorous) primates typically ingest larger volumes of food than frugivores and could therefore ingest more parasites whose infectious stages contaminate leaf material (Moore 2002). On the other hand, diets of frugivorous primates are often more varied, potentially leading to contact with a wider array of parasites, and in folivores, consumption of leaves with secondary compounds could reduce levels of intestinal parasites (e.g. Huffman 1997). Janzen (1978) even suggested that the general absence of protozoan parasites among folivorous primates could reflect a "steady flow of secondary compounds from the foliage that they eat" (p. 78).

Invertebrates, such as grubs and cockroaches, serve as intermediate hosts for trophically transmitted parasites, predicting increased diversity of these parasites among insectivorous primates. Consumption of ectoparasites during grooming should influence the distribution of ectoparasites among different primate hosts. Thus, Dunn (1968) proposed that insectivorous primates should more readily consume larger-bodied ectoparasites, possibly lowering the abundance of the larger ectoparasites among insect-eating primates.

Despite these probable links between diet and parasitism, few studies have demonstrated convincing evidence for effects of insectivory and folivory on primate exposure to infectious diseases. Two recent comparative studies found limited associations between parasite diversity and the percentages of different dietary components, with leaves positively correlated with the diversity of helminth species (particularly nematodes) in some analyses (Nunn et al. 2003a; Vitone et al. 2004), but generally non-significant for other parasite groups. In a comparative study of 23 mammals, however, basal metabolic rate exhibited a positive association with helminth richness, possibly because species with higher metabolic rates consume relatively more resources (Morand and Harvey 2000).

Other aspects of diet should influence disease risk, including prey specialization, cannibalism, coprophagy, and the need to drink water (rather than obtaining most fluids from fruit). Predation on other primates could serve as a source of new infections (Tutin 2000), as could cannibalism (e.g. Goodall 1986; Palombit 2000). Coprophagy, or the eating of feces, puts animals at risk of infection (or re-infection) with intestinal parasites if infectious stages are present in fresh feces, and this behavior has been observed in primates, including gorillas (Harcourt and Stewart 1978) and chimpanzees (Wrangham 1977; Goodall 1986; Krief et al. 2004). In gorillas, Harcourt and Stewart (1978) documented coprophagy in all age-sex classes. In most cases the animal ate its own dung. Moreover, coprophagy was associated

with heavy rain and occurred more commonly at the end of a resting period. This behavior may serve many functions, including improved absorption of vitamins (see Harcourt and Stewart 1978) or re-ingestion of seeds passed through the intestinal tract (Krief et al. 2004). Primates that are in close proximity to humans have been observed to forage in garbage dumps, and this could expose them to infected meat or human waste (see Chapter 7 for additional details).

Finally, many primate species consume water from rivers, drinking holes, or lakes. These water sources provide opportunities for parasite infection. In Senegal, Guinea baboons (*Papio papio*) have been shown to carry *S. mansoni* (McGrew et al. 1989a), but green monkeys and patas monkeys are apparently not infected by this parasite (McGrew et al. 1989b). The authors suggested that levels of infection were higher in baboons because they more commonly used stagnant water sources (see also Altmann 1974). Green and patas monkeys, on the other hand, tended to drink from flowing or temporary water sources and showed no evidence of infection with schistosomes. Meade (1984) suggested that Amboseli baboons limit their visits to drinking holes in part to avoid moist soil that surrounds these holes and might serve as focal points for acquiring infections.

In summary, omnivorous primates with diverse diets of plants and animals might be exposed to a greater diversity of parasites (Dunn 1968), but insectivory could increase the transmission of certain types of parasites. Additional dietary behaviors, including preference for different types of water sources, coprophagy, and use of garbage dumps, should further affect disease risk in primates, although only a few links have been documented thus far. Since different populations of frugivores often have markedly different diets, future field and comparative research could provide new insights by comparing parasites among these populations.

3.3.6 Environmental factors and seasonality

Primate species, like other animals, experience dramatic variation in temperature, rainfall, and the abundance of resources. Seasonal reductions in rainfall could induce dietary stress as the availability of resources declines, increasing susceptibility to disease (Lloyd 1995; Beisel 2000; Nelson et al. 2002; Nelson 2004). These reductions could also force animals to share food and water resources with different social groups and even different species, potentially leading to more opportunities for the spread of parasites.

Vector-borne diseases are among the most likely to covary with environmental conditions (Dobson and Carper 1992; Harvell et al. 2002). Temperature and rainfall should affect arthropod vector distribution and abundance, parasite development, and parasite transmission rates (Kovats et al. 2001). Many vector-borne diseases are limited in geographic range by thermal constraints because parasites cannot complete development before the vectors die. Several vector-borne human pathogens that are also infectious to free-living primates have expanded their geographic ranges or become more prevalent in recent decades, including malaria, trypanosomiasis, yellow fever, and dengue (Gratz 1999; Lindgren et al. 2000).

A global analysis of human diseases found a strong association between parasite diversity and latitude, driven by climatic variables involving precipitation and temperature (Guernier et al. 2004, see also Chapter 8). Across primate species, a comparative analysis showed similar results, with increased parasite species richness among host species in the tropics (Fig. 3.14, Nunn et al. 2005). This pattern was strongest for protozoan parasites, perhaps due to the greater proportional representation of vector-borne parasites among protozoa recorded in primates (see Fig. 2.11). The pattern shown in Fig. 3.14 could also reflect a confounding influence of geographic range size, because when this variable was entered into the model, the latitudinal effect weakened.

Bioclimatographs that capture data on moisture and temperature have traditionally been used to predict outbreaks of gastrointestinal nematodes infecting livestock. These associations arise because intestinal macroparasites of terrestrial animals are often susceptible to variation in temperature and humidity at several stages of their life cycles (Gordon 1948; Smith 1990). In *S. mansoni*, for example, a 10º C increase in temperature can dramatically shorten development time by over two weeks (Gordon et al. 1934).

Rainfall can clear away pathogens, especially for arboreal primates exposed to contaminated vegetation. Thus, arboreal mangabeys (*C. albigena*) were found to use an area more intensively during the rainy season (Freeland 1980). Overall, however,

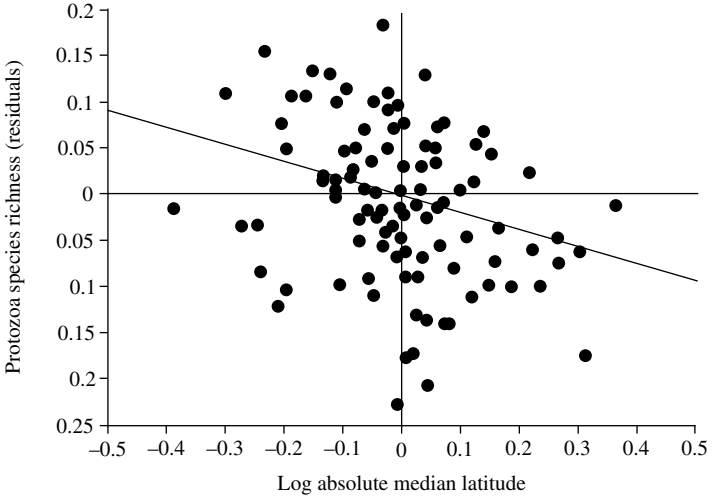


Fig. 3.14 Latitudinal gradients in protozoan parasite species richness. Points represent independent contrasts. Increases in median absolute latitude are associated with decreases in the size of the protozoan parasite community. In this plot, parasite species richness was measured as least-squares residuals following regression analysis of protozoan parasite richness and a measure sampling effort for each host species. From Nunn et al. 2005. Printed from *Diversity and Distributions*, with permission from Blackwell Publishing.

the parasite-related costs of increased moisture probably outweigh any potential benefits that rainfall might provide by removing parasites from the environment (Freeland 1980). Because many nematodes require strict moisture levels for development, Hausfater and Meade (1982) predicted that baboons would avoid contaminated sleeping sites more often in the rainy season than in the dry season—a prediction that was supported by their data. Similarly, several studies of arboreal primates showed a positive relationship between moist environments and intestinal macroparasite infections (Stuart et al. 1993, 1998; Stuart and Strier 1995; Stoner 1996). As noted above, intestinal parasite infections among howlers at La Selva (a wetter environment) were greater than among howlers at La Pacifica (a drier habitat). Furthermore, at La Selva, a river troop exhibited higher intensity of nematode infection than a forest group (Stoner 1996). Similar effects have been documented in terrestrial primate species, with nematode prevalence and intensity generally greater among baboons and chimpanzees at Gombe, as compared to populations inhabiting the drier conditions at Mt Assirik (McGrew et al. 1989a). Finally, in a recent comparative study of white blood cell counts in 33 primate species, lymphocyte and phagocyte concentrations correlated positively with rainfall (Semple et al. 2002).

Seasonal cycles can generate periodic transmission opportunities for some human and wildlife pathogens (Dowell 2001; Altizer et al. 2004). In chimpanzees, Huffman et al. (1997) found that the prevalence of infection by the nematode *Oesophagostomum stephanosomum* increased during the wet season in two years, with sharp peaks in egg production in infected individuals occurring 1–2 months after the onset of rains. Two other nematodes (*Trichuris trichiura* and *Strongyloides fuelleborni*) showed no seasonal variation in this population. In gorillas, Watts (1998) found that the incidence of respiratory infections (and deaths) were associated with annual periods of high rainfall, a pattern also suggested for geladas (Ohsawa and Dunbar 1984) and chimpanzees (Boesch and Boesch-Achermann 2000). Botfly infections also vary in abundance seasonally, being more common toward the end of the dry season (Smith 1977) and showing up to three cycles per year (Milton 1996). Meade (1984) found that spirurid nematode prevalence increased in the dry season, and Pettifer (1984) found that worm burdens in chacma baboons were higher during the wet season for *Bertiella studeri* and *Oesophagostomum bifurcum*, but the hookworm *Trichostrongylus falculatus* was more common in the dry season. Other studies have found no striking differences across seasons in the presence of macroparasites (intestinal parasites in chimpanzees, McGrew et al. 1989a; and schistosomes in baboons, Müller-Graf et al. 1997).

Additional effort should focus on examining environmental factors at regional and global scales using phylogenetic methods (Box 3.2) and geographic information systems (GIS), as discussed in Box 3.3. It is important to recognize that not all parasites will be sensitive to environmental factors or will show seasonal variation. Thus, some parasites, such as the nematode *Trichuris*, have thick shells that make them resistant to desiccation and may reduce the magnitude of the impact of seasonal

fluctuations on survival (Meade 1984). Seasonal changes can also affect host susceptibility to infectious diseases (Combes 2000; Nelson et al. 2002; Nelson 2004). Thus, another potentially profitable direction would be to consider the links between dietary stress and disease susceptibility, particularly among primates that live in highly seasonal conditions, such as in Madagascar or desert habitats. Studies of rodents and humans suggest that immune systems are weakened during the winter (reviewed in Dowell 2001), and other environmental stressors or annual rhythms in immune function and reproduction could further weaken immunity and increase disease risk (Lloyd 1995; Nelson et al. 2002).

3.4 Summary and synthesis

In this chapter, we identified the host traits that influence patterns of parasitism and developed predictions for future research that could uncover the directional associations and mechanistic links between parasites and primate behavior and ecology. A multitude of host traits, in conjunction with environmental parameters and details on parasite transmission mode, determine encounters with and susceptibility to infectious diseases (Table 3.1). Many critical hypotheses remain untested, as summarized in the sections above. In fact, most knowledge of primate-parasite ecology has derived from studies of particular populations, whereas many questions will require analysis of cross-species data that control for confounding factors, such as sampling effort and a wide range of ecological covariates. Furthermore, studies of parasites from wild primates tend to be biased toward intestinal helminths, viruses, and vector-borne protozoa, with data lacking on bacteria, fungi, and parasites that are spread through the consumption of intermediate hosts (and therefore linked to diet). The future is likely to hold many surprises, and further investigation will undoubtedly lead to revision of the predictions presented in this chapter, while also producing new predictions to explore through field and comparative research.

Primatologists have devoted substantial effort to studying the effects of predation on primate populations (van Schaik 1983; Anderson 1986; Janson 1992). Although predation is a critical factor that undoubtedly drives patterns of primate behavior, actual cases of predation are rarely observed (Cheney and Wrangham 1987). In contrast, many field primatologists have observed animals that are obviously afflicted with intestinal parasites, bot flies, respiratory infections, or other parasitic organisms. Importantly, predation and resource competition are likely to be major ecological factors that influence patterns of sociality, and that could therefore influence the spread of disease; thus, research on parasites should be seen as one component in the integrative framework already developed to study primate socioecology.

Box 3.3 Spatial epidemiology and geographical analysis of disease risk

Spatial epidemiology aims to identify the causes of spatial variation in disease risk including large-scale landscape variables and localized processes that govern transmission events (reviewed in Ostfeld et al. 2005). At one level, spatial data can be used to track the spread of disease into new areas and to guide strategies for monitoring efforts and intervention. For example, researchers have developed predictive models for the spatial spread of raccoon rabies in the eastern United States by using county-by-county dates of first appearance, information on human population density, rivers, mountain ranges, and the expected frequency of long-distance host translocation (Smith et al. 2002; Russell et al. 2004; 2005). Rivers and mountain ranges substantially slowed the movement of rabies across the landscape (Smith et al. 2002) and highlighted regions for targeting oral vaccination efforts (Russell et al. 2005).

Another approach to spatial epidemiology is to forecast epidemics and predict current and future "hotspots" of infection using key environmental parameters such as temperature, rainfall, elevation, humidity, and vegetation (Meade et al. 1988; Ostfeld et al. 2005). Spatial variation in disease risk can also arise from biological variables like the presence of vectors, other host species, human density, and habitat disturbance. Based on known correspondence between habitat characteristics and factors influencing parasite transmission, geo-referenced landscape data can be used to create habitat risk assessment profiles (see Fig. 3.15). Such methods were applied to several emerging diseases including

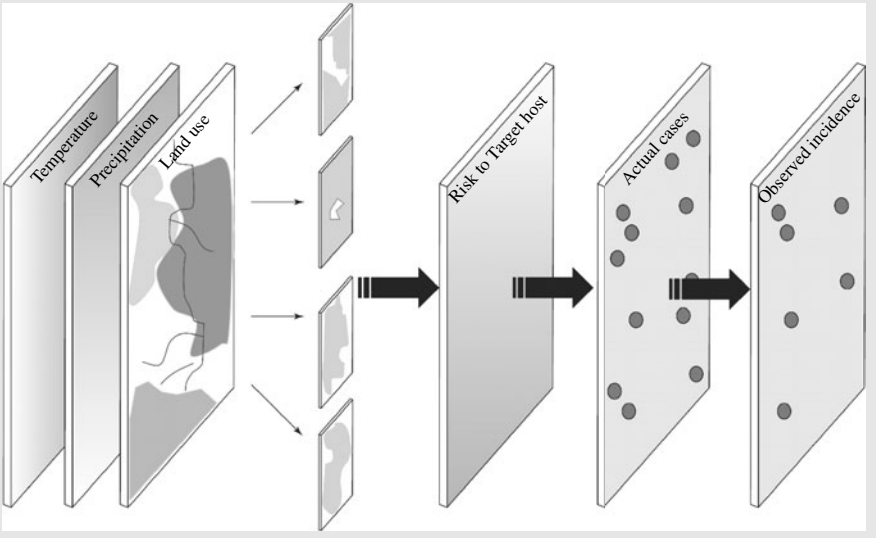


Fig. 3.15 Diagrammatic sketch of how spatial variation in environmental variables such as temperature and precipitation can be used to predict risk of acquiring infectious diseases, in this case for humans, using a GIS-based approach. Known relationships between environmental variables and the distribution of parasites or vector abundance can influence the risk of target hosts encountering the disease-causing agents. Reprinted from *Trends in Ecology and Evolution* 20, R. S. Ostfeld, G. E. Glass and F. Keesing. Spatial epidemiology: an emerging (or re-emerging) discipline, pages 328–355. Copyright (2005), with permission of Elsevier.

Box 3.3 (*cont.*)

Campylobacter infections in humans (Nygard et al. 2004) and Lyme disease in domesticated animals (Guerra et al. 2001).

Most spatially explicit methods based on ecological data use computerized GIS to input, extrapolate, and analyze information. Multiple layers of digitized map data can be obtained from existing maps of landscape features, species occurrence maps, and data tables showing climatic data records for known spatial coordinates. At large spatial scales (global or continental levels), satellite images or remote sensing technology provide information on surface temperature, rainfall, and vegetation indices (i.e. advanced very high resolution radiometer data, or AVHRR). For example, remote sensing data have been used to map the probable distribution of vector-borne pathogens of humans, including malaria, trypanosomiasis, and tick-borne diseases (e.g. Hay et al. 1996; 2002; Rogers and Randolph 2003). Because locations in close spatial proximity are not likely to be independent of one another, statistical methods are used to control for spatial autocorrelation (e.g. Guernier et al. 2004)

GIS methods have been used to to create risk assessment maps for predicting human disease occurrence in the absence of complete surveillance information. Similar approaches could be applied to wild primate hosts, asking whether measures of parasite prevalence and diversity in wild primates covary with factors such as climate, human population density, and land use, and the presence of other wildlife species. An exciting area for future research involves integration of GIS with agent-based modeling approaches (Rushton et al. 2000; Gimblett 2002). With such integration, it will be possible to study the spread of disease at a landscape level using models that encompass information on habitat and population-level characteristics, while also using agent-based models to provide details on individual interactions within and between groups.

4

Host–parasite dynamics and epidemiological principles

4.1 Introduction

How do infectious diseases spread through host populations, and under what conditions will parasites regulate host abundance? What features of host and parasite biology determine the probability of parasite invasion and persistence? As illustrated in Chapter 3, ecologists can explore factors associated with disease risk using descriptive data on host biology and parasite occurrence. Indeed, primates provide many fascinating examples of how host biology and environmental variables can influence variation in parasite occurrence. To move beyond qualitative and largely intuitive approaches, more quantitative methods can be used for investigating host–parasite dynamics. Such approaches are especially important for real-world systems where multiple ecological, behavioral, and genetic processes interact.

Much of our understanding of wildlife-pathogen systems has been shaped by mathematical models that examine how events that occur at the level of individual animals—including birth, infection, dispersal, and death—translate into population-level phenomena such as epidemic cycles or the spread of infectious diseases across a geographic region. From a practical perspective, conclusions arising from even the simplest of models can help assess the probability of parasite invasion and develop control strategies for mitigating these risks in wild populations. These approaches are also important for zoo collections or breeding facilities, where the introduction of one infected animal (or the transfer of diseases among species) can devastate an entire captive population. In a public health context, mathematical models have been applied to develop strategies for containing threats arising from pathogens like SARS, HIV/AIDS, and potential bioterror agents in human populations (Anderson et al. 1989; Halloran et al. 2002; Lipsitch et al. 2003; Smith and Blower 2004). Similar approaches can be used to predict and manage the spread of infectious diseases in primate species, given sufficient information on host and parasite characteristics and collaboration between theoreticians, wildlife veterinarians, and field primatologists (Stuart and Strier 1995; Heymann 1999).

4.1.1 An historical perspective

Traditionally, *epidemiology* refers to the study of disease processes in humans, but increasingly this term has been applied to nonhuman systems as well. The related

term *epidemic*—translated literally as "to come upon people"—defines a rapid increase in the prevalence or intensity of parasitic infection beyond what is normally present. This is in contrast to the term *endemic*, used to describe infections that are established and constantly present in a particular region and normally do not show large fluctuations in occurrence or area affected.

Many historians recognize the origins of epidemiology in the early ground-breaking work of Dr John Snow, who in 1854 used data from the location of cholera deaths to identify the Broad Street pump as the source of a cholera outbreak in London (Rosenberg 1962; CDC 2004a). Dr Snow reportedly had this pump handle removed and the outbreak subsided. His work led to the development of a new theory that cholera was transmitted primarily through contaminated water, and thus pointed the way toward public health reforms to limit disease spread, including improved sanitation (CDC 2004a). In terms of understanding the dynamics of human diseases, other groundbreaking work during this past century emerged from long-term studies of measles and other communicable childhood diseases (Soper 1929; Bartlett 1957, 1960). The dynamics of measles in European cities probably represents one of the most comprehensively studied data sets in ecology, and analyses of monthly case reports of this viral infection have tremendously advanced knowledge of host–pathogen interactions (Bjørnstad et al. 2002; Grenfell 2002). For example, Bartlett's (1957, 1960) seminal work on the epidemics of measles in English and Welsh towns before the advent of vaccination gave rise to the concept of a "critical community size," namely the minimum population size above which an infection persists in the population.

Parasitologists and veterinary workers studying infectious diseases in animals have contributed extensively to descriptions of parasite taxonomy, life cycles, pathology, and pathogen occurrence. This work uncovered important details of parasite biology from a variety of wild animals, including nonhuman primates (Fiennes 1967; Fowler 1976; Kalter 1983; Brack 1987). Also of historical note are detailed studies of gastrointestinal helminths during the last century that pointed to the role of temperature and moisture in determining parasite outbreaks in sheep and cattle (Gordon et al. 1934; Levine 1963), and more generally set the stage for later studies of the links between climate and the ecology of infectious diseases (Dobson and Carper 1992; Harvell et al. 2002). By focusing on the life history of parasites or infections within single animals, however more traditional approaches in parasitology overlooked many important ecological processes, including the role of parasites in regulating animal abundance, factors determining the spread of parasites through populations, and the potential for evolutionary change in both hosts and parasites (Anderson 1995; Tompkins et al. 2001; Hudson et al. 2002; Altizer et al. 2003a).

Beginning in the late 1970s, a synthetic view of the ecological dynamics of host–parasite interactions was initiated by a series of ground-breaking papers by Roy Anderson and Robert May (Anderson and May 1979; May and Anderson 1979). Their work joined fundamental approaches in population ecology with the biological details of host–parasite interactions using epidemiological frameworks dating back

to the first part of the twentieth century (Ross 1911; Kermack and McKendrick 1927). Anderson and May's models showed that parasite establishment in host populations is linked fundamentally to host abundance and behavior (Anderson and May 1978). These models further revealed the ways that parasites can regulate populations and identified mechanisms that limit the spread of parasites (May and Anderson 1978). A combination of modeling work and epidemiological data provided new perspectives on the dynamics of infectious diseases in humans (Anderson and May 1991; Earn et al. 2000; Grassly et al. 2005), and these general principles have been applied across a wide range of host–parasite systems. Indeed, studies of infectious disease dynamics surged during the 1980s and 1990s, and scientific investigation in this field continues to expand to this day (Figure 4.1), as evidenced by a large number of scientific books and edited volumes addressing host–parasite ecology and evolution published in the last decade (Grenfell and Dobson 1995; Clayton and Moore 1997; Frank 2002; Hudson et al. 2002; Moore 2002; Thomas et al. 2004a).

Recent progress in the field of wildlife disease ecology has emerged from efforts to apply experimental and modeling approaches to parasite spread and population dynamics in natural populations (Grenfell and Dobson 1995; Hudson et al. 2002),

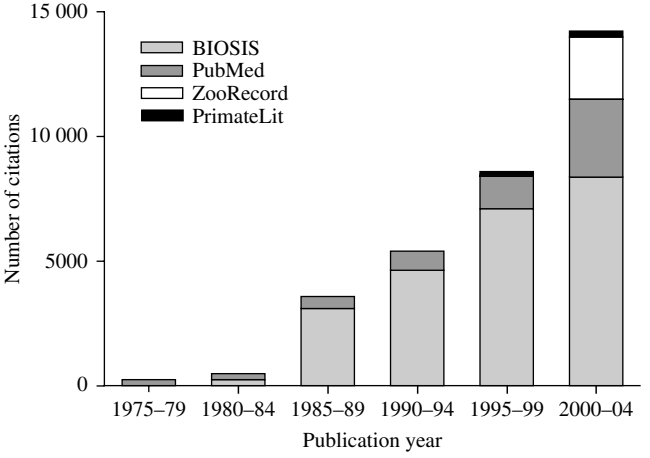


Fig. 4.1 Increase in the number of published records (citation counts) from 5 bibliographic databases addressing host–parasite ecology or evolution. Databases include BIOSIS Previews (covering a wide range of life sciences journals; OVID Technologies, Inc.), PubMed (focusing on the biomedical literature; National Center for Biotechnology Information), Zoological Record Plus (ZooRecord, focusing on publications in animal biology; CSA Illumina) and PrimateLit (covering references in primatology; Wisconsin Primate Research Center and Washington National Primate Research Center). Search terms used in each case were as follows: (infectious disease or parasite or pathogen) and (dynamics or ecology or evolution), together with the years of publication as shown on the X-axis. For PrimateLit and ZooRecord, only journal publications were extracted (i.e. not websites, conferences, books, or other sources).

and from increased interest in the joint evolution of hosts and pathogens (Hamilton and Zuk 1982; Lively 1992; Clayton and Moore 1997; Lively 1999). For example, long-term studies on the dynamics of cecal nematodes (*Trichostrongylus tenuis*) in red grouse (*Lagopus lagopus scoticus*) showed that parasites can drive host population cycles, in part due to their sublethal impacts on host fecundity and the persistence of parasite infectious stages during periods of low host abundance (Hudson et al. 1985, 1992, 1998a; Dobson and Hudson 1992). Similarly, long-term studies of genetic interactions between trematode parasites (*Microphallus* sp.) and freshwater snails (*Potamopyrgus* sp.) demonstrated that parasites can adapt to infect common host genotypes, and that frequency-dependent selection can generate evolutionary cycles in host and parasite allelic frequencies (Dybdahl and Lively 1998; Lively 1999).

Surprisingly, virtually no detailed epidemiological studies have focused on parasite dynamics in wild primate hosts. Even for primate infections of great concern to human health, such as lentiviruses, spumaviruses, and *Schistosoma* parasites, a great number of studies report data from "wild" primate hosts sampled long after they were captured in the wild and far away from the capture sites, thus calling into question whether patterns reflect those found in the wild and reducing the usefulness of prevalence data for epidemiological analysis. The shortage of studies on parasite dynamics in wild primates, including those that join modeling approaches with field data, is perhaps the greatest challenge for developing a better understanding of infectious diseases in these species.

4.1.2 Basic terminology and measures of infection

4.1.2.1 Prevalence

Several basic epidemiological parameters are important for describing parasitism in natural populations. As mentioned briefly in Chapter 1, *prevalence* is a primary measure of pathogen occurrence that refers to the proportion of hosts infected with a micro- or macroparasite. Prevalence can be estimated using any methods that discriminate infected from non-infected hosts, such as (1) outward signs of disease linked to changes in physical appearance or behavior of the host, (2) direct evidence of parasites in the blood, feces, or other host tissues, including use of PCR-based methods for detecting parasite DNA or RNA, and (3) serological methods that use antigen–antibody reactions to infer the past history of exposure to a particular agent (i.e. *seroprevalence*). These different approaches for sampling individual animals capture different phases of infection in the host (Table 4.1).

Some warnings are in order when interpreting prevalence estimated from field sampling protocols. First, inferences of disease status will depend on the method used and the hosts' stage of infection, since hosts could be sampled before developing disease or antibodies, and outward signs of infection might persist after hosts are no longer infectious (Table 4.1). Thus, multiple methods for assessing host infection status are often needed, especially when modeling approaches require information

Table 4.1 Stages of infection or disease status assignments based on different methods for examining hosts for signs of infection, including actual presence of the pathogen (using microscopy, culture, or PCR-based methods), physical or outward signs of disease, and the presence of host antibodies using serological techniques

Stage of infection	Test method		
	Presence of pathogen	Outward signs of disease	Host antibodies to infection
Susceptible	No	No	No
Exposed and infectious	Yes	No	No
Diseased and infectious	Yes	Yes	No
Diseased, infectious, and host immune response	Yes	Yes	Yes
Recovering but still diseased	No	Yes	Yes
Recovered and immune	No	No	Yes
Asymptomatic carrier state	Yes	No	Yes/No
Unrelated cause of disease	No	Yes	No

Different combinations of presence/absence information can be used to infer the infectiousness of the host and potential impacts of disease at the individual level. Note that each test method alone could correspond to multiple phases of infection in the absence of other information.

on the infection status of different individuals (see below). A second potential caveat for interpreting prevalence data is that accurate estimates of prevalence might require correcting for uneven sampling of healthy and diseased animals by researchers (Jennelle et al., provisionally accepted). This issue arises because behavioral or physical changes in diseased animals could make them more or less apparent to observers, leading to systematic biases in estimated prevalence (Faustino et al. 2004). Third, further complications occur when the infection status of animals is quantified with uncertainty, as many methods for detecting parasites are accompanied by imperfect specificity and sensitivity. In this case, *specificity* refers to the ability of a test to discriminate between true versus false positives, and *sensitivity* refers to the power of a test to detect true versus false negatives (Burr and Snodgrass 2004). Detecting infection status at different stages following host exposure can influence the sensitivity and specificity of the test.

4.1.2.2 Intensity

For microparasites, ecologists frequently assume that it is sufficient to know whether or not a host is harboring a given parasite, rather than counting the actual number of viral or bacterial particles per host. In some cases, however, high levels of pathogens in the blood or other host tissues (e.g. viremia, bacteremia, or parasitemia) can indicate particularly severe infections, with impacts on pathogen transmission and the likelihood of host survival. A second useful measure of infection status commonly

employed for many macroparasites is the *intensity* of infection, or numbers of parasites per infected host (see Chapter 1). Not surprisingly, intensity is more likely to be used for parasites that can be readily counted, such as ticks per animal or numbers of worms inhabiting a section of the gastrointestinal tract. Estimates of intensity can be measured by quantifying parasite life stages in feces, blood smears, muscles or other organs (Bush et al. 1997). Another measure related to intensity is parasite *abundance* or the average number of parasites across all hosts. Because this measure also includes non-infected hosts in the calculation, it is a composite measure of both intensity and prevalence (i.e. abundance = intensity * prevalence).

4.1.2.3 Parasite aggregation

Measures of intensity and abundance are closely tied to the fundamental ecological question: are individual organisms clumped, randomly dispersed, or evenly dispersed within host populations? Parasite aggregation is critically important to understanding the population-level impacts of parasites on their hosts (Anderson and May 1978; May and Anderson 1978). A large number of empirical studies have shown that macroparasites are almost always aggregated or clumped, with most parasites in a population found in a small number of hosts, and most hosts harboring light infections (Fig. 4.2). A key measure of parasite dispersion (or aggregation) is the ratio of the variance to the mean in parasite numbers (Shaw and Dobson 1995; Shaw et al. 1998). This ratio should be close to one when parasites are randomly distributed among hosts and much greater than one when the majority of parasites are clumped in just a few hosts. Another measure of parasite aggregation uses the negative binominal distribution (see Fig. 4.2).

Some studies of wild primate populations have provided statistics on parasite aggregation (Fig. 4.2(b)). Several processes could generate aggregated populations of parasites, including parasite recruitment into already-infected hosts through continual re-exposure. Differences in exposure could also result from behavioral variation in food or habitat preferences (Müller-Graf et al. 1996, 1997), or from patterns of dispersion linked to variation in primate mating and social systems (Stuart and Strier 1995). Heterogeneity in parasite burdens might further reflect differential susceptibility arising from genetic variation in host resistance (Patterson et al. 1998; Coltman et al. 2001), or from variation in host social status, nutrition, or stress. Traits of the parasites themselves, such as parasite mobility (Shaw and Dobson 1995), could also affect levels of aggregation in populations.

4.2 Analytical models of disease spread

Mathematical models are used in epidemiology to investigate how processes operating at the level of individuals translate into population-level phenomena. Individual-level events include transmission and the onset of infection and host recovery and death (Fig. 4.3(a)), whereas population-level outcomes capture waves of epidemics traveling through populations, host population declines, and shifts in the frequency of immune hosts (Fig. 4.3(b)). Depending on the details of the host–parasite system,

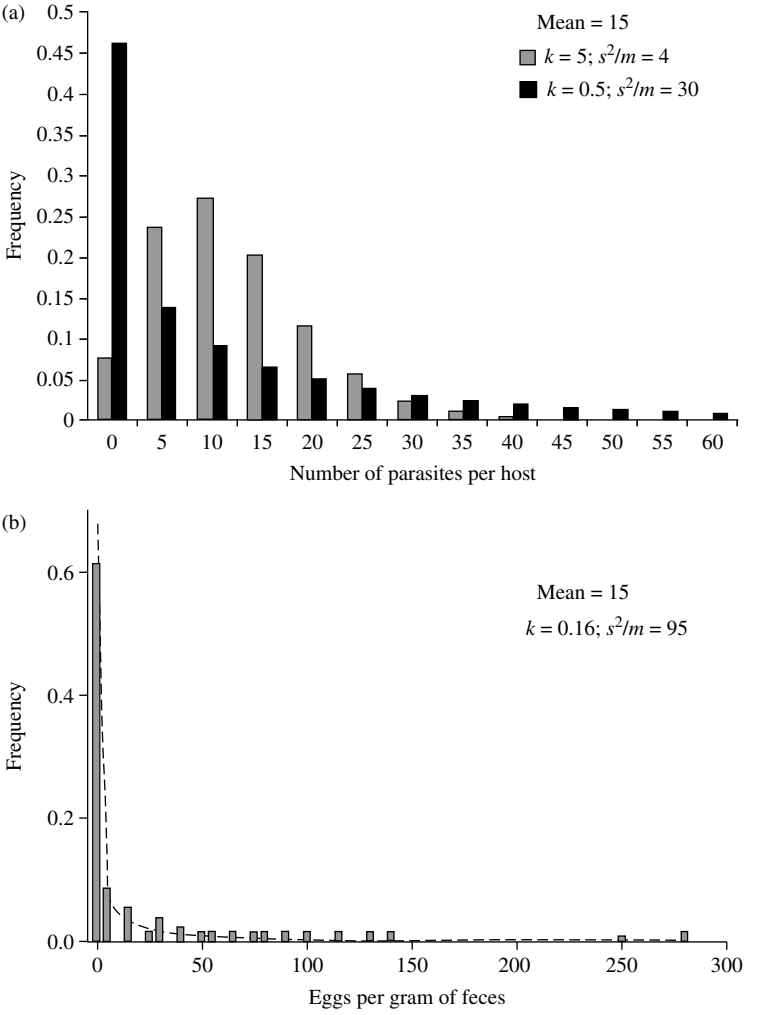


Fig. 4.2 Patterns of aggregation in macroparasites. In all cases the bars represent frequency distributions based on the proportion of hosts with a given parasite intensity. The parameter k from the negative binomial distribution provides an index of the degree of aggregation; when k is large, the distribution is approximately random (Poisson), and when k is small (less than 1) the distribution is highly aggregated (Shaw and Dobson 1995). In these plots, s^2 refers to the variance and m refers to the mean. (a) Theoretical distributions for a negative binomial process where the mean number of worms per host is 15, and the k parameter is either relatively high (gray bars; $k = 5$) or relatively low (black bars, $k = 0.5$). (b) Distribution of *Schistosoma mansoni* infection in a natural population of olive baboons (*Papio anubis*) in Gombe Stream National Park, Tanzania (Müller-Graf et al. 1997). Samples shown are worm eggs per gram of feces, from a total of 396 fecal samples collected from 206 known individuals from five different troops. In this case, the parasite shows a highly aggregated distribution ($k = 0.16$). Panel (b) reproduced from Müller-Graf et al., *Parasitology* vol. 115. Copyright (1997), Cambridge University Press.

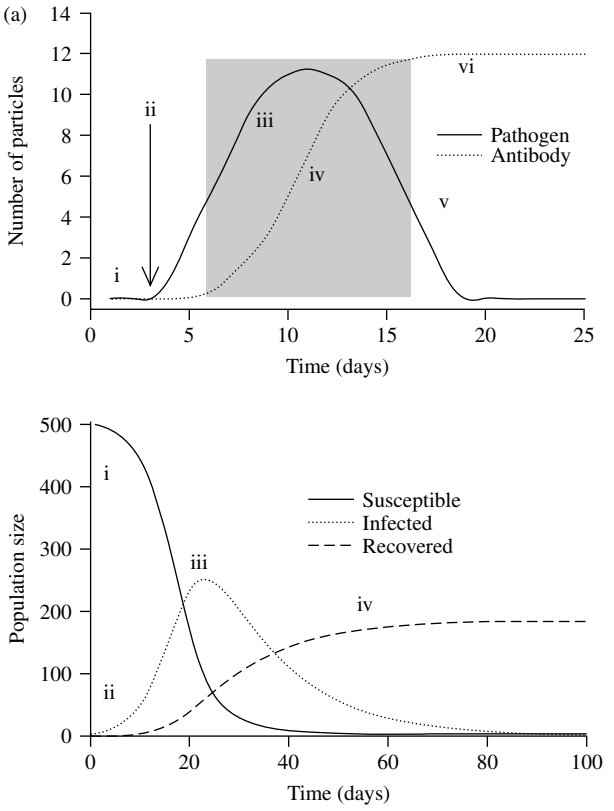


Fig. 4.3 Individual- and population-level processes associated with a generic host-microparasite interaction. (a) Processes occurring within individual hosts include: (i) a susceptible stage prior to exposure and infection, (ii) the onset of infection following transmission, and (iii) an increase and peak in parasite particles following replication within the host, which is often associated with a period of illness or disease (shaded box). Once the parasite is detected by the immune system, (iv) host antibodies are produced to help the host recognize and attack parasite stages, and this is followed by (v) a decline in the circulating levels of parasites, following which (vi) host immunity could remain high or gradually decline following recovery. (b) Population-level processes include (i) an initially entirely susceptible host population, (ii) introduction of an infected host, and (iii) an increase and peak in the numbers of infected animals following a classic "epidemic curve." This typical outcome of an SIR model (see Box 4.1) results in declining numbers of susceptible hosts and (iv) an increasing number of recovered and immune hosts.

these individual and population-level processes could occur on similar or very different time scales.

For many biologists, the utility of mathematical models for real-world infectious disease problems is not always obvious. This lack of appreciation can be partly attributed to the challenges of translating model parameters into phenomena that can

be measured in the field. These challenges can be overcome, however, and many benefits arise from using epidemiological models. Specifically, models demonstrate the mechanisms by which parasites can regulate host populations, and they can highlight processes that predict disease spread among groups or populations. Models also can be used to evaluate the costs and benefits of intervention strategies aimed at limiting disease risks to threatened host species, such as vaccination, quarantine, and culling of reservoir hosts (Chapter 7). Models of host–parasite interactions share several features in common with other mathematical models in population ecology, including a set of clearly stated assumptions, reliance well-defined variables, quantitative expression of processes influencing biological events, and a set of predictions regarding dynamical outcomes and equilibrium conditions. To that end, collaboration between modelers and field biologists is crucial, with field biologists providing key information required to parameterize epidemiological models and models pointing to predictions that are testable with field data.

Two general classes of mathematical models have been used to describe the dynamics of infectious disease in microparasites and macroparasites. For microparasites such as viruses and bacteria, where researchers are generally not concerned with the numbers of parasites per host, a *compartment model structure* divides the host population into *susceptible, infectious, and recovered* (or resistant) individuals. For macroparasites such as helminths and arthropods, models must also account for parasite eggs or larvae that persist outside of the host, as well as the frequency distribution of the number of parasites per host. Both types of models generally rely on a framework of coupled differential equations, and these can be complicated by factors such as latency or carrier states and the details of the transmission process. A full description of epidemiological models for both micro- and macroparasites is provided in Anderson and May (1991).

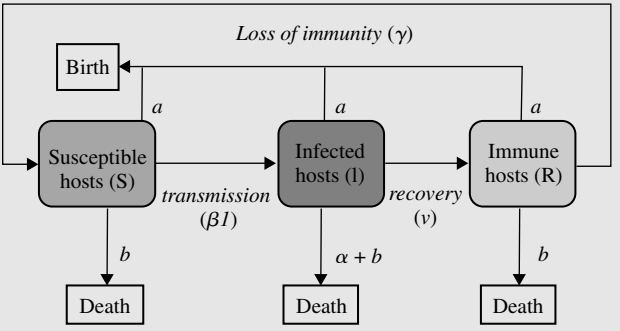
4.2.1 Microparasites and compartment models

A broad array of microparasites can infect primate hosts (Chapter 2). Mathematical models for directly transmitted microparasites typically divide the host population into susceptible (S), infected (I), and recovered/immune (R) classes and track changes in the number of hosts within each category (Box 4.1). This type of compartment model (often called an SIR model) has been developed and analyzed extensively by Anderson and May (1979, 1991), Getz and Pickering (1983), and others, drawing on classical approaches of Ross (1911) and Kermack and McKendrick (1927). For cases where hosts do not acquire immunity to re-infection (e.g. some STDs and chronic diseases, such as tuberculosis and brucellosis), the resistant class is eliminated and the equations simplify to an SI model (or SIS, for susceptible-infected-susceptible). Other complications can be added to the simple compartment model, some of which are addressed later in this chapter.

Box 4.1 Compartment models for directly transmitted microparasites

Mathematical models for microparasites divide the host population into susceptible (S), infected (I), and recovered/immune (R) classes and track changes in the number of hosts within each category. Total host population size, N, is the sum of S + I + R. Susceptible hosts arise from new births (where a is the per capita birth rate, here arising from each host class) or loss of immunity from the recovered class (γ). Individuals leave the susceptible class through natural mortality (b) or through infection after encountering an infected host (at rate βSI). Infected hosts are lost through natural death (b), disease-induced mortality (α) or through recovery (ν) to an immune state. Arrows indicate movement between host states, and the differential equations express these processes in mathematical terms. This model assumes that hosts are uninfected at birth, that pathogens do not affect host fecundity, and that host populations are large enough that stochastic processes can be ignored. The simple SIR model shown here is useful for parasites with density dependent transmission, which is a "mass action" process where transmission increases directly with host population density.

Many complications can be added to the simple compartment model framework. For example, a disease may reduce the fecundity of infected hosts, or be associated with a long latent period. Age or social structure may complicate among-host contact rates and parasite transfer. In addition, the density-dependent mixing assumed by this model is often inappropriate to describe the transmission dynamics of many pathogens. Other transmission modes can have profound effects on the invasion, persistence, and temporal dynamics of disease, and their consequences have been explored in theoretical and comparative studies (described in Box 4.3). Additional factors that increase the realism and complexity of host–parasite interactions are described in Section 4.4.



$$\frac{dS}{dt} = a(S+I+R) - bS - \beta SI + \gamma R$$

$$\frac{dI}{dt} = \beta SI - (\alpha + b + \nu)I$$

$$\frac{dR}{dt} = \nu I - (b + \gamma)R$$

$$\frac{dN}{dt} = (a-b)N - \alpha I$$

Fig. 4.4 Schematic diagram and differential equations for a typical SIR compartment model for a directly transmitted microparasite.

4.2.1.1 Basic reproductive number

The basic SIR model gives rise to several key principles that characterize host–pathogen interactions and have important consequences for infectious disease dynamics in wild populations. Probably the most important issue for any infectious disease is whether it will invade and establish in the host population. A related question concerns how fast it spreads. Both of these issues can be addressed by the basic reproductive number, R_0, which sets the conditions under which pathogens can increase in prevalence when the disease is initially rare. Formally defined, R_0 is the number of secondary infections produced by a single index case introduced into an entirely susceptible host population (Anderson and May 1991; Dietz 1993; Heesterbeek 2002). This is estimated by multiplying the expected number of new infections from a single infected host (βS, where initially $S \approx N$, the total population size) by the average duration of infectiousness, D, where $D = 1/(\alpha+b+\nu)$. Thus, for the SIR model in Box 4.1,

$$R_0 = \frac{\beta S}{\alpha+b+\nu} \tag{4.1}$$

As in Box 4.1, β corresponds to the pathogen transmission parameter, α denotes disease-induced mortality rate, b captures host background mortality rate, and ν corresponds to host recovery rate from infection. In a deterministic system, R_0 defines a break-even point above which the pathogen will establish in the population and below which the pathogen will decline to extinction. In other words, R_0 must exceed 1.0 for the disease to invade (although in a stochastic system, the pathogen could go extinct even if $R_0 > 1$, and could increase if $R_0 < 1$, albeit with low probability; Lloyd-Smith et al. 2005).

Values for R_0 clearly differ among infectious diseases and also can change over space and time for the same pathogen (Dietz 1993). For the model in Box 4.1, the form of Equation (4.1) suggests that pathogens with high transmission rates (β), low virulence (α), and low host recovery (ν) should have the highest R_0 values, and that pathogen spread will also be favored by high host population size and low host background mortality. Approaches for deriving expressions for R_0 in more complicated systems (such as when host populations are structured by age, sex, or other heterogeneities) have been developed by Diekmann *et al*. (1990), Hasibeder and Dye (1988), and others.

Once an epidemic has started, the larger the size of R_0, the faster the disease will spread, although this will depend on whether R_0 is large due to a longer infectious period or because of greater transmission potential. Thus, pathogens with low values of R_0 should generally cause longer epidemics with lower peak prevalence, and pathogens with high R_0 values should initiate rapid epidemics with higher peak prevalence. Once an epidemic is underway, a parameter defined as R measures the number of subsequent cases following the initial secondary infections. In the absence of control measures, $R = R_0 s$, where s is the remaining proportion of susceptible hosts in the population. This is an important concept and shows that the per

capita rate of spread of a pathogen will decrease over time as animals are removed from the susceptible class. For most directly transmitted pathogens, the expectation is that the susceptible class will eventually be reduced to a break-even point that roughly corresponds to $R = 1$, and this also corresponds to the threshold population size described in Equation (4.2) below.

Estimating R_0 is an important step toward management and intervention of epidemic pathogens (Table 4.2), but it has rarely been calculated in wild primate populations. In a perfect scenario, known parameter values for transmission (β), host population size, and the duration of the infectious period (D) can be used to evaluate expressions such as Equation (4.1). On the other hand, this information is usually incomplete and reliable values for β are extremely elusive (Heesterbeek 2002). Several methods for estimating the reproductive number rely on detailed knowledge of host longevity or retrospective studies of epidemics that recently subsided. For well-studied endemic

Table 4.2 Estimated values of the basic reproduction number, R_0, for some infectious diseases in humans and wildlife

Pathogen	Site	Time	R_0	Reference
Pathogens in human populations				
Measles virus	England	1950–68	16–18	Anderson and May 1991
Polio virus	USA	1955	5–6	Anderson and May 1991
Smallpox virus	Developing countries	Pre-1960s	3–5	May 1983
Malaria, *Plasmodium falciparum* and *P. malariae*	Nigeria	1970s	16–80	Anderson and May 1991
Hepatitis C Virus, subtypes 1a,b	Southeast Asia Africa, Global	1900–2000	2–4	Pybus et al. 2001
Ebola virus	Congo, Uganda	1995, 2000	1–2	Chowell et al. 2004
SARS virus	Singapore, Hong Kong	2002–03	~3	Lipsitch et al. 2003
Pathogens in wildlife or domesticated animals				
Phocine distemper virus	North Sea	1988	2–3	Swinton et al. 1998
Foot and mouth disease	Europe	2001	4.5	Ferguson et al. 2001
Bovine tuberculosis	South Africa	2004	2–2.5	P. Cross, personal communication
Bovine spongiform encephalopathy (BSE)	Europe	1988[1]	10–12	Ferguson et al. 1999
Rabies	Kenya	1992–1993[1]	2.4	Kitala et al. 2002

[1] Values shown for before control measures were set in place.

pathogens infecting host species such as humans, where detailed demographic data are available, R_0 can be estimated as the host life expectancy (L) relative to the average age of infection (A, that is, $R_0 = L/A$), assuming that the pathogen is constantly present and that host demographic rates are relatively unchanging (Anderson and May 1991). This approach has been applied to a variety of human pathogens including measles virus, poliovirus, and HIV-1 and 2 (Table 4.2).

Observed changes in the number of cases early in an epidemic can also be used to estimate R_0 from the rate of exponential growth of the pathogen (r), assuming that the infectious period, D, is also known (Keeling et al. 2003; Lipsitch et al. 2003). It has even become possible to use gene sequence data to estimate R_0 and temporal changes in pathogen population size (Pybus et al. 2001; Yusim et al. 2001). In this approach, coalescent theory is used to infer historical changes in pathogen population size (the "effective number of infections") from molecular phylogenies constructed using pathogen gene sequence data, as based on comprehensive sampling of contemporary cases. Results provide estimates for the pathogen growth rate, from which R_0 can be determined using plausible information on D (reviewed in Holmes 2004). Finally, retrospective approaches can be used to estimate R_0 for newly emerged pathogens in situations in which there is lifetime immunity (Swinton et al. 1998; Gani and Leach 2001). One approach is to sample a host population after an epidemic wave has subsided and ask what fraction of animals remain susceptible and hence unexposed (Tompkins et al. 2002). Assuming the entire population was susceptible at the onset of the outbreak, greater values of R_0 will result in lower fractions of susceptible hosts after the epidemic has run its course.

4.2.1.2 Threshold population size and pathogen persistence

The establishment and persistence of many directly transmitted parasites can be related to a critical population density of susceptible hosts below which $R_0 < 1$. The break-even point at which a parasite can just invade the system is known as the threshold host density that must be exceeded for parasites to increase (N_T). Assuming that the population is homogeneously mixed (as in Box 4.1), N_T is calculated as:

$$N_T = \frac{\alpha + b + \nu}{\beta} \tag{4.2}$$

Thus, pathogens that are highly virulent (high α) or have lower transmission rates (low β) should require much higher host densities to establish than those that are highly transmissible and relatively benign. Comparison of Equations (4.1) and (4.2) shows that pathogens with high R_0 values tend to be those with low threshold density requirements.

Evidence for threshold host densities has been documented for several microparasites infecting wild mammal populations. Fox rabies in Europe and brucellosis in American bison appear to be unable to establish in areas where the density of susceptible hosts is too low (Anderson et al. 1981; Dobson and Meagher 1996a). In Serengeti lion populations, outbreaks of several viruses (including coronavirus,

calicivirus, parvovirus, and canine distemper virus) coincided with periodic accumulation of susceptible animals born into the population, and each virus appeared to have its own threshold number of susceptible animals beyond which outbreaks occurred (Packer et al. 1999).

Relative to establishment, predicting pathogen persistence is more challenging, as this can depend on chance encounters between a few remaining infectious hosts and susceptible individuals. These encounters can be highly variable and will be complicated by the finite nature of new births and the spatial distribution of susceptible animals left in the population (Keeling et al. 2001). In addition, threshold population sizes for persistence will be higher than invasion thresholds if recovered hosts maintain lasting immunity, so that new births are required to rebuild the susceptible population.

Persistence thresholds for human diseases are related to the concept of a *critical community size*, which reflects the smallest number of susceptible hosts in a given population below which infectious diseases are likely to go extinct, and above which they are likely to persist or remain endemic (Bartlett 1960; Keeling and Grenfell 1997b). Persistence thresholds have been demonstrated for human diseases like measles and whooping cough that can persist in large cities but "fade out" in smaller towns (Keeling and Grenfell 1997b; Rohani et al. 2000). Among wildlife populations, mathematical models were used to show that the persistence thresholds for phocine distemper virus (PDV) in harbor seals exceeded the global population size of this host species (Swinton et al. 1998), pointing to introductions from other host species as a requirement for initiating new outbreaks. For many wildlife disease systems, however, thresholds for parasite invasion and persistence are difficult to detect, particularly for small or subdivided host populations (Lloyd-Smith et al. 2005).

Finally, the threshold density for pathogen persistence is relevant for the use of vaccination programs to control infectious diseases (Box 4.2), as eradication requires reducing the density or frequency of susceptible hosts below a level at which the parasite can no longer maintain chains of transmission. Vaccination strategies have been employed to control diseases like measles and polio in human populations, and were instrumental in the worldwide eradication of smallpox (discussed in Chapter 8). Among wildlife populations, vaccines distributed with oral bait have been successful in slowing or halting the spread of rabies in foxes and raccoons (see section 7.4.5), but widespread vaccination programs to limit pathogen persistence have rarely been employed in wild primates.

4.2.1.3 Frequency- and density-dependent transmission

Parasite transmission strategies determine the rate at which susceptible animals become infected and are arguably the most important factor governing the spread of infectious diseases (Begon 2002). A fundamental issue for transmission concerns how host contact rates change in response to host population size or density (Box 4.3, McCallum et al. 2001). In most simple models of contagious infections, transmission is assumed to occur via a "mass action" process in which random

Box 4.2 Host immunity and vaccination

Theoretical models show that if recovered hosts gain lasting immunity to future infections, then a significant number of hosts at equilibrium can be resistant to infection. The presence of lasting immunity is important because this can affect both temporal dynamics and management of disease outbreaks using immunization strategies. Systems characterized by lasting immunity following recovery can express marked cycles in prevalence (Anderson and May 1991). These oscillations result because parasites spread and exhaust their base of susceptible hosts rapidly, and after recovery these hosts are removed from the susceptible class. The number of susceptible hosts can slowly recover through new births or loss of immunity, eventually resulting in enough hosts to sustain another outbreak (Grenfell and Bjørnstad 2005). The effects of lasting immunity on disease dynamics will depend on recovery rates, whether or not recovered hosts gain life-long immunity to infection, and host turnover rates in the absence of disease.

Host immunity and the concept of a threshold density phenomenon are also closely related to the idea that vaccination-based efforts can limit the spread of parasites or eradicate them by reducing the abundance of susceptible hosts (see section 4.2.1.2). More precisely, the critical proportion of a well-mixed population that should be immunized to allow eradication of a directly transmitted disease is $p_c = 1 - (1/R_0)$, with the goal of driving susceptible host density below N_T (i.e. $p_c = N/N_T$). Even if the fraction of hosts immunized does not reach this critical level, vaccination programs can still slow the spread of disease considerably at the population level by reducing the effective R_0 of the pathogen. Similarly, *herd immunity* is a phenomenon whereby susceptible hosts are protected from infection due to a high frequency of immune individuals in the population (Anderson and May 1991).

encounters between infected and susceptible hosts increase directly with greater host density (a phenomenon called *density dependent transmission*; illustrated in the SIR model outlined in Box 4.1). In this case, the number of new infections per unit time is modeled as βSI, or a product of the transmission parameter β and the number of susceptible (S) and infected hosts (I). Although some confusion exists regarding whether S and I refer to overall population size or density (numbers per unit area), this transmission function has been used to model a large number of host–parasite systems.

On the other hand, for infections limited by more fixed numbers of contacts—as might result from restricted behavioral processes such as mating—the transmission process is not expected to increase directly with host population size or density (Box 4.3). Instead, an individual animal's probability of encountering the pathogen will depend on the relative probability that a particular encounter is with an infected host. In the case of sexual transmission, for example, the rate at which animals encounter an infected mate depends more on the chance that any given mate is infected rather than on total host density (unless, of course, animals mate more often in more dense populations). In this case, new infections arise according to the frequency of infected hosts ($\beta SI/N$). This process has been termed *frequency-dependent transmission* (Getz and Pickering 1983), and it probably characterizes

Box 4.3 Modeling pathogen transmission and host contact rates

For parasites transmitted by host contact, a general way of describing the process that leads to new infections is to consider the number of new infections (λ) as a function of the contact rate (C(N)), per contact transmission probability (ϵ), and the chance that any given encounter will be with an infected host (I/N).

$$\lambda = C(N)\epsilon\frac{I}{N} \tag{4.3}$$

The contact rate $C(N)$ describes the relationship between the number of host contacts per unit time and host population density (Getz and Pickering 1983; Heesterbeek and Metz 1993; Thrall et al. 1998). This contact rate can increase directly with host population size [$C(N) = cN$ for density-dependent transmission], or remain constant over a wide range of population densities [$C(N) = c$ for frequency-dependent transmission]. Note that for density-dependent transmission, equation (3) reduces to $\lambda = \epsilon cSI$, which can also be written as βSI. By comparison, for frequency-dependent transmission, equation (3) reduces to $\lambda = \epsilon cSI/N$, otherwise written as $\beta SI/N$. The distinction between these two transmission strategies emphasizes that the transmission parameter β is actually a composite variable that captures multiple processes, and that the units of β differ for density- and frequency-dependent transmission (Begon et al. 2002)—a point that is highly relevant to estimating transmission rates in captive and wild systems (Knell et al. 1998; Caley and Ramsey 2001).

When transmission is decomposed into contact rates and per contact transmission probabilities, it is possible to capture a range of strategies along a continuum between density and frequency-dependent processes (Dietz 1982). This is important because in reality, parasite transmission is neither purely frequency- nor density-dependent, but is probably a complex function of both, with spatial or behavioral processes tending to produce transmission rates that are intermediate between density- and frequency-dependence (Antonovics et al. 1995; Knell et al. 1996; Begon et al. 1999; McCallum et al. 2001; Fenton et al. 2002). Where the parasite lies on the density- to frequency-dependent continuum is a crucial determinant of host–parasite dynamics. For example, Begon et al. (1999b) studied the transmission dynamics of cowpox virus (family Orthopoxviridae, related to smallpox virus) within and between wild populations of bank voles and wood mice in Britain. This virus is directly transmitted by close contact, and hence new infections might have increased directly with host density. Counter to expectations, however, results showed that a model based on frequency-dependent transmission provided a better fit to the data than one based on density-dependent transmission. Similar approaches could be taken for directly transmitted pathogens in primates, such as SIV, STLV, and hepatitis viruses, to explore whether the incidence of infection changes as a function of host density, or whether it depends more closely on the proportion of infected animals and rates of specialized encounters.

In the case of vector-borne diseases like malaria and Dengue fever, the risk of infection is a complex function of the vector biting rates (i.e. number of bites by vectors per host per unit time), and the proportion of vectors that are infectious based on their previous contact with an infected host (Macdonald 1957). In some cases, the transmission of vector-borne diseases can share features similar to frequency-dependence if the vector actively searches for hosts and compensates for decreased host density by increasing its movement among hosts (Antonovics et al. 1995). For many helminths or diarrheal diseases that have free-living stages that persist outside of the host, these stages can be modeled explicitly in terms of their rates of accumulation, persistence in the environment, and uptake by susceptible animals (Anderson and May 1980). Although we do not describe their dynamics in detail here, the consequences of these and other transmission strategies have been explored in many theoretical and comparative studies (Getz and Pickering 1983; Molineaux 1985; Thrall et al. 1993a; Lipsitch et al. 1995b).

many STDs (Thrall et al. 1993a; Antonovics et al. 1995; Thrall and Antonovics 1997).

Several studies have contrasted host–parasite dynamics for STDs characterized by frequency-dependent transmission with the dynamics of ordinary infectious diseases (OIDs) characterized by density-dependent transmission (Box 4.3, Getz and Pickering 1983; Thrall et al. 1993a). Perhaps the most striking result is that the host density threshold expressed in Equation (4.2) disappears if parasites are transmitted by a frequency-dependent rather than a density-dependent process (Getz and Pickering 1983). In this situation, the spread of pathogens with frequency-dependent transmission remains relatively constant over a range of host densities, so that in deterministic systems, parasites with frequency-dependent transmission should invade and persist at arbitrarily low host densities. Using a modeling approach, Thrall and Antonovics (1997) derived conditions under which an STD could invade and displace a direct-contact pathogen. Compared to an OID, invasion by the STD was easier in smaller populations associated with lower rates of contact. Conversely, the OID could invade more easily in larger host populations characterized by higher contact rates (Fig. 4.5). In a later paper, these authors proposed the concept of a social-sexual crossover point (SSCP). Increased sexual transmission was always favored if the equilibrium population size was less than the SSCP; otherwise, non-sexual transmission was favored (Thrall et al. 1998).

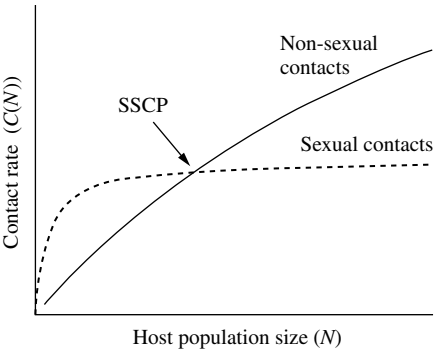


Fig. 4.5 Relationship between effective contact number (the number of contacts per unit time that actually result in disease transmission) and host population size (N), which refers to the number of animals in proximity to a target host with which it could potentially interact. The arrow indicates the social-sexual crossover point (SSCP) where the number of nonsexual contacts exceeds the number of sexual contacts. Because even at low population densities, individuals will still actively seek out sexual contacts for reproductive purposes, the number of sexual contacts is generally assumed to initially increase rapidly even at low host density, but to reach an asymptote at lower total numbers (due to longer contact periods associated with sexual versus nonsexual contacts). Figure modified from Thrall, P. H., Antonovics, J., Wilson, W. G. "Allocation to sexual vs. nonsexual transmission." *American Naturalist* 151: 29–45.

4.2.2 Macroparasite models

In contrast to many microparasites, macroparasites like worms and arthropods cause persistent infections, and their aggregated distributions mean that a small fraction of the host population usually accommodates most of the parasites (Fig. 4.2). Furthermore, because effects on host fitness and the production of infectious stages depend on the number of parasites harbored by individual hosts (Chapters 1 and 2), macroparasite population models must account for variation in the numbers of parasites per infected animal. The biology of macroparasites with direct life cycles (see Fig. 2.2) is relatively straightforward to translate into a mathematical framework, with adult worms inside host animals releasing infectious stages into the environment and new infections resulting when hosts encounter or ingest parasite eggs or larvae (Box 4.4).

Macroparasite models typically track the density of the entire host population (H), the abundance of adult parasites within hosts (P), and the number of free-living parasite stages in the external environment (W). The model in Box 4.4 also assumes that parasites are aggregated within hosts according to the negative binomial distribution, where the degree of aggregation varies inversely with k (see Fig. 4.2). As indicated by the equations, the mortality of adult parasites is affected by within-host clustering, with parasite mortality increasing when k is small (i.e. when parasites are highly aggregated).

The basic reproductive number of macroparasites is the product of the mean number of new infections produced by a single adult parasite and the average life expectancy of adult and larval stages:

$$R_0 = \frac{\beta \lambda H}{(\mu + b + \alpha)(\gamma + \beta H)} \tag{4.4}$$

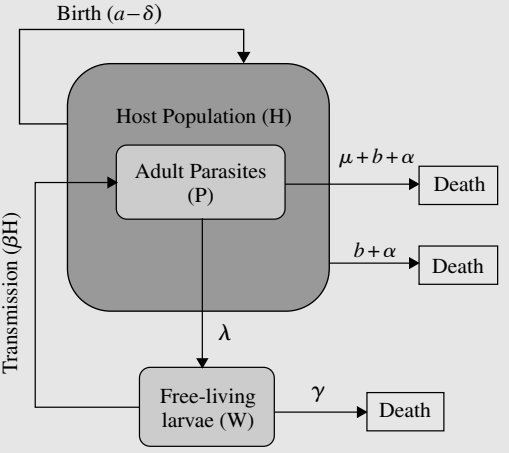
As with microparasites, Equation (4.4) must exceed 1.0 for the parasite to establish when rare. Therefore, parasite invasion and persistence depend strongly on the rate of production of eggs or larval stages (λ), the rate at which hosts consume parasite infectious stages (β), and the survival of infective stages outside of the host (1-μ). The threshold host population necessary to sustain infection is:

$$H_T = \frac{\gamma(\mu + b + \alpha)}{\beta(\lambda - (\mu + b + \alpha))} \tag{4.5}$$

Because the mortality rates of adult and larval parasites are likely to be low (larval parasites often have long-lived resistant stages and adult worms can live for years within their hosts), and the transmission rate of macroparasites is relatively high (especially when infective stages actively seek out their hosts), this model predicts that macroparasites should be able to persist at lower host population densities than many directly transmitted microparasites.

Box 4.4 Models for host-macroparasite interactions

Mathematical models for host-macroparasite infections often track the numbers of adult worms inside host animals and the size of the host population. Adult worms release infectious stages into the environment, and hosts become infected through encounters with parasite eggs or larvae. This diagram depicts a host population of size H, harboring an adult parasite population of size P. As in the microparasite model (Box 4.1), per capita host birth and death rates are denoted by a and b, respectively. Adult parasites give birth to free-living infective stages at rate λ, and die as a result of three different processes: parasite background mortality (μ), host background mortality (b), and parasite-induced host mortality (α). Thus, the model assumes that when hosts die so do their parasites. Free-living egg and larval stages die in the external environment at rate γ and are encountered by hosts at rate β, thus giving rise to new adult infections. Adult parasites can induce host sterility and mortality at rates δ and α, respectively; these are per capita rates induced by each individual parasite and assume that overall host death rate rises linearly with parasite burden. Relatively simple host-macroparasite models developed by Anderson and May (1978) have been modified by Dobson and Hudson (1992), Roberts and Grenfell (1992), and others to incorporate the presence of free-living infective stages, arrested parasite development, and complex life cycles (Fig 4.6).



$$\frac{dH}{dt} = (a-b)H-(\alpha+\delta)P$$

$$\frac{dP}{dt} = \beta WH-(\mu+b+\alpha)P-\alpha\,\frac{P^2}{H}\,\frac{(k+1)}{k}$$

$$\frac{dW}{dt} = \lambda P-\gamma W-\beta WH$$

Fig. 4.6 Schematic representation of host and parasite life cycle for macroparasitic infections and accompanying differential equations.

4.3 The role of parasites in regulating host populations

Because parasites are rarely seen and frequently cause only mild or sublethal effects, it is commonly thought that their impacts on animal abundance are minor, perhaps accounting for occasional mortality among very weak, young, or old animals. Counter to this view, epidemiological models and a growing number of wildlife-parasite examples point to a number of conditions under which parasites can regulate host population size (Scott and Dobson 1989). In some extreme cases, infectious agents have caused precipitous losses of 50% or more of existing host populations, as occurred with morbillivirus epidemics in black-footed ferrets and harbor seals and more recently with transmissible facial tumors affecting Tasmanian devils (Thorne and Williams 1988; Harding et al. 2002; Bostanci 2005). In other cases, removal of endemic parasites revealed that parasites were a significant factor depressing host population size or were responsible for generating dramatic population cycles in host abundance (McCallum and Dobson 1995; Hudson et al. 1998a). It is important to note that host regulation can arise from both within-species processes, such as competition for limited resources, and from species interactions like predation, interspecific competition, and parasitism. Confusion in identifying regulatory mechanisms often arises because most species are affected by a combination of biotic density-dependent factors and extrinsic environmental variation (May 1983; Bjørnstad and Grenfell 2001), making it difficult to tease apart processes that contribute to population dynamics in non-experimental systems.

4.3.1 Theoretical predictions

Parasites can impact total host population size (N) through their effects on individual host fitness, including parasite-induced host mortality and reductions in host fertility. To illustrate this mathematically for the microparasite model shown in Box 4.1, the change in total host population size can be written as,

$$\frac{dN}{dt} = (r - \alpha y)N \tag{4.6}$$

where the intrinsic growth rate of uninfected hosts is $r = a - b$, the prevalence of disease is $y = I/N$, and α is disease-induced host mortality. Equation (4.6) implies that one mechanism by which parasites regulate their hosts is through disease-induced mortality (α) that offsets the host's intrinsic growth rate. Somewhat surprisingly, if pathogens affect host mortality alone, those with intermediate virulence will depress host density to a greater degree (the upper-right face of Fig. 4.7). This is because more lethal parasites are more likely to also kill their hosts before transmission to other hosts occurs (Anderson and May 1979; Anderson 1982a; McCallum 1994), so that the more virulent a parasite, the lower its expected prevalence in the population. Indeed, highly virulent parasites do not appear to reduce equilibrium host density, although they could induce short-term population declines.

A striking element of Fig. 4.7 is that equilibrium host abundance is lowest when parasites completely sterilize infected animals with no additional host mortality (as shown in the lower corner of this graph). Such negative effects on host reproduction have been demonstrated across a range of animal–parasite systems including helminths infecting red grouse, hares, and reindeer (Hudson et al. 1985, 1992; Stien et al. 2002; Newey and Thirgood 2004). Further investigation of these issues in wild primates would undoubtedly produce similar examples (e.g. Milton 1996). In the case of helminth infections, parasite-induced reductions in host fecundity can also trigger oscillations in host abundance (May and Anderson 1978; Hudson et al. 1998a), especially when parasites have long-lived infectious stages that persist in the environment (Dobson and Hudson 1992). Collectively, these points suggest that infectious diseases with low or moderate effects on host survival or those that sterilize their hosts may cause far greater conservation concerns and should not be overlooked when assessing potential causes of wildlife declines.

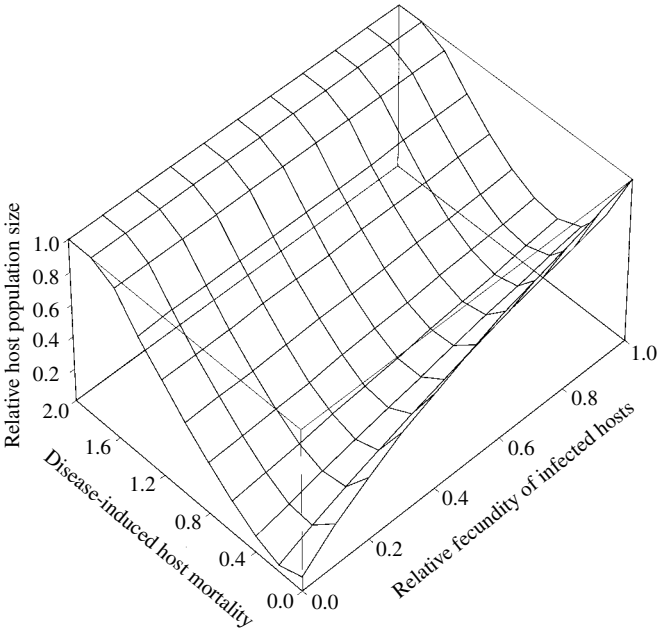


Fig. 4.7 Parasite-mediated reduction of host population size in relation to disease-induced host mortality and the relative fecundity of infected hosts. Higher values of host mortality (towards the left) and lower levels of fecundity (to the bottom) indicate greater negative effects on the host (i.e. virulence). Results are based on a modified version of the model in Box 4.1, with frequency-dependent transmission and density-dependent births (i.e. additional host regulation in the absence of disease). Shown on the vertical axis is host population size relative to the disease free carrying capacity (i.e. N^*/K) in the presence of the pathogen. Other parameters used were: $a = 0.5$, $b = 0.35$, and $\beta = 3$.

Simple inferences about host regulation assume that parasites have a narrow host range and cannot rely on a reservoir host for persistence. As discussed below, pathogens with a wide host range that are relatively benign in reservoir hosts can have severe consequences for endangered or rare species (McCallum and Dobson 1995). Furthermore, parasites whose transmission is density-dependent should have stronger effects on high-density host populations (Anderson 1978; Getz and Pickering 1983), and can induce striking host population cycles. Because density-dependent diseases in theory require a threshold host density for establishment and persistence, they should be unlikely to cause host extinction when acting alone (Anderson and May 1979). Pathogens with frequency-dependent transmission, on the other hand, can persist and continue to spread even in low-density host populations.

Relative to microparasites, host regulation by macroparasites further depends on the degree to which parasites are aggregated among hosts (Anderson and May 1978; May and Anderson 1978; Tompkins et al. 2001). This effect arises because hosts that harbor high numbers of parasites are most likely to be removed from the population, whereas host with few parasites might experience little or no reductions in fitness. When a large proportion of a macroparasite population is aggregated in a small proportion of the hosts, stable regulation is more likely, although at the other extreme, parasites can be so aggregated that the host escapes regulation entirely. As most macroparasites show aggregated distributions (Shaw and Dobson 1995; Shaw et al. 1998; Wilson et al. 2001), it seems probable that these parasites play some role in regulating wild populations. A related point is that wildlife managers might expect regulating parasites to be abundant in a high proportion of the host population, including a large number of dead animals. Counter to this expectation, mathematical models suggest that regulation by endemic macroparasites is probably more likely when high parasite burdens are seen in only a few infected animals (McCallum and Dobson 1995).

4.3.2 Regulation in experimental and natural populations

A common misconception is that parasite effects on host abundance can be inferred using information on prevalence alone, or observations of parasite-induced host mortality (McCallum 1994; McCallum and Dobson 1995). Unfortunately, modeling approaches suggest that counter to common wisdom, the most frequently observed causes of mortality are not necessarily the most important regulatory factors (Anderson and Gordon 1982). In natural systems, therefore, observing host population abundance and demographic rates in both the presence and absence of parasites is probably the best way to examine the population-level impact of infectious disease (Scott and Dobson 1989; Tompkins and Begon 1999; Hochachka and Dhondt 2000).

Only a handful of studies have been conducted to examine the population level effects of disease in wild populations. In extreme cases, the effects of disease on host abundance are obvious, as when populations of European rabbits (*Oryctolagus cuniculus*) in Australia and Europe collapsed following the intentional introduction of myxoma virus during the 1950s, and later, calicivirus during the late 1990s

(Fenner and Fantini 1999). Similar dramatic declines in host abundance were observed when populations of harbor seals in the North Sea crashed during outbreaks of phocine distemper in 1988 and 2002 (Heide-Jorgensen et al. 1992; Jensen et al. 2002). One thorough and groundbreaking analysis quantified the impacts of a bacterial eye disease (caused by *Mycoplasma gallisepticum*) that emerged in wild house finches (*Carpodacus mexicanus*) in North America starting in 1993. Researchers used observed prevalence and host abundance data at a continent-wide scale to show that as this disease spread across the house finches' eastern range, host populations dropped sharply to around 40% of their expected disease-free abundance (Hochachka and Dhondt 2000). This analysis also showed that higher density populations suffered more severe declines, relative to areas with lower host density. Evidence indicates that the eye disease probably caused host population declines through effects on individual survival rather than fecundity, as the timing of outbreaks generally occurred during the fall and winter (outside of the breeding season, Altizer et al. 2004) and birds with severe infections, where one or both eyes swelled shut, probably died of exposure, starvation, or predation (Dhondt et al. 2005).

Although a few studies have the advantage of comparing host abundance before and after pathogen introduction, experiments are essential to document parasite effects to the exclusion of other regulatory factors, in part because it is difficult to establish regulation when populations harboring endemic parasite infections are in equilibrium (Tompkins et al. 2002). In manipulative experiments, researchers treat a fraction of animals or a subset of populations—either by experimentally adding parasites or by using anti-parasitic drugs or vaccination to lower infections—and treat other animals (controls) with placebos. Survival and fecundity at the individual level, together with population size and growth rates, can be compared among treatment and control groups. A classic experimental study of population regulation by parasites was conducted in a freely breeding colony of mice. In large arenas housing up to 1000 individual mice, Scott (1987b) introduced a helminth (*Heligmosomoides polygyrus*) that parasitizes mice in the wild. Whereas the unexposed control population increased and maintained a high population size, the parasite-treated populations crashed rapidly to very low abundance (Fig. 4.8), only recovering after antihelminthic treatment was given. Because mice in these enclosures reproduced freely and had access to abundant resources, this study underscored the potential importance of parasites relative to competition for food or space. In the field, experimental approaches have demonstrated impacts on host survival or population size induced by nematode parasites on feral Soay sheep (see fig. 1.5, Gulland 1992; Gulland et al. 1993b), botfly parasites in wild mice (Munger and Krasnov 1991), and caecal nematodes on population cycles of red grouse (Hudson et al. 1998a).

We currently have limited knowledge of parasite-induced population regulation in primate hosts, but this should not discourage experimental work on suitable primate subjects (Janson 2000). Although some researchers have proposed that parasites can regulate primate populations (Freeland 1976; Smith 1977; Milton 1996), no experimental studies of population regulation in wild primate have been conducted to date. Records of severe population-level mortality have been recorded in a number of primate populations (summarized in Chapters 1 and 7). In the absence of experimental

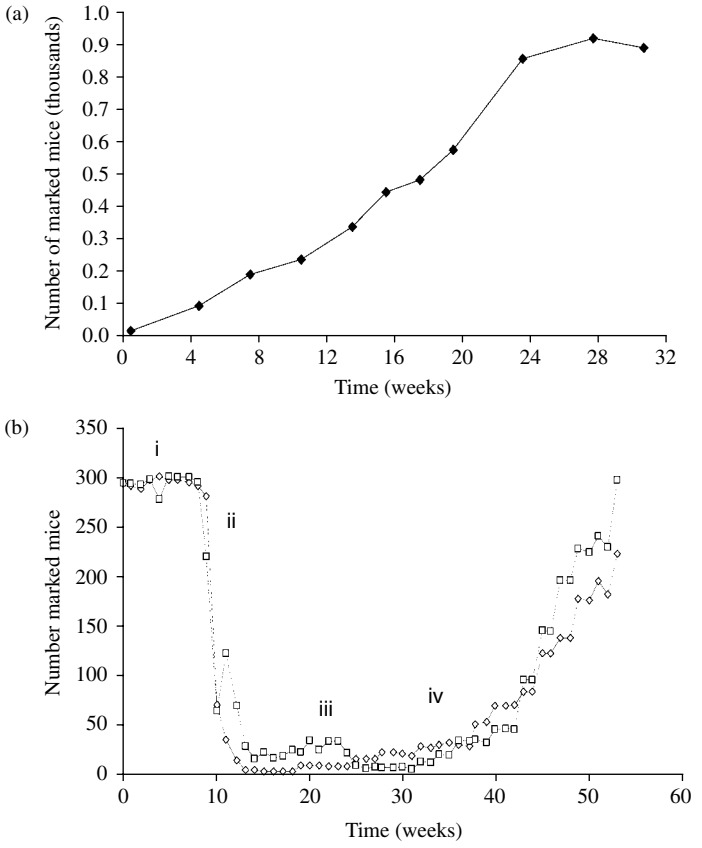


Fig. 4.8 Effect of the nematode parasite *Heligmosomoides polygyrus* on the abundance of mice in experimental enclosures in a parasite addition-removal study. (a) Number of mice in an uninfected population over time (in thousands). (b) Number of mice in two experimentally treated populations. (i) Mice were maintained at N = 300 during the first 5 weeks, after which time (ii) parasites were added, and this was followed by a dramatic crash in population size (iii) which then remained low. During phase (iv), mice were treated with an antiparasitic drug, after which population size increased rapidly. Data from Scott (1987a). Modified from Scott, M. E. "Regulation of mouse colony abundance by *Heligmosomoides polygyrus*." Parasitology 95: 111–124. Copyright (1987) with permission from Cambridge University Press.

data, researchers can only extrapolate from experimental studies in other taxa to understand likely patterns of regulation in natural populations of primates. Clearly, many primate parasites cause significant pathology, and combining limited information on transmission and virulence with theoretical modeling approaches could allow researchers to draw inferences for parasite-mediated impacts on abundance of primate populations, as has been done for other species (Anderson and Gordon 1982; Scott and Dobson 1989). In some cases, wild primates have been vaccinated against disease—including mountain gorillas vaccinated against measles following an outbreak

attributed to human introduction (Hutchins et al. 1991, Chapter 7). It is conceivable that experimental "removal" approaches, similar to those described above, could be adapted to study parasite-induced population dynamics of primate hosts in long-term wild populations or free-ranging populations, such as among the rhesus macaques on Cayo Santiago. Another useful approach for primates involves using radio tracking and visual observations to monitor the behavior and vital rates in animals with known parasite burdens (Faustino et al. 2004). These studies should obviously be conducted in populations in which comprehensive long-term monitoring is possible.

4.4 Heterogeneities and dynamical complexities

The dynamics and persistence of infectious diseases cannot be understood without considering the role of ecological and genetic heterogeneities that influence parasite transmission dynamics (Rand et al. 1995; Hagenaars et al. 2004). Unlike the relatively simple homogeneous populations described earlier, populations of wild primates are stratified by age, sex, social rank, or clumped spatially due to naturally fluctuating resources or habitat fragmentation. Further complications arise when pathogens can infect multiple host species, requiring that researchers consider transmission heterogeneities among multiple host species and the consequences for parasite spread and persistence. Here, we briefly examine three factors that should be important for patterns of disease spread in free-living primates: spatial heterogeneity (including landscape features and metapopulation dynamics), host social system, and parasites capable of infecting multiple host species. Several approaches have been developed to examine how different sources of ecological heterogeneity influence disease spread, including metapopulation models, mixing matrices, individual-based models, and social network theory. Not surprisingly, advances gained by modeling approaches have rapidly outpaced field and experimental work. Thus, empirical studies in natural systems are badly needed to identify which heterogeneities are likely to be most relevant in wild primate populations, and how control strategies might be implemented in response to pathogens in heterogeneous environments (Chapter 7).

4.4.1 Spatial heterogeneity: landscape features and metapopulation dynamics

In many other wildlife systems, spatially explicit models have been used to understand the influence of landscape ecology and host dispersal patterns on the spread of newly introduced diseases across a geographic region (Shigesada and Kawasaki 1997; Russell et al. 2004). Perhaps the best examples include rabies infecting foxes (Murray et al. 1986) and raccoons (Smith et al. 2002), where transmission is highly local and host movement is affected by natural barriers like rivers or mountain ranges (see Box 3.3). Consideration of these factors requires information on the spatial configuration of host populations, rates of local and long-distance host

dispersal, and potential natural barriers to host movement. Spatial simulations could point to sites for implementing physical barriers or intensive vaccination efforts to slow or stop pathogen spread (Russell et al. 2005). Detailed records of habitat use, spatial distributions, and between-group contact necessary for such simulations already exist for several wild primate species (Waser 1976; Kappeler 1998b; Di Fiore 2003; Dias and Strier 2003), and these can be augmented by gene flow estimates derived from molecular data (Gagneux et al. 2001). In other cases, monitoring data that track the spatial spread of novel pathogens like Ebola virus can be used to parameterize models, and thus used to predict where new outbreaks might occur and how fast the pathogen will spread in populations of susceptible hosts.

Beyond the details of landscape features, models have also been used to examine disease spread in the context of metapopulation processes more generally (Hess 1996; Carlsson-Graner and Thrall 2002; McCallum and Dobson 2002; Park et al. 2002). In the case of primates, metapopulations (defined as a group of populations or patches between which dispersal can occur) might arise from naturally patchy habitats or the subdivision of host populations into social groups. Loss of suitable habitat caused by forest fragmentation and other habitat changes can further isolate primate individuals or groups into remaining patches, as documented for primate species such as *Cercopithecus mitis, Procolobus badius*, and *Macaca silenus* (Lawes et al. 2000; Singh et al. 2002; Galat-Luong and Galat 2005).

Insights from metapopulation models point to the joint roles of two key processes on pathogen establishment and persistence: (a) within-patch dynamics and (b) local colonization and extinction (Hess 1996; Grenfell and Harwood 1997; Carlsson-Graner and Thrall 2002; Gog et al. 2002). One consequence of metapopulation dynamics is that subdividing a host population into smaller units can increase the critical community size required for pathogen persistence (Park et al. 2002). Thus, local population sizes might be too small for pathogens to persist, and limited movement among patches could further reduce pathogen spread at the entire population level (Hess 1996; Gog et al. 2002). Other models show that host movement among local patches can be crucial to re-colonization following local extinction, allowing hosts to escape to areas not yet affected by parasites, while also facilitating the spatial spread of alleles determining host resistance and pathogen infectiousness (Hassell et al. 1991; Hess 1996; Grenfell and Harwood 1997; Thrall and Burdon 1997). Metapopulation approaches and concepts have tremendous importance for examining the role of habitat fragmentation and isolation in host–pathogen dynamics, including in primates (Cowlishaw and Dunbar 2000). In the context of disease and primate conservation, these issues are addressed in more detail in Chapter 7.

4.4.2 Host social system

Primates are generally social animals, and as such they might experience greater infectious disease risk through increased local density, close proximity, or higher contact rates among host individuals (Anderson and May 1979; Arneberg 2002, see Chapters 3 and 6). The details of host social systems will determine how diseases

spread through populations; pathogens spread within groups through a network of social and mating contacts and between groups through dispersal. Patterns of transmission will also depend on the type of contact and characteristics of interacting individuals. For example, infections are more likely to spread from mother to dependent offspring, or between preferred mating partners, than between individuals that avoid one another at food resources or sleeping sites. Information on the frequency of pairwise contacts can often be extracted from existing data sources on primates, such as grooming matrices or records of group composition and intergroup movements (Sugiyama 1971; Pusey and Packer 1987; Rowell 1991; Isbell and VanVuren 1996).

Several modeling approaches have been applied to capture heterogeneity in patterns of social contact, focusing primarily on the spread of contagious infections in human populations. One strategy is to group individuals into classes (e.g. social status, kinship, or sexual activity) and describe contacts among classes in terms of a "mixing matrix," where the entries in each of the cells describe the frequency distribution of contacts per unit time (Blower and McLean 1991). The most important insight gained from these models is that the pattern of contacts between different activity classes has a major impact on parasite spread (Jacquez et al. 1988). Specifically, a high degree of mixing within an activity class results in a more rapid initial spread but a lower population-wide prevalence, as compared to a higher degree of mixing among activity classes. Despite their importance in human epidemiology, mixing matrices have not been applied widely to animal social and mating systems because detailed information for their construction (contact rates within and among social classes or mating groups) has generally not been available. In the context of a female-bonded primate species, this approach could be applied by developing matrices that measure contact rates among females within and across matrilines, among males, and among males and females.

Stimulated in part by increasing computational power, agent-based or individual-based modeling approaches have been increasingly applied to problems in epidemiology to simulate more realistic contact patterns (Keeling 1999a; Koopman et al. 2002). These models essentially assume that individual animals interact with one another using simple local rules for group formation, within-group contact, and among-group dispersal (see Grimm and Railsback 2005 for more details on individual based models in ecology). For example, Thrall et al. (2000) used individual-based models to show how the spread of an STD in a polygynous host was influenced by variance in male mating success and migration of females among mating groups (Box 4.5). Other individual-based models have been applied to understand patterns of disease spread in social insects (Naug and Camazine 2002; Pie et al. 2004). These models showed that division of labor, limited worker activity, and spatial separation of units within a colony could slow or diminish disease outbreaks. Although these simulation-based approaches can provide insights into the consequences of heterogeneities in behavior, they are relatively data-hungry in terms of the number of traits, and detailed measures of these traits, that are required for model parameterization.

Box 4.5 Dynamics and evolution of STDs

STDs are increasingly recognized as an important parasite group with potentially large impacts on host reproduction and evolution (Smith and Dobson 1992; Lockhart et al. 1996). The characteristics and dynamics of STDs differ from many other infectious diseases. STDs have smaller host ranges, longer infectious periods, and are less likely to cause host mortality or induce protective host immunity (Oriel and Hayward 1974; Smith and Dobson 1992; Lockhart et al. 1996). Characteristics of many STDs also cause their dynamics to differ from other directly transmitted parasites. In particular, STDs tend to persist as endemic (rather than epidemic) infections, with transmission relatively unaffected by increased host density or crowding. They have been described as a unique class of pathogens well adapted to persisting in small, low density host populations (Smith and Dobson 1992), although their presence in large populations is not theoretically precluded. Animals with promiscuous mating systems (or species in which females engage in frequent extra-pair copulations) are predicted to experience a greater risk of acquiring STDs. However, empirical patterns illustrating potential links between host mating behavior and infectious disease risk have not been well documented in mammals or other vertebrates.

The dynamics of most STDs in humans requires consideration of heterogeneities in sexual activity (Anderson and May 1991). For this reason, population models developed to predict the dynamics and control of HIV, syphilis, gonorrhoea and other STDs have focused on human sexual contact patterns (Anderson et al. 1988, 1989; Boily and Masse 1997; Hethcote and Yorke 1984; Garnett et al. 1997). Mathematical models that incorporate heterogeneity in mating behavior show that STD transmission increases with increasing variance in partner exchange rates, and that highly promiscuous individuals ("superspreaders") can facilitate STD persistence even when the mean number of sexual partners is low (Anderson and May 1991). Consistent with models that predict a higher risk of infection among more promiscuous subgroups, surveys of HIV and other STDs in human populations show that prevalence increases with increasing numbers of sexual partners per year (reviewed in Anderson and May 1991). One might expect this generalization to apply to wild mammals with polygynous mating systems, with variance in male mating success at the population level being proportional to increased transmission of STDs.

Using an individual-based simulation model of polygynous mating systems, Thrall et al. (2000) examined how variance in male mating success (i.e. mating skew) affects the spread of STDs, and how this interacts with longevity and the migration of females among mating groups. Their model assumed that males varied in their attractiveness to females, that females had only one mate per breeding season, and that females could change groups between breeding seasons. Two mating system parameters were examined: variation in male mating success (degree of polygyny) and variation in female fidelity to males (dispersal to new groups between mating systems). When females moved frequently among groups, variance in male mating success had a weaker effect on prevalence of infection in females. When intergroup movement was limited, parasites spread more rapidly and reached higher prevalence in groups with more females (i.e. greater polygyny) (Fig 4.9).

A notable outcome of the model by Thrall et al. (2000) was that equilibrium STD prevalence was significantly greater in females than in males. When variance in male mating success was high, many males remained unmated, lowering the equilibrium prevalence among males relative to females. Using published data on two sexually transmitted retroviruses in wild primate populations (SIV and STLV), Nunn and Altizer (2004) found support for the prediction that STD prevalence is higher in females than in males among

Box 4.5 (*Cont.*)

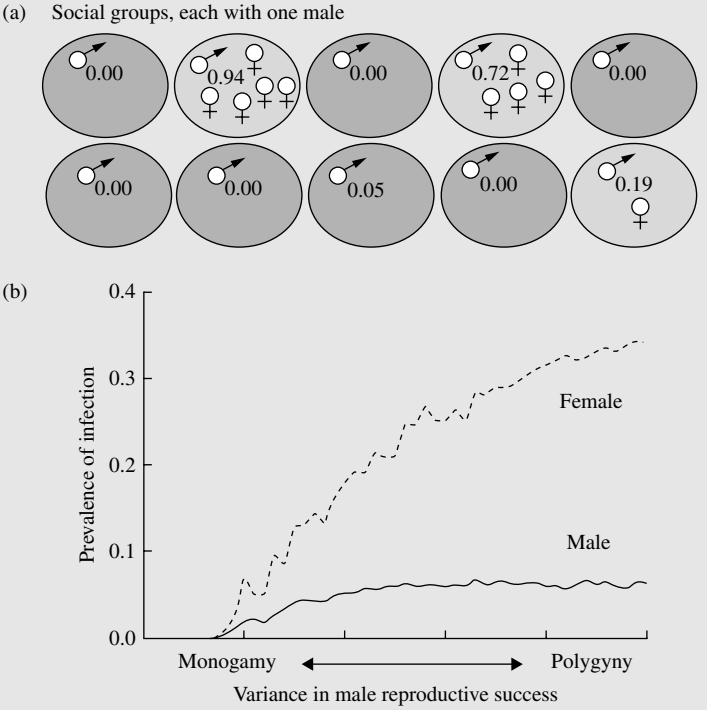


Fig. 4.9 Schematic diagram (a) and results (b) of an individual-based simulation model used to investigate the spread of an STD in males and females within the context of variance in male mating success, female dispersal between groups, and mortality. (a) Each male was assigned an attractiveness score from 0 to 1, and more attractive males were assigned greater numbers of females. The number of males was equal to the number of females. (b) Model results showing the change in population-wide STD prevalence in males and females separately, in relation to overall variance in male mating success. Note that the left side of this figure reflects a more monogamous situation, in which males tend to have single mates, and the right reflects extreme polygyny, in which a few males monopolized all the females in the population. Bottom figure redrawn from Thrall, P. H., J. Antonovics, and A. P. Dobson. Sexually transmitted diseases in polygynous mating systems: prevalence and impact on reproductive success. *Proceedings of the Royal Society London B.*, 267, 1555–1563. Fig 1(a), Copyright (2000) The Royal Society.

non-monogamous species. (see Fig. 3.11). Although these analyses were consistent with the model predictions, alternative explanations are possible, including the possibility that females are more susceptible to STDs. Higher STD prevalence among females has also been reported among captive breeding primate colonies, including sooty mangabeys and baboons (Levin et al. 1988; Fultz et al. 1990).

Box 4.5 (*Cont.*)

Differences in STD prevalence between males and females are more striking because theory predicts the opposite pattern for OIDs, with higher prevalence in males due to energetic costs associated with competition for mates or the deleterious effects of testosterone on immunocompetence (see Chapter 3). Other observations show that males might not only account for more infections, but also contribute disproportionately to the transmission of macro- and microparasites (Perkins et al. 2003a; Ferrari et al. 2004a). Further studies are needed to determine the mechanisms and consequences of sex-biased susceptibility, including its role in the evolution of mate choice and traits that signal parasite infection (see Chapters 5 and 6).

An individual-based simulation model was recently used to investigate how mating group size, group composition, and dispersal rates influenced the ability of a highly pathogenic disease to spread through a susceptible population of primates (Nunn et al. in review). In this model, females were assumed to disperse to new groups when the number of males in their group dropped to zero, which could happen during disease epidemics when the harem-holding male dies. The results from this simulation model revealed that introduced pathogens such as Ebola virus spread the fastest in host systems characterized by highly polygynous groups (Fig. 4.10).

Social network theory represents a third approach that allows researchers to focus directly on how interactions among individuals influence the spread of disease (Moore and Newman 2000). This strategy is borrowed from sociological methods in which researchers investigate relations and connectedness among individuals (Wasserman and Faust 1994), and this basic approach could be applied to model contagious agents in primate social groups. In the most basic sense, network data can be captured by a square array of values, where both rows and columns are the same individuals or subjects, and each cell of the array defines the relationship between two individuals. In this case, each animal or person becomes a point (or node) in a network, and lines (or edges) represent relationships between subjects (Fig. 4.11). In these networks, some animals might have few connections whereas others have many, essentially representing hubs of activity or potential "super-spreaders" of infectious disease. Network models can simulate realistic social and sexual interactions (Jones and Handcock 2003; Cross et al. 2004; Eubank et al. 2004). This approach has been used to evaluate strategies for limiting the spread of human pathogens, including emerging respiratory infections, HIV/AIDS, and potential bioterror agents such as smallpox (Ancel Meyers et al. 2003; Jones and Handcock 2003; Eubank et al. 2004). Information on pairwise relationships between individuals in nonhuman primates could be used to explore disease spread in the context of social interactions (e.g. using grooming matrices, Hemelrijk and Lutejin 1998).

4.4.3 Multi-host dynamics

The majority of parasites examined to date, including many emerging diseases and over 60% of pathogens infecting humans and nonhuman primates, are capable of infecting more than one host species (Murphy 1998; Cleaveland et al. 2001; Dobson and Foufopoulos 2001; Pedersen et al. 2005). These *multi-host parasites* tend to pose problems for a wide array of wildlife species, as evidenced by population declines or high mortality in African carnivores caused by rabies and canine distemper virus, sea otters infected with *Toxoplasma*, and black-footed ferrets infected by canine distemper (Roelke-Parker et al. 1996; Harvell et al. 1999; Daszak et al. 2000; Jensen et al. 2002; Miller et al. 2002). In some cases, outbreaks originate from livestock or animals kept as pets, from recently introduced exotic hosts, or from pathogen exchanges following contact between wild host species that do not normally interact with one another. Despite their apparent importance, however, the dynamics of multi-host parasites in wild animal populations are not well understood (Desdevises et al. 2002), in part because conventional studies focus mainly on single host–pathogen systems (Anderson and May 1991; Bull 1994; Day 2001).

Adding multiple host species to an infectious disease system introduces another level of heterogeneity that can have major impacts on pathogen spread and evolution, as researchers must account for transmission within and between host species and differential effects of parasites on each host (Frank 1993; Begon et al. 1999; Woolhouse et al. 2001; Antonovics et al. 2002; Gandon 2002, 2004; Holt 2003). Theoretical studies point out several key dynamical properties of multi-host pathogens (Dobson 2004; Fenton and Pedersen 2005). First, the presence of reservoir hosts can lead to periodic pathogen resurgence following long durations of disease-free periods in highly susceptible host species (Cleaveland and Dye 1995; Keeling and Gilligan 2000; Haydon et al. 2002a; Swinton et al. 2002). Second, parasites in multiple host systems can intensify disease impacts on sensitive wildlife species (Greenman and Hudson 2000). This effect arises because a pathogen restricted to a rare species is unlikely, by itself, to drive the species to extinction; on the other hand, if the pathogen can infect a common host species, then infections to a less common species can remain high even if that species is declining toward extinction (McCallum and Dobson 1995). Third, host–parasite interactions involving more than two host species can yield complex dynamical outcomes, and often support the proverb that "my enemy's enemy is also my friend" (Dobson and Crawley 1994). For example, parasites can reverse the outcome of competition between host species sharing the same resource if the dominant competitor is more susceptible to infection. *Apparent competition* is a related phenomenon whereby two or more hosts not directly competing for resources are affected by the same parasite, but to different degrees (Holt and Pickering 1985; Greenman and Hudson 1999; Gilbert et al. 2001). In this case, generalist parasites that are relatively benign in one host species may depress the density of other hosts for which they are more pathogenic. These general insights indicate that many threatened species, including a number of

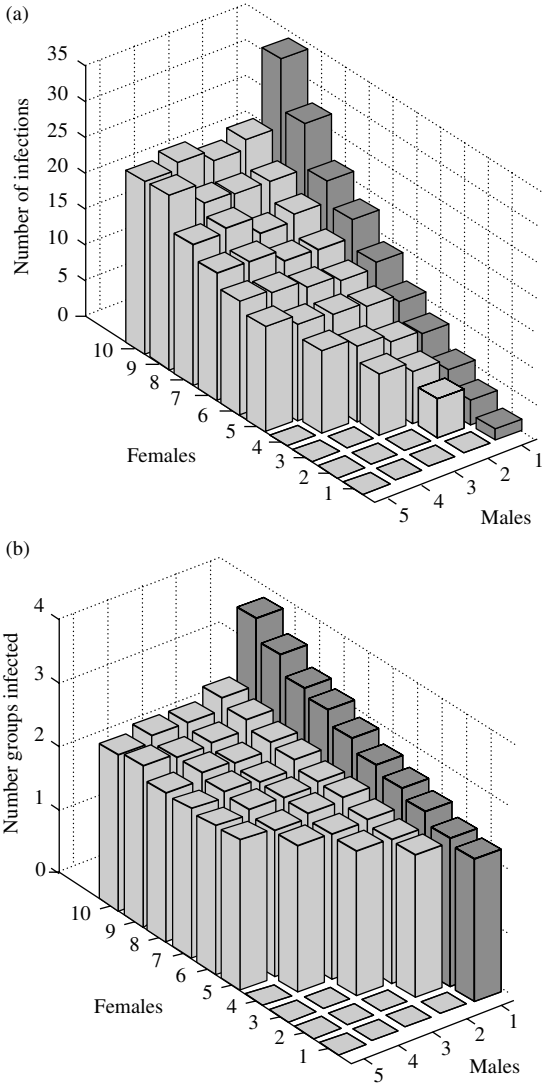


Fig. 4.10 Disease emergence following the introduction of a novel parasite into a susceptible host population defined by different average numbers of males and females per group, and with female dispersal among groups. Plots show (a) average number of infections and (b) average number of groups infected at the end of the simulation, relative to variation in the number of males and females. The parasite establishes more readily in single-male systems (darker bars) due to dispersal of females from groups following the death of the male. Groups were formed and the infection was initiated in one randomly chosen individual, with a user-defined incubation period, disease-induced host mortality rate (virulence), and within-group transmission rate. In this spatially explicit simulation model, dispersing individuals were assumed to move in a random walk through the population until they encountered another group with one or more opposite-sexed individuals. (Nunn et al. in review).

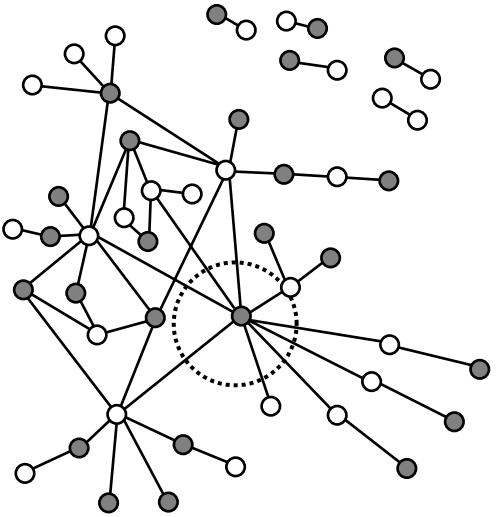


Fig. 4.11 Example of a social (in this case, sexual) network for modeling the spread of directly transmitted infections. In this diagram, the solid circles are males and open circles are females, and the lines connecting individuals indicate sexual relationships. Note that in this network, the typical individual has relatively few partners per year, but there are a few individuals that connect many of the nodes, including the male in the dotted circle who has had mating contacts with nine other partners and represents a major link among these individuals. Modified from Jones, J. H. and Handcock, M. S. "An assessment of preferential attachment as a mechanism of human sexual network formation. *Proceedings: Biological Sciences*. 270: 1123–1128.

primates, may be at risk from generalist parasites held in reservoir populations (addressed in Chapter 7).

Multi-host parasites are often transmitted by vectors or via long-lived infective stages that persist in the hosts' environment. Although many researchers assume that adding multiple host species to parasite transmission dynamics will have negative effects on vulnerable wildlife species, in the case of vector-borne diseases this effect could be reversed. Thus, Rudolf and Antonovics (2005) developed a general host–pathogen model to show that under the assumption of frequency-dependent transmission (which probably characterizes many vector-borne pathogens, see Box 4.3), adding a second host species to the system could actually prevent the pathogen-mediated extinction of a more vulnerable host. Their study emphasizes the need for empirical data on the role of host diversity in the dynamics and impacts of multi-host parasites.

For some vector-borne pathogens, such as *Borrelia burgdorferi* (a tick-borne bacterial pathogen and the causative agent of Lyme disease), a greater diversity of host species might reduce pathogen prevalence and impacts on humans or species of conservation concern (Schmidt et al. 2000; Logiudice 2003). This occurs in part through a mechanism termed the "dilution effect," whereby high host species diversity reduces parasite prevalence by limiting the effects of competent reservoir hosts.

In the Lyme disease system, for example, white-footed mice are the most competent host for *Borrelia* replication. As the number of non-mouse species increases, more contacts are likely to occur between the deer tick vectors and less competent reservoir hosts, thus tending to reduce prevalence in the ticks, the non-competent reservoirs, and the mice. Although host species diversity could play a similar role in reducing the transmission potential of other vector-borne diseases, including parasites that infect a range of primate hosts, its general importance in wild animal populations is largely unknown.

The presence of multiple host species could also impact the evolution of pathogen virulence (Woolhouse et al. 2001; Gandon 2004). For parasites infecting a single host species, theory predicts that they should evolve to optimum levels of virulence as determined by tradeoffs between virulence and transmission (or by different levels of within-host competition, see Chapter 2). On the other hand, the presence of multiple host species allows parasites with unusually high virulence to persist in some "dead end" hosts or those that contribute only weakly to parasite transmission, provided that they have weaker effects in a reservoir host. Indeed, this could explain die-offs caused by some multi-host pathogens in primates, including outbreaks of Ebola and related filoviruses in humans and apes (Sanchez et al. 1995; Leroy et al. 2004a), Sin Nombre Virus outbreaks in humans in the southwestern United States (Khan et al. 1996), and high mortality induced by yellow fever virus among monkeys and humans in Central and South America (Chapter 1). These and other consequences of parasite interactions with multiple host species remain largely unstudied at an empirical level.

Finally, it is important to keep in mind that the interplay between parasitism and multi-host systems can have major repercussions for biodiversity and stability of ecological communities (Holt and Pickering 1985; Begon and Bowers 1994). Thus, parasites could prevent any single species or group of species from dominating communities, allowing many species to coexist at relatively low densities. Several empirical observations illustrate the role of pathogens in determining plant and animal community structure and modifying ecosystems. Pathogens that attack key herbivores can have major effects on plant recruitment and abundance (Dobson and Crawley 1994), and can also impact the density of predators and other natural enemies (Dobson and Hudson 1986). One example is furnished by the myxoma virus epidemic in rabbits in southern England. Although a high abundance of rabbits in the mid-1900s prevented the regeneration of woody plants in grassland habitats, myxoma virus (introduced in the 1950s) led to a scarcity of rabbits for the next 15 years. Remarkably, in areas where rabbit grazing had previously prevented tree establishment, a cohort of oak seedlings grew into forests following the initial epidemic (Dobson and Crawley 1994). Similar cases can be found in East Africa, where rinderpest and bacterial pathogens caused changes in herbivore abundance and radically altered the structure of plant communities. Although these examples are cases where pathogens have generated striking changes in community structure, the vast majority of host–parasite interactions are likely to yield more subtle yet still substantial effects on the assembly of ecological communities.

4.5 Summary and synthesis

A general understanding of parasite ecology and epidemiology is essential for managing infectious diseases in nonhuman primates and other wild animal populations, both in terms of detecting disease threats for vulnerable species and implementing control measures to decrease pathogen pressure. Basic epidemiological models give rise to several key principles that characterize host–parasite interactions. These include the concept of the basic reproductive number, R_0, which sets the criteria for parasites to establish in a population and also provides information on how rapidly pathogens will spread in a naïve population. Mathematical models point to situations in which parasites will regulate or reduce the size of host populations and show when social and spatial heterogeneities are likely to be important in wildlife–pathogen systems.

Among wild primates, a large number of field studies have examined patterns of habitat use, demography, and social interactions. We also know that primates harbor an incredible diversity of parasites and infectious diseases (Chapman et al. 2005a; Nunn and Altizer 2005). Yet surprisingly few studies have linked host characteristics, including abundance, life history traits, and behavior with patterns of parasite occurrence. Furthermore, no comprehensive experimental studies addressing parasite ecology have been conducted in wild primate populations (even though such experiments are feasible, Janson 2000). Inferences of the population impacts of primate parasites are therefore made indirectly, except where conspicuous epidemics have decimated previously intact primate populations (Chapter 1). One priority for the future is to collect comprehensive monitoring data for a variety of disease-causing agents in wild primates (Chapter 7), including those shared with human hosts (Chapter 8, Wolfe et al. 1998).

For species of conservation concern like many primates, non-invasive sampling techniques should prove to be extremely useful for monitoring the occurrence of infectious diseases (Makuwa et al. 2003). One promising example is the use of fecal samples for epidemiological studies of a range of gut-dwelling parasites. More recent molecular techniques have proven useful for extracting DNA or RNA of viral pathogens from fecal material, including agents not typically associated with gut infections, such as SIV infections in wild chimpanzees and sooty mangabeys (Ling et al. 2004; Nerrienet et al. 2005). The advantage is that researchers could determine the hosts' infection status, and by amplifying portions of the parasite's genome, could also obtain molecular data useful for investigating the epidemiology of parasite populations. Studies of feces could be further used for assessing the magnitude and timing of host responses by detecting the presence of host mucosal antibodies to particular pathogens, and by measuring levels of stress hormones, such as corticosterone, present in fecal material. Host genetic data has been obtained from non-invasive samples such as hair and feces in several primate species, including baboons, Barbary macaques, chimpanzees, and gorillas (Smith et al. 2000; Jensen-Seamann and Kidd 2001; Lathuilliere et al. 2001; Morin et al. 2001; Lukas et al. 2004). Combining host genetic data with monitoring of parasites in wild primate

populations could potentially point to factors that underlie primate susceptibility to infectious diseases, and would allow biologists to explore the consequences of disease for shifts in the genetic composition and long-term viability of primate populations (Altizer et al. 2003a).

The shortage of detailed studies of primate–parasites dynamics calls for better integration of quantitative theoretical approaches and records of parasitism in natural populations. For example, it is difficult to relate categorically defined mating systems (e.g. polygyny, serial monogamy) and social organization (e.g. solitary, fission–fusion communities) to the spread of parasites in wild populations. More precise measures of parameters suggested by theoretical models are needed from wild mammal populations, including inter- and intra-group contact rates, dispersal rates and distances, contact durations for different types of social interactions, and better measures of variance in male and female mating success. Moreover, model parameters that define contacts leading to parasite transmission must reflect biologically realistic and estimable processes, which can be achieved by increasing interactions between primatologists and epidemiologists. Indeed, perhaps the greatest challenge in moving forward studies of parasite–pathogen interactions is to increase communication and collaboration between mathematical ecologists studying the dynamics of infectious diseases, veterinary workers collecting samples from the field, and behavioral ecologists collecting detailed records of primates in their natural environments.

5

Host defenses: the immune system and behavioral counterstrategies

5.1 Introduction

Like other animals, primates employ an impressive battery of defenses to prevent or respond to attacks from disease-causing organisms. These anti-parasite strategies include immune defenses to combat infections and behavioral defenses to avoid parasites in the environment. Some host defenses have a strong genetic basis, as illustrated by the importance of diverse genes at the major histocompatibility complex (MHC) in the ability of vertebrate animals to recognize and respond to diverse pathogens (Hedrick and Kim 2000; Knapp 2005). Other defenses are phenotypically plastic or learned, such as when primates use medicinal plants to eliminate gastrointestinal helminths (Huffman et al. 1996), or when they avoid parasites spread through fecal contamination of the environment (Freeland 1980; Hausfater and Meade 1982). In many cases, resistance-conferring traits are costly in terms of time or energy that could otherwise be spent foraging, reproducing, or defending territories (Webster and Woolhouse 1999). Inducible immune or behavioral defenses activated upon infection might be less costly and relatively effective in responding to rare or unpredictable risks of infection (Harvell 1990).

Disease-causing organisms enter their hosts using a variety of mechanisms, and these entry points act as selective pressures on immune and behavioral defenses. Some parasites gain access through portals provided by cuts and skin abrasions. Vector-borne parasites like malaria enter when biting arthropods pierce the skin and effectively inject the parasite, potentially favoring behavioral strategies to avoid contact with the vectors. Similarly, cercariae (free-swimming intermediate stages of schistosomes) and hookworm larvae burrow directly into the skin of vertebrate hosts (Schmidt et al. 2000), possibly leading to selection on animals to avoid prolonged contact with water and moist soil. Parasites can also enter their hosts through mucous membranes at epithelial sites in the respiratory, gastrointestinal, and urogenital tracts. Once inside a host, parasites move to the blood, lungs, digestive tract, or other host tissues to initiate growth and replication.

In this chapter we examine the incredible array of defenses employed by free-living primates to prevent initial infection and limit subsequent parasite replication. We begin by considering strategies for parasite removal, including immune responses, self-medication, and grooming behavior. In the second section, we review behavioral

strategies that primates use to limit the risk of encountering parasites. Finally, we investigate the links between sexual selection and parasites, focusing on mate choice related to parasite avoidance, selection of healthy caregivers, and the indirect benefits of "good genes." This chapter focuses primarily on individual-level strategies, such as the immune system and behavioral defenses. Chapter 6 builds on these ideas by considering properties of mating and social systems that serve as defenses to infectious disease.

When reading this chapter, it is essential to remember that host behavioral and immune defenses are part of a coevolutionary "arms race" that takes place between hosts and parasites (Hamilton 1982; Hart 1994; Frank 2002). Parasites influence host immunity and other host defenses, which exerts reciprocal selection pressure on the parasite, including selection for alternative transmission strategies, manipulation of host behavior, and changes in virulence (Knell 1999; Mackinnon and Read 2004). Another crucial aspect of behavioral and immune defenses is that they are often costly to implement in terms of energy expenditure, life history tradeoffs, and opportunity costs (Hart 1994; Sheldon and Verhulst 1996; Moret and Schmid-Hempel 2000). Moreover, defenses employed against one parasite could increase vulnerability to other parasites, and an important area for future research involves developing a better understanding of costs of resistance and tradeoffs in host–parasite interactions. Such investigations require means of reliably measuring both immune and behavioral defenses in the wild and their correlations with other fitness-related traits (Norris and Evans 2000).

5.2 Responding to infections: strategies for parasite removal

5.2.1 Immune defenses

Knowledge of the molecular and physiological mechanisms of host immunity might seem immaterial to primatologists who are mainly interested in explaining variation in host behavior. Yet understanding host immune defenses is fundamental for researchers working at the interface of ecology, behavior, and evolution. Indeed, ecologists have shown growing interest in the evolutionary ecology of immune defenses (i.e. *ecological immunology*), including studies of factors that maintain variation in resistance in wild populations and the consequences of such variation for host survival and life-history tradeoffs (Sheldon and Verhulst 1996; Norris and Evans 2000; McDade 2003; Schmid-Hempel and Ebert 2003). Understanding host immunity is also essential for evaluating the degree to which immune defenses can be used as predictive measures of disease risk in empirical studies (Nunn et al. 2000; Nunn 2002a, b; Semple et al. 2002; Sorci et al. 2003).

The immune system has been relatively well studied in humans and captive nonhuman primates (Wakelin 1996; Roitt et al. 1998; Parham 2005), but virtually nothing is known about how primate immunity functions in response to natural infections in the wild. Thus, biomedical researchers who study captive monkeys have

gained major insights into host immune cells important to the progression of AIDS by comparing the course of simian immunodeficiency virus (SIV) infection in natural African primate hosts, in which immune deficiency fails to develop, relative to Asian macaques that develop a disease similar to AIDS (Rey-Cuille et al. 1998; Hirsch et al. 2004). Because many excellent textbooks cover the biology of the vertebrate immune system (e.g. Roitt et al. 1998; Goldsby et al. 2002; Parham 2005), here we provide only a brief overview of the two major arms of the immune system (Fig. 5.1). These are

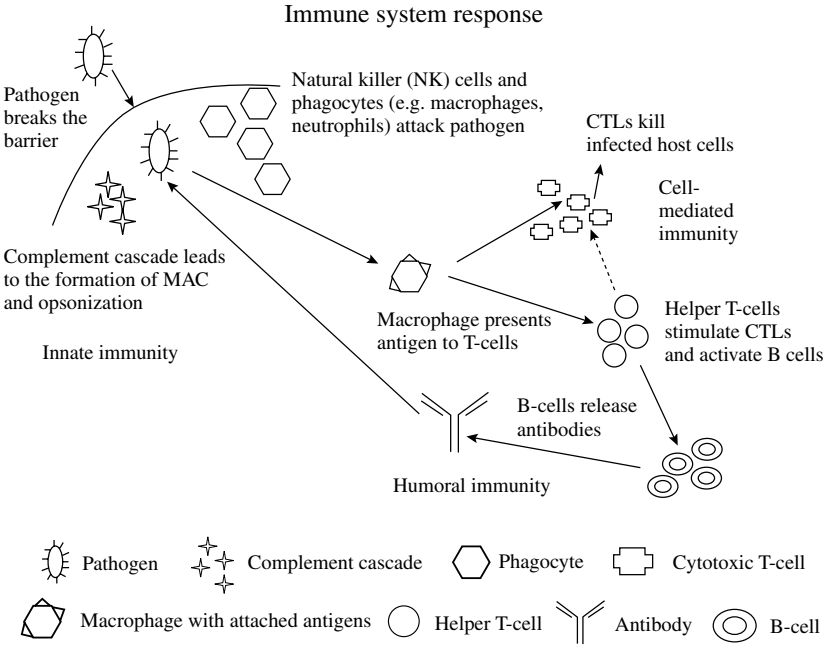


Fig. 5.1 A simplified representation of the major arms of the vertebrate immune system, including innate and adaptive defenses. Innate defenses involve phagocytic activity by cells such as neutrophils that attack pathogens and natural killer (NK) cells that destroy infected host cells. The complement cascade, another component of innate immunity, is made up of serum proteins that form the membrane attack complex (MAC) and also opsonize (mark for destruction) invading pathogens. The combination of leukocyte migration and the complement cascade often results in inflammation at the site of infection. Phagocytic cells also signal the adaptive immune system that a pathogen has invaded by presenting antigens (pathogen proteins) to T-cells. Adaptive defenses can be divided into two branches: cell-mediated immunity and humoral immunity. In cell-mediated immunity, T-cells detect antigens presented by macrophages; helper T-cells respond to extracellular invaders by activating B-cells and stimulating cytotoxic T-cell (CTL) proliferation and maturation, while the cytotoxic T-cells destroy intracellular pathogens by lysing infected host cells. In humoral immunity, activated B-cells secrete antibodies into the plasma and lymph. These antibodies recognize particular antigens and opsonize the invading pathogens, signaling to phagocytes in the innate immune system to destroy them. Figure provided by C. Bradley, University of Georgia.

Table 5.1 Major cell types of white blood cells (leukocytes) involved in innate and adaptive immunity in mammalian hosts. See also Fig. 5.2

Cell type	Immune system component	Function
Neutrophil	Innate	Short-lived phagocyte; binds to and ingests extracellular bacteria
Eosinophil	Innate	Attacks large extracellular parasites such as helminths by injecting destructive enzymes into parasite tissues
Basophil	Innate	Enhances inflammatory response
Monocyte	Innate + adaptive	Long-lived phagocyte; engulfs and destroys foreign particles; moves into host tissues and develops into macrophages; macrophages present antigens from destroyed pathogens to T-cells
Lymphocyte		
B-lymphocytes	Adaptive—humoral	Counters extracellular pathogens by encoding and producing antibodies
T-lymphocytes	Adaptive—cell-mediated and humoral	Controls B-cell development (CD-4); kills viral-infected cells (CD-8 or T-cytotoxic cells)

often referred to as innate (or non-specific) and adaptive (or specific) immunity—although it is important to note that some immune mechanisms classified as innate defenses actually have some inducible and specific properties. Many defenses involved in Fig. 5.1 are mediated by white blood cells (WBCs), also called *leukocytes* (Table 5.1). At the most general level, all immune defenses require a system for recognizing that infection has occurred and attacking the parasites or destroying infected host cells at the site of infection (Roitt et al. 1998). Thus, the defenses that are most effectively employed will depend on the characteristics of the parasite, including whether the pathogen develops within or outside of host cells and its point of entry in the host.

5.2.1.1 Innate immunity

Innate immune defenses represent the first line of defense against a wide range of parasite types (Roitt et al. 1998). Three major elements of innate defenses are phagocytosis, inflammation, and the complement cascade. Phagocytic leukocytes, such as neutrophils and monocytes (Table 5.1; Fig. 5.2), directly engulf foreign material, including pathogen particles, outside of host cells (Wakelin 1996; Goldsby et al. 2002). This baseline and relatively generalized defense probably represents an important barrier against extracellular stages of pathogens (Box 5.1). A second component of innate immunity is the inflammatory response, resulting in increased blood flow and migration of phagocytic cells to the site of infection or damaged tissue. The complement system of serum proteins (also known as the complement cascade) helps to regulate immune reactions, destroy foreign cells, and generate inflammation (Goldsby et al. 2002). Part of this complement cascade involves opsonization, whereby serum molecules attach to the exterior of target foreign cells to make them

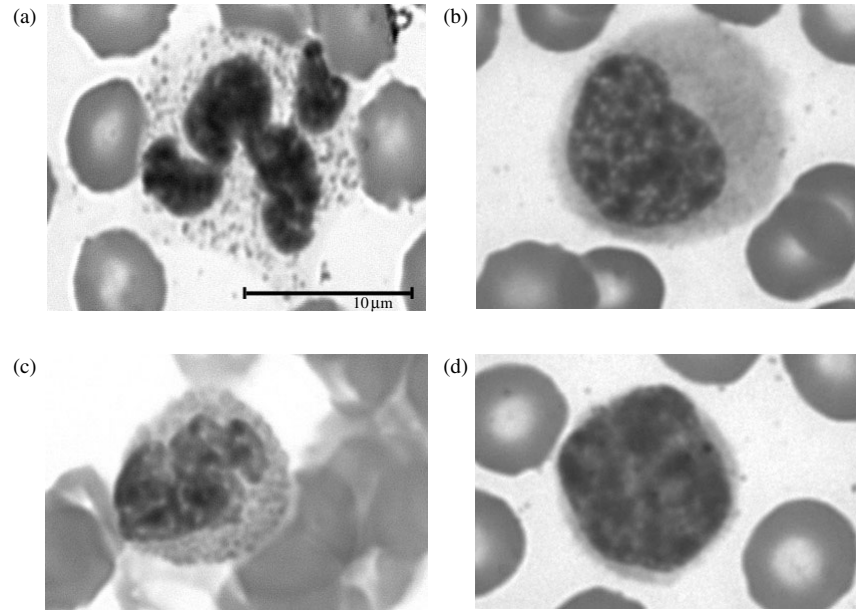


Fig. 5.2 Four types of leukocytes, or white blood cells (WBCs), from a rhesus monkey (*Macaca mulatta*). All images are given to the scale shown in the first panel. (a) Neutrophils are the most common WBC type (50–70% of WBCs), and are characterized by a multi-lobed nucleus (with 3 or more distinct lobes) and pale-staining, small granules in the cytoplasm. (b) Monocytes are considered agranulocytic (though they may contain some very small granules), and generally have a kidney- or U-shaped nucleus. The cytoplasm of monocytes is abundant, and may contain vacuoles (non-staining areas) that help to distinguish smaller monocytes from large lymphocytes. Monocytes are rare in the bloodstream (3–9% of WBCs). (c) Eosinophils, like neutrophils, are granulocytic, but have larger granules and only two nuclear lobes. Eosinophils are much less common (<5% of WBCs) than neutrophils. (d) Lymphocytes are distinguishable from other WBC types by their large, somewhat round nucleus that takes up most of the cell, and a thin pale band of cytoplasm at the periphery of the cell. Lymphocytes come in two varieties, B-cells and T-cells, that are morphologically indistinguishable from each other through a microscope. Photomicrographs courtesy of AnaPatricia Garcia, Yerkes National Primate Research Center.

more easily ingested and to attract phagocytic leukocytes. Also important is the membrane attack complex (MAC) that demolishes the lipid membranes of gram-negative bacteria and viral envelope proteins (Fig. 5.1).

5.2.1.2 Adaptive immunity

The second major arm of immune defenses is known as *acquired* or *adaptive immunity*. Adaptive components of the immune system recognize an incredible diversity of pathogen types based on their antigenic markers, and in many cases allow hosts to retain a memory of past infections (Roitt et al. 1998). Adaptive immunity is further divided

Box 5.1 Comparative studies of baseline leukocyte counts in primates

The cross-species association between overall white blood cell (WBC) counts and measures of mating promiscuity in primates described in Chapter 1 (Fig. 1.3) supports the hypothesis that promiscuous species experience greater disease risk—and hence have higher concentrations of circulating leukocytes (Nunn et al. 2000; Nunn 2002a). However, this comparative pattern also raises questions about mechanisms underlying this association (Read and Allen 2000b; Anderson et al. 2004). Specifically, why would higher levels of basal WBCs improve defenses to parasites, and in particular, defend against STDs? One possible explanation relates to the timing of the vertebrate immune response relative to the within-host course of infection for many STDs. For instance, among healthy, captive animals, levels of WBCs could indicate the capacity of innate immune cells (monocytes, granulocytes, or natural killer cells) to respond quickly to infections. Such generalized defenses could be critical to STD prevention because, unlike the "hit-and-run" strategy of many direct contact pathogens, STDs are difficult to eradicate once they become established. In fact, many STDs result in life-long infections (Lockhart et al. 1996), and by stockpiling basal defenses, higher WBC counts could be essential in preventing the initial establishment of an STD.

WBCs might also play a role in removing sperm and seminal fluid from the female reproductive tract, in part to reduce infection risk, but could also eliminate incompatible sperm as a form of cryptic female choice (Eberhard 1985). Immediately following copulation, massive numbers of WBCs are known to inundate the female reproductive tract, where they actively engulf sperm and seminal fluid (Phillips and Mahler 1977; Pandya and Cohen 1985; Barratt et al. 1990). Neutrophils are a primary phagocytic cell in this process, which is relevant because analyses of neutrophil counts provided the most consistent results in phylogenetic comparative tests involving both primates and carnivores (Nunn et al. 2000; Nunn 2002a, 2003b). Given that infectious stages of many STDs are present in seminal fluid (Holmes et al. 1999), a plausible interpretation is that active and immediate phagocytosis of ejaculate functions to reduce the risk of STD infection.

Finally, Anderson et al. (2004) emphasized that the mechanism underlying the association between WBC levels and mating promiscuity remains unclear, suggesting that social factors rather than sexual factors might play a role in explaining variation in WBC counts. For example, promiscuity could increase the transmission of pathogens with non-sexual transmission modes, and differences in stress levels across species could arise through competition for mates in more promiscuous species. Similarly, if restricted from mating with multiple partners in captivity, individuals of a promiscuous species could become stressed, much as carnivores with larger home ranges experience greater stress when held in confined conditions, such as zoos (Clubb and Mason 2003). Future research should therefore evaluate the mechanisms that account for variation across species in WBC counts, including potential biases resulting from captive housing of primates with different mating systems, as the source of WBC counts is usually from captive populations (International Species Information System 1999; Nunn et al. 2000; Semple et al. 2002; Anderson et al. 2004).

into two major types of inducible defenses, referred to as *cell-mediated* and *humoral immunity*. Both of these components involve the recognition of antigen-presenting cells, but a major difference is that humoral immunity operates through antibodies circulating in blood plasma and lymph to attack extracellular parasites, whereas cell-mediated immunity depends on lymphocytes that recognize and attack pathogens developing inside host cells (Goldsby et al. 2002, Fig. 5.1).

The adaptive immune response is mediated by two main types of lymphocytes called *T-cells* (or T-lymphocytes) and *B-cells* (or B-lymphocytes; Table 5.1). There are two main types of T-cells (CD-4 and CD-8), distinguished by their membrane-bound surface molecules. CD-8 T-cells function in cell-mediated immunity and can destroy host cells invaded by pathogens, whereas CD-4 T-cells help activate B-cells, which in turn generate antibodies involved in humoral immunity. Thus, in the antibody response, B-cells are activated by binding to CD-4 cells that themselves have recognized *antigens*, or surface molecules of pathogens that evoke the hosts' immune system. These activated B-cells differentiate into plasma cell clones that produce serum antibodies specific to the antigens that stimulated their production (Graham 2002). Each antibody type released into the blood recognizes and binds to a single antigenic site on a parasite's surface, but a diversity of antibodies can recognize a multitude of components of infectious organisms. Antibodies defend against extracellular pathogens by binding to surface antigens to block active sites on pathogen membranes. Through a process called agglutination, antibodies also attach to pathogens and facilitate their recognition by phagocytic cells (Fig. 5.1).

Five classes of antibody molecules are produced by the hosts' immune system; these molecules vary in size and their general location in the body (Bush et al. 2001). The different classes of antibodies—called *immunoglobulins* or Ig for short—are distinguished by their "heavy chains" and referred to as IgA, IgD, IgE, IgG, and IgM. The relative abundance of different types of antibodies can provide information regarding the cause of infection and indicate whether the hosts' immune system is functioning normally (Table 5.2). For example, high levels of IgG can indicate long-term chronic infections such as HIV, and high levels of IgE can indicate infection with larger parasites, allergic reactions, or certain autoimmune diseases, in which self-recognition mechanisms fail and the immune system attacks the host's own body (Roitt et al. 1998).

Table 5.2 Five classes of immunoglobulins, or antibody molecules[1]

Type	Representation[2]	Description and Function
IgG	70–75%	Part of the intra- and extra-vascular pools, IgG is the major antibody of humoral immune responses. Maternal IgG provides immunity to neonates in early life.
IgM	10%	Mainly found in the intravascular pool and commonly used in response to antigenically complex parasites.
IgA	15–20%	Found in sero-mucous secrections, including saliva and in secretions of the genital tract.
IgD	<1%	Present in greater amounts on the membrane of B-cells. The function of this immunoglobulin is largely unknown.
IgE	<1%	Uncommon in blood serum, but found on the membrane of some immune system cells and mucosal surfaces. Associated with defenses against helminths as well as allergic reactions.

[1] Taken from Roitt et al. (1998).
[2] Proportional representation of immunoglobulins in normal human blood serum, based on Roitt et al. (1998).

Antibodies involved in humoral immunity can attack extracellular parasites, but cell-mediated immunity is necessary to destroy pathogens within host cells (Fig. 5.1). This latter type of adaptive immunity involves cytotoxic T-cells that recognize and respond to antigens expressed on the surface of infected cells. In this way, they bind to and destroy infected host cells, thus preventing further within-cell replication and exposing pathogens to circulating antibodies (Roitt et al. 1998).

Important features of adaptive immunity are the ability to recognize and respond to a high diversity of antigens, and the high level of specificity of inducible responses. Perhaps the most important feature in terms of protecting against future infections is immune memory. During an immune response, memory T-cells are produced that remain in the lymph nodes, and together with longer-lived memory B-cells, allow the immune system to mount a faster and stronger response following subsequent exposures to the same (or similar) antigens.

5.2.1.3 Organs and tissues involved in immune defense

Key organs and tissues involved in both innate and adaptive immune defenses include the spleen, thymus, and bone marrow. The spleen stores blood cells, including those used in immune defense and detection of blood-borne antigens. The thymus and bone marrow represent sites of lymphocyte development, with the thymus linked most strongly with T-cell development and bone marrow associated with B-cell production. Following their development, lymphocytes and other blood cells typically move around the body and can migrate to peripheral tissues including lymph nodes and lymphoid tissues. This migration is important in facilitating rapid responses to infectious agents, as cells involved in the immune system and located in different organs can respond to antigens circulating in the blood, on the surface of leukocytes, or on mucosal surfaces in the body.

5.2.1.4 Costs and tradeoffs of immune defenses

Immune defenses must be rapidly deployed against foreign organisms, but an overly strong response can be harmful to the host. Thus, many non-infectious diseases are the result of a hypersensitive immune system (autoimmune diseases). Moreover, vertebrate immune defenses are themselves costly to implement (Lochmiller and Deerenberg 2000; Derting and Compton 2003). For this reason, hosts cannot simply set immunity to a maximum level, and they therefore "turn down" the immune system until defenses are needed.

The idea that immune defenses are costly has been supported by a number of studies showing that animals invest less energy in reproduction or growth when maintaining high immune defenses, and vice versa. For example, experimental increases in reproductive activity can reduce levels of innate, humoral, and T-cell mediated immunity (reviewed in Lochmiller and Deerenberg 2000; Norris and Evans 2000). Such tradeoffs lie at the core of research on ecological immunology (Sheldon and Verhulst 1996; Norris and Evans 2000; McDade 2003), and given the potential costs of immunity, we would expect animals to invest in greater defenses

only when the risk of pathogen infection is high. Despite the importance of evolutionary tradeoffs for explaining natural patterns of host immunity, studies assessing these costs in wild mammal populations are rare (Saino et al. 2000). Nevertheless, ecologists have implemented a growing number of techniques for assessing immune parameters in wild vertebrate hosts (Box 5.2 and Table 5.3), opening the door for future work in captive and wild primates.

Box 5.2 Quantifying immune defenses in wild vertebrate animals

To understand how primate immune systems defend against different pathogens and respond to environmental variables, and to evaluate the costs of immune system parameters for reproductive fitness, ecologists must quantify levels of innate, cell-mediated, and humoral immunity in wild animals—in addition to collecting measures of infection status, body condition, or stress (Krief et al. 2005). Researchers often define immunocompetence as a host's investment in baseline immune defenses or ability to mount an immune response following exposure to a pathogen (Sheldon and Verhulst 1996; Roitt et al. 1998; Zuk and Stoehr 2002). Two general approaches to measuring immunity in an ecological context include point-estimates of immune parameters and assessing the response to immune system challenges (reviewed in Norris and Evans 2000). As expected, many immunodiagnostic techniques have been used extensively in humans and domesticated animals (Edwards 2000; Harvey 2001; Thrall et al. 2004), and ecologists have employed a number of methods in studies of wild birds (reviewed in Norris and Evans 2000).

Monitoring techniques often require collecting a small blood sample (e.g. 0.1–1.0 ml) from which several hematological parameters can be measured (Table 5.3). These include total white blood cell (WBC) counts and differentials (i.e. numbers of each type of WBC) as measures of innate immunity, in addition to ratios of neutrophils to lymphocytes, which have been used as an index of stress across a variety of vertebrate animals (Morrow-Tesch et al. 1993; Reichert et al. 2002; Weber et al. 2002). If blood is collected in microcapillary tubes, a hematocrit centrifuge can be used to obtain a hematocrit reading (based on the separation of plasma, red and white blood cells into different layers), providing information on possible anemia and leukocyte abundance (Table 5.3). Serological tests can be used to assess current antibody levels to particular pathogens, including serum or rapid plate agglutination (SPA/RPA) and ELISA (enzyme-linked immunosorbent assay), thus providing information on current or previous exposure to known infectious agents (Edwards 2000). Blood serum proteins, including albumin and globulin, can also be separated to measure levels of circulating transport proteins and antibodies (Thrall et al. 2004).

Relative to monitoring techniques, challenge methods involve exposing animals to stimulants to trigger an immune reaction. The overall strength of response is usually taken as an indication of the level of immuncompetence. These methods require either holding animals temporarily in captivity, or reliably recapturing challenged individuals in the field, which might make this approach difficult for some larger-bodied primates. A common method for assessing antibody production (humoral immunity) is to inject animals with a harmless protein or cell type and assess the antibody response. Many researchers use the sheep red blood cell (SRBC) hemagglutination assay, where SRBCs are injected into animals and resulting production of specific antibodies is measured at a later time by collecting blood and performing a hemagglutination assay or ELISA test (Cichon et al. 2002). Cell-mediated immunity can be assayed by injecting animals sub-dermally with a substance known to trigger cell division, such as phyotohemagglutinin (PHA), which

Box 5.2 (*Cont.*)

stimulates T-lymphocytes to migrate to and proliferate at the site of injection (Lewis et al. 2000). The level of inflammation or thickness of skin at the injection site (relative to a control site) indicates the strength of the T-cell response.

Each method for assessing host condition and immune defenses has advantages and drawbacks. Monitoring techniques are often faster and less invasive, and provide a snapshot of immune status when samples were collected in the field. However, these point-estimates will be influenced by an animal's overall condition and the history or presence of any current infections, making it difficult to interpret these measures unless concomitant data on the infection status of animals are also available. For example, an animal might have high leukocyte counts due to a current infection or because of high baseline investment in innate immunity. Challenge methods, on the other hand, can measure adaptive immunity (either humoral or cell-mediated) by exposing hosts to antigens and measuring the subsequent response. Although favored by immunologists or veterinary workers, challenge techniques can be more invasive and could induce stress or elevate natural mortality by holding or recapturing animals between the time when a challenge is applied and when the response is measured.

Cross-species comparisons of leukocyte counts and the relative size of immune system organs (i.e. thymus and spleen) have been used to investigate whether features of host behavior or ecology are associated with the risk of parasite infection and host immune defenses (Møller et al. 1998a; Nunn et al. 2000; Nunn 2002a). However, a critical task that remains is to determine which parameters in primates and other wild mammals are linked with greater investment in immune defenses, and which cell types and immune system components play significant roles in responding to different types of infectious diseases (see Box 5.1). This is difficult in part due to a lack of information on the function of different cell types in wild animals, and due to species-level heterogeneity in baseline measures of many of these defenses.

Finally, it is important to note that blood samples collected for immune system assays can be used for other purposes, including host genotyping or PCR-based tests to probe for pathogen-specific markers. These samples can also be used to assess levels of stress hormones (i.e. glucocorticosteroids), thus providing information on acute or chronic stress responses (Table 5.3, Sapolsky et al. 2000; Romero 2004). Increasingly, non-invasive techniques using information acquired from feces can provide information on levels of adrenal and gonadal hormones associated with physiological stress, levels of pathogen infection (including pathogen DNA), and the presence of mucosal antibodies (reviewed in Wasser et al. 2002). Such non-invasive sampling techniques are probably crucial for primate species of conservation concern, or those that are difficult to capture or restrain for blood collection.

5.2.1.5 MHC and the genetics of immunity

The genetics underlying variation in host immunity have attracted much recent interest, including studies focusing on the evolutionary maintenance of immunological variation (Frank 2002). Among vertebrate animals in particular, genetic loci associated with the MHC play a key role in acquired immunity (Box 5.3), and the extreme polymorphism of MHC class I and II genes is important for recognition and response to a wide diversity of pathogens (Nei and Hughes 1991; Hedrick and Kim

Table 5.3 Methods used to measure immune defenses in wild or captive animals

Type	Sample	Technique	Description
Monitoring—innate immunity	Blood: smear	WBC counts and differentials	Total numbers of WBCs per blood volume, and the proportion of each leukocyte type, such as neutrophils, monocytes and eosinophils. From these counts, the numbers of neutrophils divided by lymphyocytes has been used to assay chronic stress. Elevated total WBC counts can indicate a current infection, as can high counts of certain WBCs (e.g. neutrophils in response to bacterial infections)
Monitoring—innate immunity	Blood: hematocrit tube	Hematocrit reading	Separates red blood cells, plasma, and WBCs into different layers; ratio of red blood cells to plasma indicates anemia; buffy coat layer indicates WBC abundance
Monitoring—humoral immunity	Blood: serum or plasma	Antibody tests	Serum or rapid plate agglutination tests (SPA, RPA) and enzyme-linked immunosorbent assay (ELISA) used to detect or quantify antibody production against specific antigens
Monitoring—humoral immunity	Blood: serum	Serum proteins	Albumin and globulin (separated from blood serum) indicate levels of circulating transport proteins and antibodies (i.e. immunoglobulins)
Monitoring—stress hormones	Blood plasma or feces	Stress hormone assay	Concentrations of glucocorticosteroid hormones (cortisol, corticosterone) from blood plasma or feces; can indicate acute stress response or chronic stress depending on sampling protocols
Monitoring/ Measuring—immune organs	Spleen or thymus	Size of organ	Measuring size of organ relative to body size indicates investment in the production of immune system cells
Challenge—response of humoral immunity	Blood: serum	Sheep red blood cell (SRBC) hemagglutination	Inject novel antigen (e.g. SRBC) and measure levels of antibody production over time
Challenge—response of cell-mediated immunity	Dermal thickness	Phytohemagglutinin assay (PHA) or Delayed hypersensitivity test	Inject mitogen (e.g. phytohemagglutinin or other substance that induces cell division) into sensitive skin area and measure swelling to assess T-cell migration and replication

The type of assay refers to whether the test provides a point-estimate of immune status (monitoring) or involves a challenge test, and also whether the test quantifies elements of innate, humoral, or other aspects of immunity. Sample refers the type of tissue or component of the blood that is examined. Technique refers to the name or abbreviation of the test, and description provides a brief explanation of what is measured or how tests are performed (modified after Norris and Evans 2000). WBC refers to white blood cell (leukoctye).

2000). Multiple lines of evidence support a role for MHC in responding to pathogen infections. In captive experiments with mice, for example, MHC heterozygotes were more resistant to multiple-strain bacterial infections (Penn et al. 2002). Recent studies of vertebrates further suggest that MHC heterozygosity and the occurrence of specific alleles or genotypes provide resistance to a variety of pathogens in the wild (Paterson et al. 1998; Hedrick et al. 2001; Froeschke and Sommer 2005).

In humans, researchers have identified an extraordinary number of alleles across three MHC Class I loci, which in humans are called HLA for Human Leukocyte Antigen region (HLA-A, HLA-B, and HLA-C genes, Robinson et al. 2003). These extremely high levels of variation at MHC loci could result from balancing selection based on a combination of frequency-dependent selection (as pathogens evolve to escape common MHC genotypes) and selection resulting from heterozygote advantage (heterozygotes have a greater diversity of MHC types). In nonhuman primates, MHC genes also appear to be highly polymorphic, but levels of variation differ tremendously among species (Knapp 2005). For example, common marmosets (*Callithrix jacchus*) are used in biomedical research as models for several human diseases, and in captivity show high vulnerability to a range of parasites, including enteric bacteria (Potkay 1992). Relative to other primates, this species showed evidence for fewer alleles across several MHC Class II genes and at least one nonfunctional region (Antunes et al. 1998).

An important question, therefore, is whether populations of threatened primates and other declining species will suffer disproportionate impacts from infectious disease due to loss of variation across MHC loci. Indeed, allelic diversity at these loci has been shown to be lower than expected among endangered species, such as those that have undergone population bottlenecks, longer-term genetic drift, or inbreeding following declines in population size (Hedrick et al. 1999). On the other hand, recent studies of populations of endangered salmon, Arabian oryx, red wolves, and desert bighorn sheep indicate that strong positive and balancing selection has maintained a surprisingly high diversity of MHC genotypes (Hedrick et al. 2000, 2002; Garrigan and Hedrick 2001; Gutierrez-Espeleta et al. 2001), and this pattern is in direct contrast to the level of diversity of other genes that are not affected by natural selection. In the most striking example documented to date, Aguilar et al. (2004) demonstrated that despite extreme monomorphism at selectively neutral loci in the San Nicholas Island fox (*Urocyon littoralis dickeyi*), animals showed remarkably high levels of variation across five MHC loci. The authors concluded that this pattern was best explained by an extreme population bottleneck (ca. < 10 individuals) followed by intense balancing selection to maintain MHC variation. This and other studies imply that a goal of captive breeding and conservation efforts for wild primates should be to characterize and maintain existing levels of MHC variation that are present in the wild. To balance this view, some authors suggest that MHC is but one of many fitness-related loci, and some controversy has emerged regarding whether conservation genetics should focus on maintaining MHC variation versus genome-wide heterozygosity in captive breeding programs (see O'Brien and Evermann 1988; Hughes 1991; Miller and Hedrick 1991; Vrigenhoek and Leberg 1991).

Box 5.3 MHC genes in pathogen resistance, host behavior and evolution

Major histocompatibility complex (MHC) molecules are immune proteins that are crucial to the process of specific or adaptive immunity. These molecules recognize and bind to pathogen proteins (antigens) inside infected host cells and transport these antigens to the outer membrane of the cell where they are presented to T-cells to initiate humoral and cell-mediated immune responses (Parham and Ohta 1996). Most nucleated host cells produce MHC class I molecules that are recognized by cytotoxic T-cells, which then destroy the infected antigen-presenting host cells. In contrast, MHC class II molecules are produced only by certain lymphocytes (macrophages, B-cells and dendritic cells) to aid in antibody production. Specific MHC molecules preferentially bind to specific pathogen peptides, and hence different MHC alleles can confer resistance to different pathogens. Individual hosts that are heterozygous across multiple MHC loci should be able to recognize and present a greater diversity of pathogen peptides than homozygous individuals (Doherty and Zinkernagel 1975). Similarly, high levels of MHC allelic variation at the population-level will reduce the chance that a single pathogen can affect the majority of hosts, and may be adaptive in the face of unpredictable and frequent disease outbreaks (Hedrick and Kim 2000).

Among primates, variation and function in the relatively large MHC coding regions or "gene families" have been characterized in several species, including chimpanzees, yellow baboons, and several macaque species (reviewed in Knapp 2005). As expected, most studies of MHC variation focus on humans, where this complex is called the HLA (human leukocyte antigen region, encoding MHC class I, II, and III molecules). In humans, over 200 tightly linked genes (defined as potentially coding sequences, although only a subset have known immunological functions) have been identified across the HLA complex, and collectively these are associated with more than 1500 alleles or molecular variants (Robinson et al. 2003; Yuhki et al. 2003). Evidence for the selective maintenance of variation at these loci comes from several sources, including a high frequency of non-synonymous nucleotide substitutions at sites that encode peptide-binding regions (Hughes and Nei 1988), and studies showing that individuals homozygous for one or more HLA class I loci are more vulnerable to infectious diseases, including more rapid progression of AIDS following infection with HIV-1 (Carrington et al. 1999).

Surprisingly few studies of MHC variation have been conducted in wild primates. Future studies of the role of MHC polymorphism in relation to pathogen-mediated selection in wild primates could include comparative differences among primate species that differ in known levels of pathogen exposure. The prediction would be that species with greater MHC variability (in terms of number of alleles and frequency of heterozygotes) should be those that have been historically exposed to a broader spectrum of parasites. It is important to note that results could depend on the specific loci examined and the pathogen(s) of greatest relevance. For example, certain MHC genes in humans are associated with protection against malaria and heptatitis B virus (Hill et al. 1992; Thursz et al. 1995), and in rhesus macaques (*Macaca mulatta*), particular MHC class I and II alleles are linked with slower progression of SIV-associated disease (Sauermann et al. 2000; Carrington and Bontrop 2002). Strong pathogen-mediated selection could therefore lead to a high frequency of resistance-conferring alleles and the concomitant loss of others. Such an event could have occurred among wild chimpanzees as a result of selection by a retrovirus related to SIVcpz. In this case, de Groot et al. (2002) showed that relative to humans, chimpanzees exhibit reduced allelic variation at several MHC loci. The authors argued that this may indicate a "selective sweep" induced by widespread viral infection following a hypothesized ancient pandemic of SIV, although other explanations are possible.

Box 5.3 (*Cont.*)

Other studies have pointed to assortative mating and kin recognition in maintaining heterozygosity and allelic variation across the MHC. Studies focusing mainly on mice showed that MHC variation is related to mate choice and inbreeding avoidance, and that mice can discern individuals with similar or dissimilar MHC genotypes based on olfactory cues (Boyse et al. 1987; Potts et al. 1994; Carroll et al. 2002). Perhaps the most celebrated of these studies focused on humans and provided evidence that females prefer scents of males with dissimilar MHC genotypes (Wedekind et al. 1995). Limited evidence from wild primates points to a similar role for mate choice and MHC compatibility in maintaining MHC heterozygosity (Knapp et al. 1996).

Finally, tiny amounts of tissue, including those extracted from hair follicles or animal feces collected in the field, can be used to amplify fragments of DNA for MHC typing in wild primates (Lukas et al. 2004; Knapp 2005). Because MHC genes are tightly linked and are generally inherited as large segments of DNA (i.e. as intact haplotypes), these genes are useful in paternity studies for identifying haplotypes transmitted from male and female parents (Walsh et al. 2003a). Thus, MHC genes could offer a powerful tool for assessing patterns of relatedness and sociality in wild populations (Nurnberg et al. 1998) in addition to investigating patterns of genetic variation relative to current and past pressures from infectious diseases.

5.2.1.6 Parasite evasion of host immunity

Despite sophisticated and varied host defenses, some parasites can persist and replicate within hosts, even over extended periods of time. On the one hand, this could result from individual host characteristics. With respect to immune defenses, chronic stress and nutritional shortfalls depress the immune system and increase susceptibility to infection (e.g. Koski et al. 1999; Koski and Scott 2001; Padgett and Glaser 2003). Studies have shown that psychological stress can alter immune responses and the course of infection in humans (e.g. Cohen et al. 1991), and stress in animals reduces vaccine responses, slows wound healing, and intensifies the pathogenesis of viruses and bacteria (Padgett et al. 1998a, b; McCabe et al. 2000). Indeed, glucocorticoid (GC) hormones like cortisol, produced by the adrenal cortex during acute stress responses, form a major link between the neuroendocrine system and the immune system (Padgett and Glaser 2003). These GC hormones provide energy for "fight or flight" responses to threats, but chronic activation of this stress response can deteriorate the expression of immunologically related genes, and GCs can also bind to and interfere with the activity of some leukocytes.

On the other hand, physiological changes associated with stress fail to explain why some parasites persist in hosts for much longer periods of time, particularly in non-stressful situations. Parasites can also evade detection by immune cells by masking their antigens, or by producing molecules so similar to the host that they do not evoke an immune response (Phillips 2002). Some parasites evade detection for a time by entering intracellular space, as happens with the invasion of red blood cells

by malaria parasites, or by taking up residence in host organs that are poorly defended, such as the eye, brain, and neural ganglia. Remarkably, some parasites avoid host defenses by changing their surface antigens, either as a facultative response (e.g. trypanosome parasites that vary their antigenic surface proteins) or through natural selection for "escape mutants"—thus staying one step ahead of the immune system (Bitter et al. 1998). This sort of parasite–immune system interaction has received much attention in studies of within-host dynamics of the Human Immunodeficiency Virus (HIV), the virus that causes AIDS. A remarkable aspect of HIV is that viral genotypes in later stages of the infection differ markedly from the initial viruses that entered the host, and evidence points to a positive role for T-lymphocytes in selecting for antigenic variants (Frank 2002). Finally, some parasites, such as flaviviruses, can decoy the hosts' immune systems into producing large numbers of lymphocyte types that are poor at clearing the virus (King et al. 2003), whereas others can actively suppress or interfere with host immunity (Bush et al. 2001). Frank (2002) described several examples in which viruses interfere with MHC presentation of antigens or with mechanisms of cell death (apoptosis) aimed at controlling infections.

In general, interactions between immune defenses and parasite infection can lead to one of three outcomes: (1) complete and rapid removal of the foreign organism, (2) total failure to control the pathogen, or (3) partial control with longer-term persistence and potential disease (Phillips 2002). These possible outcomes lead to the question, how effective is the primate immune system in combating different types of parasites? Complete immunity is documented for many viruses and other microparasites, whereas some protozoa and many macroparasites can at best illicit only partial immunity. For example, animals cannot be successfully re-infected with the protozoan *Leishmania tropica*, and partial immunity is known in schistosomiasis (Bush et al. 2001). Understanding mechanisms that influence innate and adaptive immunity, including genetic components of host resistance, may be important for protecting threatened primates from the spread of highly pathogenic diseases, such as Ebola (Walsh et al. 2003b). Characterizing variation in primate resistance or immunity among populations or species that differ in their interactions with parasites could also provide a deeper understanding of how infectious diseases have shaped the evolution of human resistance traits.

5.2.2 Physiological responses and sickness behaviors

Exposure to parasites often triggers a range of physiological changes including fever, reduction in blood plasma iron levels, reduced food intake, and diminished activity levels. Hosts initiate and maintain these "acute phase responses" through products secreted by leukocytes, and such responses often aid in recovery from infection (Johnson 2002).

Perhaps the most widely appreciated and well-established physiological response to infection is fever, defined as the elevation of core body temperatures (Kluger 1979). Induced fever response is so widespread in the animal kingdom that even

ectotherms seek warmer areas to raise their body temperatures following infection (Kluger et al. 1975; Elliot et al. 2002). Fever benefits hosts in part because most infectious microparasites have an optimal temperature for development, often at or below the hosts' normal body temperature, and replicate poorly at higher body temperatures (Kluger et al. 1975; Johnson 2002). Elevated body temperatures also can boost the immune response by enhancing the production of lymphocytes and antibodies and by increasing rates of phagocytosis (Kluger 1991).

As part of their core physiological responses to infection, mammals also exhibit a variety of outward behavioral responses that Hart (1990) termed "sickness behaviors." Sickness behaviors include sleepiness, inactivity, reduced food intake, and postures that reduce heat loss—behaviors that should be familiar to readers with past exposure to virulent pathogens such as influenza or malaria. Although sickness behaviors have been documented in nonhuman primates (e.g. Huffman and Seifu 1989), the absence of detailed reports on sickness behaviors in wild primates is more remarkable than the presence of a handful of descriptive accounts in the literature. These behaviors could be very costly, as animals exhibiting sickness behaviors might be more susceptible to predation and will lose feeding opportunities. With the goal of encouraging a closer examination of sickness behaviors in wild primates, we briefly review several benefits these behaviors could provide to primate hosts to offset these costs. At the outset it is important to note that many potential sickness behaviors could in fact represent clinical signs of disease rather than adaptive behaviors to inhibit infections. Identifying their underlying causes will require experimental determination of the net benefits of these activities to both hosts and parasites under a range of environmental conditions.

Many animals suffering from infectious diseases exhibit behaviors that can reduce heat loss. Sick chimpanzees have been reported to build and occupy nests during the day or take longer to leave a nest in the morning (Takasaki and Hunt 1987; Huffman and Seifu 1989; Krief et al. 2005), although healthy apes also build and use day nests (Fruth and Hohmann 1994). Reducing heat loss could serve to prime the fever response (Johnson 2002) so that compared to healthy animals, we expect that sick primates more frequently huddle in groups, seek sun during fair conditions, curl up to reduce surface area and lessen heat loss, and use nests or tree holes during periods when they would normally be active.

A related sickness behavior involves lethargy, characterized by prolonged periods of sleep or rest and lower rates of movement and socialization. Although inactivity could result directly from morbidity caused by pathogen infection, lethargy could also represent a strategy to reduce the demand for food and limit energetic expenditures. Several anecdotal examples are available in the literature. For instance, Altmann (1980) reported that a sick male baboon was unable to keep up with movements of other group members. More recently, Krief et al. (2005) documented a higher proportion of resting and less feeding in a chimpanzee infected with an influenza-like virus, as compared to other individuals of the same community. Their study highlights how quantitative information on activity budgets, which are commonly recorded in primate field studies, could provide new insights to sickness behaviors.

Infected animals often reduce their intake of food or specific dietary items, which could favor the elimination of certain parasites and aid in host recovery (Murray and Murray 1979; Crompton 1984; Symons 1985; Kyriazakis et al. 1998). Reduced food intake might directly starve some parasites of resources, especially for intestinal helminths and protozoa. Many bacteria require iron for successful growth and reproduction (Wright et al. 1981), and animals infected with bacteria might therefore avoid sources of iron, which for primates include many leaves and certain invertebrates (Barker et al. 1998; Rode et al. 2003). Finally, reduced foraging activity could conserve energy reserves that are better placed in maintaining body temperature to fight infections with the fever response, and might also lower the risk of predation for animals weakened by infection (Johnson 2002).

Links between the immune and nervous systems probably activate several sickness behaviors (Maier et al. 1994; Johnson 2002). Indeed, these links are extensive, bidirectional, and often involve diverse mechanisms such as hormones, release of messenger proteins from leukocytes, and direct innervation of immune system organs. Previous research has demonstrated, for example, that proteins secreted by activated macrophages serve as signals between the immune system and the brain (reviewed in Johnson 2002). In addition to changes in behaviors and physiological responses, sensitivity to pain can increase during illness or injury (Maier et al. 1994). This increased sensitivity could facilitate the conservation of energy when an animal is ill, or it may stimulate licking at the site of an injury or infection (Bolles and Fanselow 1980).

As noted earlier, it is important to consider the costs of sickness behaviors. Animals that are lethargic and not mentally alert could suffer from increased predation (Johnson 2002), suggesting that sickness behaviors could be among the most costly behavioral defenses to parasites. Altmann (1980) reported that a sick male baboon was killed by a leopard during his recovery following a viral epidemic. Animals expressing sickness behaviors are also less likely to socialize and might have difficulty caring for dependent offspring (Altmann 1980; Huffman and Seifu 1989). Lethargy and the direct effects of parasites can reduce an animal's capacity for concentration or memory (Kavaliers et al. 1999), thus posing costs for hosts that need to find food or a safe refuge. Finally, lethargic animals might not be able to perform other behavioral defenses important to countering parasite infections, resulting in greater risk of acquiring other types of infectious diseases (Moore 2002).

5.2.3 Grooming as a means of parasite removal

Grooming allows primates and other animals to remove ectoparasites, such as ticks and lice, and could also lower the risk of infection by some microparasites, especially pathogens transmitted by insect vectors and intermediate hosts (Hart 1990; Moore 2002). Although often overlooked, ticks are a major group of ectoparasites known to reduce host survival and reproduction (Lehmann 1993). As testimony to their importance, Brain and Bohrmann (1992) found that chacma baboons were

heavily infested with ticks of the genus *Rhipicephalus*, with particularly high tick loads on their ears. Two adult males examined after natural deaths harbored over 400 ticks, and more than 50% of infant deaths in this population were attributed to tick infestation, possibly due to an inability to suckle. Similarly, an experimental study using a tame redtail monkey (*Cercopithecus ascanius*) revealed that this animal acquired 8.2 ticks per hour when it was walked on a leash through Kibale Forest in Uganda (Freeland 1981a). Thus, in the absence of grooming, tick burdens in wild primates accumulate rapidly.

An individual primate can groom itself (autogrooming) or another individual (allogrooming; Figs 3.2 and 5.3). After observing three African monkey species, Freeland (1981a) suggested that autogrooming involves brushing movements to remove unattached ectoparasites and loose skin, whereas allogrooming more often involves careful searching and particle removal from fur. Relative to autogrooming, allogrooming serves both social and utilitarian purposes (Freeland 1981a; Barton 1987; Dunbar 1991). The social benefits of grooming in primates have been documented, with grooming occurring between kin, during alliance formation, and during male–female interactions (Smuts 1985; Silk 1987; Hemelrijk and Ek 1991).

The hygienic benefits of grooming seem obvious and nontrivial (Hutchins and Barash 1976; Freeland 1981a; Barton 1985; Reichard and Sommer 1994). For example, in a study of captive primates, Barton (1985) found that allogrooming was concentrated on body areas that animals cannot access on their own. After taking into account the area available for grooming, nearly 90% of allogrooming focused on these inaccessible sites. Zamma (2002) also found that grooming was concentrated in regions of highest louse density in Japanese macaques (*Macaca fuscata*), and Freeland

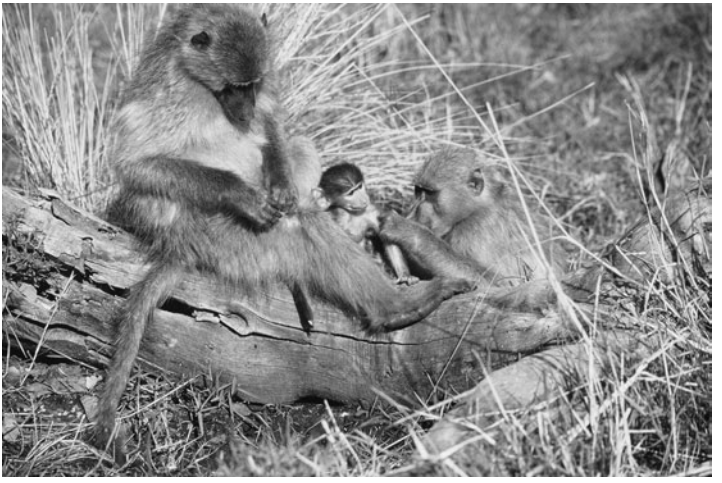


Fig. 5.3 Chaema baboons showing both autogrooming and allogrooming. Image courtesy of D. Kitchen, The Ohio State University.

(1981a) found similar results based on a study of three species of free-ranging catarrhines. Other studies have been more critical in their assessment of the hygienic benefits of grooming, although many arguments are based on anecdotal evidence. For example, Brain and Bohrmann (1992) reported that baboons actually *avoided* removing ticks from one another, even though allogrooming could have resulted in parasite removal (cf. Struhsaker 1967; Hausfater and Sutherland 1984). The authors proposed that animals might avoid removing ticks due to the foul taste of ticks when the mouth is used, and due to pain and bleeding in the recipient that follows tick removal.

In a comparative study of 44 primate species, Dunbar (1991) observed that grooming was correlated positively with group size but not body mass among Old World primates, consistent with a social rather than a hygienic function (unless, as acknowledged by Dunbar, the spread of ectoparasites increases with group size). On the other hand, the same study showed that among New World primates, grooming was more strongly related to body mass and therefore more likely to serve a hygienic function. Motivated in part by these results, Sanchez-Villagra et al. (1998) investigated patterns of grooming and ectoparasite loads in five groups of red howler monkeys in Venezuela. These authors found evidence consistent with both social and hygienic functions of grooming. Hygienic benefits were supported by the finding that animals spent the largest amount of time grooming inaccessible areas, and males that had recently become solitary exhibited higher rates of parasite infestation, presumably because they lacked grooming partners (see also Struhsaker 1967). Counter to expectations, however, there was no association between ectoparasite load and body mass of the animal being groomed, and the "beard" received little attention despite the high number of nits and lice found in this region.

As already noted, host defenses are costly, and grooming is no exception (Moore 2002). Some costs of grooming involve opportunity costs, such as time spent grooming that could be spent foraging. Other costs are physical, including the energy and concentration required to perform the activity, and even the loss of saliva during oral grooming (in rats: Ritter and Epstein 1974). Grooming also increases exposure to other parasites. Thus, ectoparasites and other infectious organisms could be transmitted during allogrooming, or the consumption of ectoparasites could lead to ingestion of parasites carried by arthropod intermediate hosts (Moore 2002). Fecal contamination of the fur provides a potential transmission route for intestinal parasites. Similarly, grooming wounds and surrounding tissue could expose groomers to blood-borne infections (Tutin 2000), and increased proximity during grooming episodes could facilitate transmission of respiratory diseases.

One conspicuous behavior of many mammals involves oral self-grooming of the genitals, particularly after mating. In an experimental study on male rats, Hart et al. (1987) used a restraining collar to prevent grooming after the male mated with a female that was vaginally inoculated with a bacterial marker organism. Compared to controls, experimentally restrained males were more likely to acquire the infection. Moreover, rat saliva was shown to be effective in killing two pathogens thought to cause genital infections in rats (Hart et al. 1987), possibly through anti-pathogen substances such as lysozyme and lactoferrin (Baron et al. 2000).

Fig. 5.4 Male genital grooming following mating. The image shows a male ringtailed lemur at St. Catherines Island, Georgia, orally grooming his genitals following mating. Picture provided by J. Parga, University of Texas.

Many primate species exhibit stereotyped genital self-grooming after mating, using their hands or their mouths (Fig. 5.4), and this behavior has been observed in both sexes (Vick and Conley 1976; Foerg 1982; Perry et al. 1992). Using phylogenetic comparative methods, Nunn (2003) tested whether genital grooming is more commonly reported among primate species in which individuals are more likely to be exposed to sexually transmitted diseases (STDs)—specifically those species in which females mate promiscuously with multiple partners. Promiscuity was quantified using data on relative testes mass (controlling for body mass) and the duration of estrus, as both of these measures are known to correlate with female mating promiscuity (Harcourt et al. 1981, 1995; van Schaik et al. 1999; Nunn et al. 2000). Counter to predictions, however, measures of promiscuity were unrelated to patterns of genital grooming, with the behavior only common in prosimians and callitrichids (Fig. 5.5). These results could indicate that smaller-bodied primates benefit more from allogrooming, or that many larger-bodied primates are biomechanically constrained in their ability to orally groom their own genitals. Moreover, because oral grooming was concentrated phylogenetically in prosimians and callitrichids, these species offer an opportunity to investigate individual variation in grooming behavior relative to disease risk, ideally using an experimental approach (Hart et al. 1987).

Many primates also orally groom wounds elsewhere on their bodies, potentially benefiting from anti-microbial factors in saliva (Baron et al. 2000). For example, Ritchie and Fragaszy (1988) described observations of a mother capuchin monkey

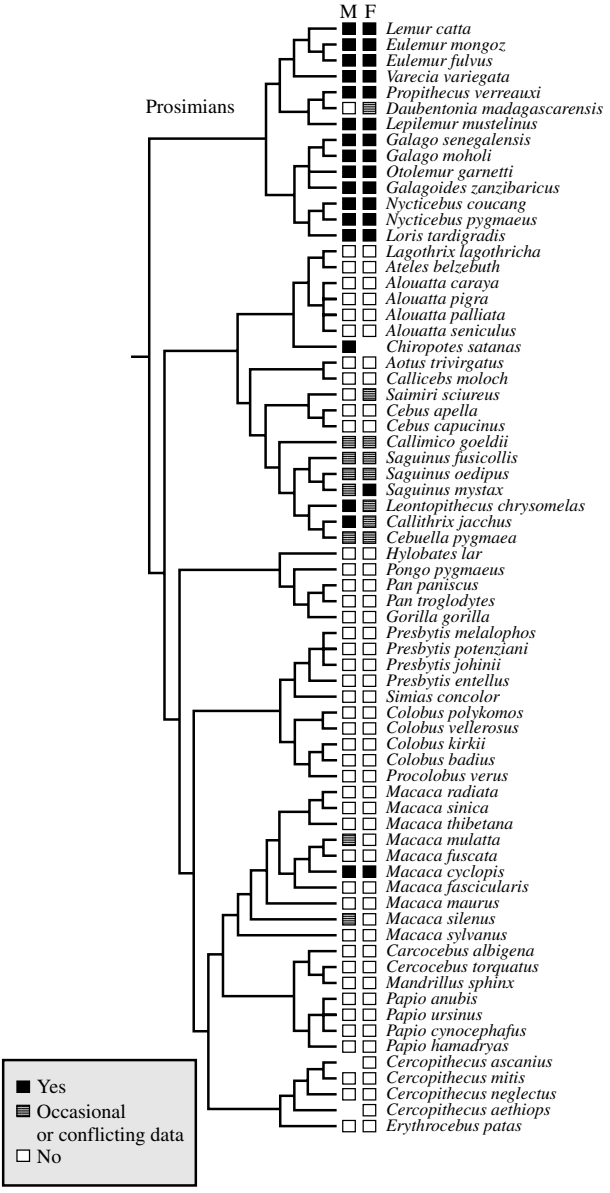


Fig. 5.5 The phylogenetic distribution of oral genital self-grooming in primates shown for males (M) and females (F) separately. Filled boxes indicate the presence of oral genital grooming, open boxes indicate absence, and no box represents missing data. Hatched boxes indicate species in which observers reported conflicting patterns of behavior or intermediate values of the trait. Reprinted from *Animal Behaviour*, Vol. 66, C. Nunn, "Behavioral Defences Against Sexually Transmitted Diseases in Primates," pp. 37–48, Copyright 2003, with permission from Elsevier.

(*Cebus apella*) orally grooming her infant's head wounds, including possible application of saliva to a stick that was used as a "grooming tool."

In summary, grooming serves a variety of social functions in primate groups, but abundant evidence also supports hygienic benefits of grooming. Many questions remain unanswered and deserve further investigation. Important among these are the tradeoffs that animals face in grooming, in particular because close contact between individuals could spread other directly transmitted diseases. Moreover, we know little about the effectiveness of genital grooming in eliminating STDs in primates, or the host characteristics that account for striking variation in these behaviors across species (Fig. 5.5 and Nunn 2003a). Finally, a wide variety of other behaviors documented in non-primates could provide hygienic benefits, including dust bathing, swimming, and applying ants to the skin (Hart 1997; Moore 2002). With a few exceptions (e.g. Longino 1984; Valderrama et al. 2000), we lack knowledge of these and related behavioral defenses in primates.

5.2.4 Medicinal plant use

Ecologists have long recognized the potential role of plant secondary compounds in eliminating parasites and reducing pain. However, only recently have systematic investigations of medicinal plants taken place, and there is much room for experimental testing of several exciting ideas. Janzen (1978) was among the first to suggest that consuming certain plants benefited animals in their battles against parasites. Noting that tannins and other substances in plants confer resistance to fungi and other microbes led him to propose, "certain tropical mammal-dispersed fruits should be a major source of antibiotics of all kinds . . ." (p. 75). He further speculated that a species of legume acts as a pain killer for elephants, that leaf-eating monkeys have fewer parasites than omnivores due to increased consumption of secondary compounds, and that feral pigs consume roots to combat helminth infections. Janzen also hypothesized that primates and other animals consume particular plants to facilitate food passage through the gut.

In primates, research on self-medication, including plant and soil consumption, has expanded significantly in the past two decades (Krishnamani and Mahaney 2000; Huffman 2006). Studies on wild primates have mainly focused on chimpanzees (Wrangham and Nishida 1983; Huffman and Wrangham 1994; Huffman 1997), with additional studies on, for example, baboons (Phillips-Conroy 1986), sifakas (*Propithecus verreauxi*, Carrai et al. 2003), bonobos (Dupain et al. 2002), gorillas (Fossey 1983; Mahaney et al. 1990), colobine monkeys (e.g. *Presbytis entellus, P. rubicunda*, and *Colobus guereza*, Oates 1978; Davies and Baillie 1988; Newton 1991), muriquis (Strier 1992, 1993), mantled howler monkeys (Glander 1994), and macaques (e.g. *Macaca fuscata* and *M. radiata*, Mahaney et al. 1993; Voros et al. 2001; Wakibara et al. 2001). Evidence consistent with some form of self-medication therefore has been documented in all major lineages of primates, with existing reports probably covering only a small fraction of the actual occurrence of medicinal plant use. Deeper questions have been raised about the actual benefits

Fig. 5.6 A chimpanzee chewing on the bitter pith of *Vernonia amygdalina*. Bitter pith chewing is thought to help control nematode infections (see Huffman 1997, 2006). Image courtesy of M. Huffman, Kyoto University.

obtained from consumption of putatively medicinal plants, with an absence of experimental tests fueling skepticism and calls for increased rigor in testing hypotheses concerning medicinal plant use (Sapolsky 1994; Lozano 1998; Hutchings et al. 2003), although the ideal experimental tests are unlikely to be feasible (or ethical) for many wild primates.

Several major types of self-medication have been suggested in primates, including eating berries, chewing plant pith (Fig. 5.6), swallowing leaves, eating bark, and consuming soil. The mechanisms of self-medication generally fall into three categories: (1) plant compounds that pharmacologically kill parasites (e.g. bitter pith chewing), (2) rough surfaces that help expel gut parasites (e.g. whole-leaf swallowing), and (3) substances that alleviate discomfort, such as pain or stomach upset, rather than reducing parasite loads (e.g. consumption of clay soils). Any given medicinal item could provide more than one benefit, and animals might use these items to prevent infection or they might be used therapeutically, that is, to treat infections (Lozano 1998). It is not our intention to summarize all examples of self-medication in primates, which have been reviewed elsewhere (Newton 1991; Huffman and Wrangham 1994; Huffman 1997; Lozano 1998; Huffman 2001). Instead, we give an overview of the diversity of medicinal plant use and the possible mechanisms involved in fighting parasites.

One of the first studies of medicinal plant use in primates focused on schistosome infections in baboons. In this study, Phillips-Conroy (1986) noted that baboons along the Awash River in regions at greatest risk of infection with *Schistosoma* consumed the fruits and leaves of *Balanites aegyptiaca*. Interpreting these results is complicated

because two different baboon species (and their hybrids) were studied, raising the possibility that behavioral variation unrelated to parasite avoidance accounted for the observed differences (see also Newton and Nishida 1990). Mechanistically, the steroidal saponin in *Balanites aegyptiaca* (diosgenin) is known to be toxic to infectious stages of schistosomes and could affect the development of the schistosome in the definitive host, possibly by changing the host's hormones or by affecting parasite attachment to the host. In a later experimental study in mice, however, Philips-Conroy and Knopf (1986) found that ingestion of the putatively active chemical agent actually *increased* the number of eggs released by infected hosts, casting doubt on the initial correlative study in baboons (although it is important to note that egg production might not be linearly related to numbers of adult worms).

Other researchers have conducted detailed studies of self-medication in chimpanzees (Huffman and Wrangham 1994; Huffman 1997), where several behaviors alerted investigators that consuming certain materials might not be tied strictly to food acquisition. For example, chimpanzees meticulously process shoots of particular species and chew on the bitter pith inside the shoots of plants (Huffman and Seifu 1989), or swallow leaves whole (Wrangham and Nishida 1983; Huffman and Caton 2001). Bitter-pith chewing (Fig. 5.6) is likely to provide pharmacological benefits, including alleviating stomach upset (Huffman et al. 1993; Huffman 1997), and swallowing whole leaves could help remove intestinal parasites (Huffman and Caton 2001), probably through physical action rather than chemical processes (Huffman et al. 1996; Page et al. 1997). Specifically, trichomes on certain whole leaves passing through the digestive tract might disrupt intestinal nematodes that are less firmly attached to the intestinal lining, probably by inducing diarrhea and leading to the expulsion of parasites in the feces (Huffman and Caton 2001; Huffman 2006). Whole leaves could also disrupt the attachment of tapeworms, although simple occurrence of proglottids (i.e. reproductive stages of tapeworms) in the feces does not necessarily indicate effective control of the actual parasites, since they will be found in feces whenever hosts are infected (Wrangham 1995). In addition, by slowly chewing plants or keeping them in the mouth before swallowing or spitting them out, secondary compounds may be absorbed by the oral mucosa, much as nicotine is absorbed from chewing tobacco, or nitroglycerine is absorbed under the tongue and used to treat individuals with heart conditions (Newton and Nishida 1990).

Many primates consume soil, a behavior known as geophagy (e.g. Knezevich 1998; Krishnamani and Mahaney 2000; Aufreiter et al. 2001; Ketch et al. 2001; Voros et al. 2001; Wakibara et al. 2001). A variety of hypotheses have been proposed to account for soil consumption, including acquiring minerals and detoxifying compounds in plant materials (e.g. Kreulen 1985). Medicinal benefits also have been proposed, specifically that soil alleviates diarrhea, isolates microorganisms, prevents toxin uptake, and buffers the stomach against gastric upset (Krishnamani and Mahaney 2000). Thus, Knezevitch (1998) proposed that high rates of soil consumption by free-ranging rhesus macaques account for the low levels of diarrhea found in these animals on Cayo Santiago. Although 89% of the animals in one study group were infected with parasites that cause diarrhea, the occurrence of diarrhea was low

(2%), and 76% of individuals practiced geophagy. Similarly, Bicca-Marques and Calegaro-Marques (1994) proposed that their observations of geophagy in black howler monkeys (*Alouatta caraya*) could be related to the presence of large numbers of cestodes in the feces of their study animals. Many researchers have suggested that soils alleviate physical discomfort from gastrointestinal upset (Mahaney et al. 1999; Ketch et al. 2001; Wakibara et al. 2001). It is important to remember that as with other behavioral counter-strategies, ingesting soil also has costs, particularly if infectious stages of parasites are consumed incidentally along with the soil. Red colobus monkeys in Zanzibar have been observed to consume charcoal (Cooney and Struhsaker 1997), which might function in ways similar to soil consumption in other primates.

A critical issue involving the use of medicinal plants concerns how this knowledge is acquired and transmitted to conspecifics (Huffman and Wrangham 1994; Huffman 1997; Huffman and Hirata 2003). Individual primates could select plants based on innate preferences for particular tastes as their health status changes, much as women often exhibit preferences for different foods when they are pregnant. Other researchers have considered socially driven mechanisms of cultural transmission (Huffman and Wrangham 1994; Huffman 1997, 2001). One recent study investigated the foundations and propagation of medicinal plant tradition (Huffman and Hirata 2004). Using a captive group of 11 chimpanzees, these authors introduced a locally available plant species with leaf characteristics that are virtually identical to leaves that are swallowed whole in wild chimpanzees. Remarkably, despite having never used this plant before, two of the chimpanzees were observed to swallow the plant whole, using behaviors similar to those documented in the wild. This suggests that chimpanzees exhibit an innate tendency to fold and swallow leaves with a rough texture. Moreover, Huffman and Hirata (2004) documented the spread of leaf-swallowing behavior to other individuals in the captive group, probably through observation of others. In terms of broader patterns of cultural transmission, offspring might learn the behavior from their mothers, or adults could learn from one another, and the trait would spread through the population via individual dispersal and group fission. Individuals must learn not only what plants to consume and when to consume them, but also the manner in which to process and consume the plants, for example, by chewing the pith, or overcoming their natural tendency to chew and instead fold and swallow whole leaves (Huffman and Wrangham 1994; Huffman 1997; Lozano 1998).

A number of important research directions are needed to better understand medicinal plant use in primates. First, we need to know whether the use of putatively medicinal plants actually assists animals in recovery and improves their health (Krief et al. 2005). Even though sick animals might use plants with medicinal properties, the lack of experimental protocols pose challenges for determining the effects of plant consumption on individual health (see Huffman 1997). Ultimately, researchers must show that the plant in question alleviates signs of infection or eliminates parasites to a greater extent than other plants in the host's diet (Lozano 1998). Second, there is an urgent need to increase our understanding of the origins and propagation

of medicinal plant use within and across populations of primates (Huffman and Hirata 2003, 2004), which Huffman (1997) noted is "one of the most challenging questions which needs to be investigated" (p. 192). Third, detailed studies on the mechanisms by which plants aid in the recovery from parasites are needed to provide evidence for the effectiveness of self-treatment. Although the use of plants by local humans will point the way toward plants with potential medicinal uses in nonhumans, ultimately it is necessary to demonstrate the mechanisms that underlie the effect of the plant on parasites. Finally, do animals ever use plant parts as stimulants or recreational drugs? One study raised this possibility after finding a "low but persistent intake" (p. 912) of hallucinogenic plants in free-ranging baboons (Hamilton et al. 1978).

5.3 Preventing infections: strategies for parasite avoidance

Among humans, behaviors such as avoiding contact with visibly sick individuals, sterilizing drinking water, washing hands, and applying insect repellant can limit exposure to infectious diseases. In this section, we review behaviors used by nonhuman primates that lower their risks of encountering parasites.

5.3.1 Habitat use and ranging behavior

5.3.1.1 Movement patterns and fecal contamination

Several investigators proposed that some aspects of primate movement patterns represent responses to variation in disease risk. A study of mangabeys (*Cercocebus albigena*) found that feces landed on branches used for locomotion in over 40% of observed defecations (Freeland 1980). Mangabeys remained in an area for a longer duration of time during the rainy season, which Freeland attributed to two factors: rain probably washed fecal material from vegetation, and fungal activity during damp conditions increased the mortality of infective protozoa. Freeland (1980) ruled out several alternative explanations that could also generate this pattern, including decreased movement of mangabeys when vegetation is wet and lower predation risk during periods of rain. Curiously, however, the animals showed little outright avoidance of fecal contamination during normal ranging, despite the potential for odors to demarcate fecal remains. Moreover, a recent study in the same species found the opposite pattern, with animals ranging more widely during the wet season (Olupot et al. 1997). Additional predictions of the "parasite avoidance" hypothesis were tested but not supported in this later study; instead, fruit availability was found to be a better predictor of ranging patterns. Thus, it remains unclear whether risk from intestinal parasites influences ranging patterns in this species.

In a study of red howler monkeys, Gilbert (1997) found that animals defecated selectively in areas where feces were more likely to fall unimpeded to the ground, reducing the potential for fecal contamination of arboreal pathways and food

resources. Before defecating, animals moved away from the resting area, looked down, and avoided soiling branches used for travel and resting. Mantled howling monkeys also show defecation patterns consistent with avoidance of gut parasites. They tend to defecate lower in the canopy and at more peripheral areas of the canopy, making it less likely that they will contaminate food resources (Henry and Winkler 2001). Braza et al. (1981) documented defecation behaviors in another study of red howler monkeys. The function of defecation behaviors in this latter study appeared to be territorial rather than hygienic, because particular locations near the monkeys' sleeping trees were used as latrines, and "after defecating, the howlers sometimes rubbed their anuses on the branches, which then took on a characteristic odour . . ." (p. 469). Obviously, anal marking of branches is not necessarily an example of "good hygiene," unless those same branches are subsequently avoided in locomotion.

Links between ranging patterns and parasitism have rarely been considered in primates (e.g. Stoner 1996), but one exemplary study focused on African bovids (Ezenwa 2004). These species show variation in grouping tendencies and patterns of ranging behavior, which is linked to territorial behavior (discussed in Chapter 6). Among individuals, Ezenwa (2004) found that territorial gazelles experienced higher parasite intensity. Across multiple bovid species, territoriality also correlated with parasitism, with more territorial host genera experiencing higher infection with strongyle nematodes. Grouping tendencies of the genera (gregarious versus solitary) showed effects that appeared to be independent of territoriality in some tests (Fig. 5.7) and interactive effects in other tests (e.g. for the effect of mean individual parasite richness, which was highest in territorial-gregarious hosts).

More intensive use of a range may therefore favor greater selectivity in contact with soil, water, or vegetation (Hart 1994). The timing of parasite development and survival in the hosts' environment probably determine the relative effectiveness of different patterns of avoidance and habitat use. Parasites could also influence patterns of migration and habitat use at a larger scale, which is relevant for some primates with large home ranges. For example, Folstad et al. (1991) proposed that the post-calving migration in reindeer (*Rangifer tarandus*) allows them to escape from warble fly (*Hypoderma tarandi*) infections by leaving behind areas contaminated with parasites.

5.3.1.2 Sleeping site selection

In his study of mangabeys, Freeland (1980) found that sleeping areas were heavily contaminated with parasites, so that animals might benefit from seeking uncontaminated sleep sites. In a later study, Hausfater and Meade (1982) investigated the links between sleeping trees, ranging patterns, and parasites in yellow baboons at Amboseli National Park, Kenya. When the baboons used the same sleeping trees on consecutive nights, infectious stages of nematodes accumulated in the surrounding soil. Animals contacted this soil when they sunned and foraged after leaving the sleeping site. Hausfater and Meade (1982) found that the nematodes *Oesophagostomum,*

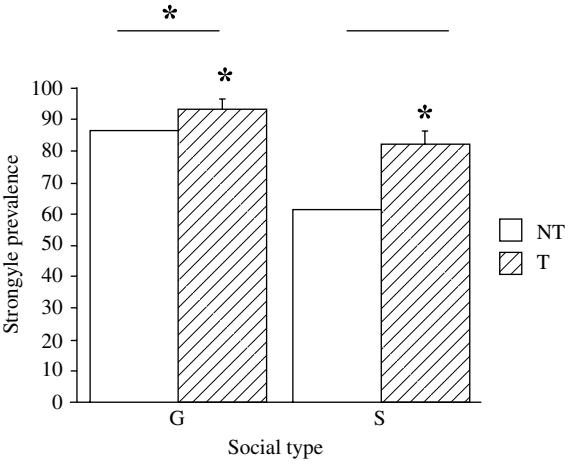


Fig. 5.7 Effect of social grouping and territoriality on strongyle prevalence in African bovids. Bars show mean prevalence (+/−SE) in a comparison of 8 African bovids that differ in social type (G = gregarious, S = solitary) and territoriality (NT = non-territorial, T = territorial). More gregarious genera and territorial genera have higher prevalence of infection. Taken from Ezenwa, V. Host social behavior and parasitic infection: a multifactorial approach. *Behavioral Ecology*, 15, 446-454. Copyright (2004) by the International Society for Behavioral Ecology.

Strongyloides, and *Trichostrongylus* become infectious to primates several days following defecation. The authors proposed that risk of acquiring infectious nematodes influenced the baboons' use of different sleeping groves, with animals rotating among sleeping trees within the range relative to parasite buildup in the soil (see also Hausfater and Sutherland 1984).

Subsequent studies failed to support the role of parasites in determining primate sleeping tree selection, whereas other studies demonstrated additional factors that could be more important. First, a group of baboons at Amboseli that foraged at a garbage dump (Lodge Group) used only a single tree repeatedly (S. Alberts, personal communication and Hahn et al. 2003). This group was found to have levels of parasitism that were comparable to other free-ranging groups in the population (Hahn et al. 2003). Second, a study of sleeping behavior in Guinea baboons (*Papio papio*) also revealed more regular use of sleeping sites and less alternation of sleeping trees (Anderson and McGrew 1984). Third, a study of sleeping site selection by golden-handed tamarins (*Saguinus midas*), a small-bodied arboreal species from South America, produced results consistent with parasite avoidance, but also highlighted predation and proximity to food resources as factors that influence the selection of sleeping sites (Day and Elwood 1999). Finally, Di Bitetti et al. (2000) failed to find any support for the parasite avoidance hypothesis in tufted capuchins (*Cebus apella*), another Neotropical, arboreal primate. Instead, sleeping site selection

Fig. 5.8 Image of a gray mouse lemur (*Microcebus murinus*) in a tree-hole. Photo by U. Walbaum, taken at Kirindy, Madagascar.

was most consistent with predation avoidance. Di Bitetti et al. (2000) noted that parasite-mediated pressure to select new sleeping sites may exist only in terrestrially foraging species, as these animals are most likely to contact parasites in the soil beneath sleeping sites.

Although the majority of studies conducted to date have not supported the initial results of Hausfater and Meade (1982), future tests could examine the effect of substrate use by focusing on terrestrial species and simultaneously quantifying the parasite communities in the hosts, in the soil, and on vegetation surrounding sleeping sites (Hausfater and Meade 1982). One potential explanation for the conflicting results is that sleeping sites are likely to play different roles in different species, and even among different populations of the same species. Understanding will probably only be achieved when predation risk and other factors that influence sleeping site selection are simultaneously quantified.

5.3.1.3 Nest-use

All species of great apes build nests, whereas many prosimians and monkeys use nest holes or other "shelters" (Fig. 5.8, Kappeler 1998a; Anderson 2000). Nest-use could reduce parasitism by providing a barrier between primate hosts and infectious stages of parasites in the soil or in vegetation (Landsoud-Soukate et al. 1995), and primates that build new nests every night should experience lower exposure to parasites that accumulate in the hosts' environment (MacKinnon 1974). Tree holes probably offer further protection from environmental conditions, such as rain and cold

temperatures, and might reduce attacks from arthropod vectors (see Section 5.3.3.2) or other insects (Whitten 1982). However, repeated use of the same tree hole could facilitate infection with ectoparasites (Dunn 1968) or fecally transmitted parasites that accumulate in the nest, thus pressuring animals to change sleeping sites when old ones become infested or contaminated (Butler and Roper 1996; Moore 2002). Some animals line their nests with materials that repel or damage parasites. Studies of birds have found some support for this "nest fumigation hypothesis" (Wimberger 1984; Hart 1997), but the idea has yet to be tested in primates.

5.3.2 Diet

Given that infectious stages of many parasites are ingested through contaminated food and water, surprisingly few studies have considered strategies that primates might use to avoid parasites while foraging (Lozano 1991; Hutchings et al. 2003), with most attention focused instead on medicinal plants that can reduce existing infections (see above). Several aspects of foraging behavior could reduce contact with parasites, including avoidance of infected prey and potentially contaminated fruit, leaves, and water.

5.3.2.1 Infected prey

At first glance, it seems plausible that predators should avoid vertebrate and invertebrate prey that serve as intermediate hosts for trophically transmitted parasites (e.g. Lozano 1991). Using a theoretical model, however, Lafferty (1992) showed that selective pressure for predators to avoid infected prey may be weak, particularly when parasites are not costly to definitive hosts, and when parasites enhance their transmission by manipulating the behavior of intermediate hosts (see Chapter 2 and Moore 2002). Under these conditions, the benefits of increased access to prey can outweigh the costs of becoming infected or, as noted by Lafferty (1992), "The parasite provides a delivery service for hard-to-get prey" (p. 862).

On the other hand, when predators and prey are closely related, the risk of contacting a harmful pathogen could be high, in part because species with more similar phylogenetic backgrounds are likely to be susceptible to similar infectious organisms (Southwood 1987; Pfenning 2000). Primates are known to hunt and consume other primates as prey, including chimpanzees that actively hunt red colobus monkeys (Stanford et al. 1994; Mitani and Watts 1999). Thus, we might expect to find more similar parasite communities among primate predators and their primate prey. Interestingly, some molecular and phylogenetic evidence supports this possibility. In one case, researchers found that blood serum samples from a yellow baboon reacted strongly to SIV from vervet monkeys, and based on these results, the authors proposed that baboons have acquired this virus through predation on vervet monkeys (Kodama et al. 1989). Another widely publicized example is the role of bushmeat hunting in exposing humans to infectious diseases from nonhuman primates, including multiple introductions of SIV/HIV, Ebola hemorrhagic fever, and Simian Foamy Viruses (e.g. Wolfe et al. 2004, see Chapters 7 and 8).

Fig. 5.9 Primates, such as these chacma baboons can be exposed to parasites through contact with slow moving, standing, or stagnant water. Image courtesy of D. Kitchen, The Ohio State University.

5.3.2.2 Contact with contaminated water

Another potential source of infection involves drinking or other physical contact with water. Whereas many primates obtain sufficient water from their diets, others utilize water sources (Fig. 5.9), including non-flowing lakes (Ransom 1981) or seasonal pools (Hall 1965). Concentrations of primates and other mammals at water sources during the dry season could also increase contact among hosts (Struhsaker and Gartlan 1970; Hamilton et al. 1976), facilitating the spread of disease within and across species. Primates may prefer flowing water sources to non-flowing or stagnant sources as a means to reduce contact with the molluscan intermediate host of schistosomiasis (McGrew et al. 1989b), and they may limit their time at the edge of water sources, as these areas provide suitable conditions for the development and survival of a number of parasites (Meade 1984). Similarly, hamadryas baboons have been reported to dig holes for drinking water rather than drink from slow-moving rivers during the dry season (Kummer 1968). However, at least once study concluded that "in general, baboons did not seem deliberately to avoid contaminating the water" with their own urine and feces (p. 6.12, Sharman 1981). As compared to other terrestrial primate species, baboons may be more susceptible to some water-borne parasites, such as schistosomes, due to greater reliance on water sources and an omnivorous diet that can include aquatic intermediate hosts, such as snails (Nelson 1960).

5.3.2.3 Ingestion of parasites on leaves and fruit

Animals could avoid food items that are common sources of parasites (Lozano 1991; Hutchings et al. 2003), although resource-limited animals may also benefit from eating foliage even when it is contaminated with parasites (Hutchings et al. 2003),

especially when nutritional stress acts to further increase disease risk (Gulland 1992; Milton 1996; Koski and Scott 2001; Chapman et al. 2005a). Ungulates are known to avoid foraging near feces (Hart 1994; Moore 2002), and the risk of fecal contamination may account for the use of "latrines" by a wide variety of mammals, such as raccoons (*Procyon lotor*, Page et al. 1999) and badgers (*Meles meles*, Stewart et al. 2002). In many species, however, latrines also provide social information to conspecifics through olfactory signals (Stewart et al. 2002), therefore potentially increasing exposure to parasites when conspecifics investigate these signals.

Primates are known to avoid eating potentially toxic plants, and in some cases they actually prepare foods to remove more toxic parts (Freeland and Janzen 1974; Wakibara et al. 2001). Thus, it is reasonable to propose that primate hosts avoid obvious sources of parasites either through diet choice, or by inspecting, cleaning, and preparing dietary items. Little is known about how primates avoid encounters with parasites on food resources, although observations of macaques washing potatoes in both salt and freshwater suggest that this might confer hygienic benefits (in addition to improving the taste of food items; Nakamichi et al. 1998). This and other behavioral strategies could be examined experimentally in wild and captive primate populations.

5.3.3 Avoidance of arthropod vectors and parasites

Arthropods serve as vectors for several major groups of infectious diseases, including blood-borne protozoa (e.g. malaria, trypanosomiasis), viruses (dengue and yellow fever), and helminths (filarial worms). These important parasite groups should select for host avoidance mechanisms that reduce bites from the arthropod vectors that transmit them (Moore 2002). Here we consider individual-level deterrents to insect pests. Later, in Chapter 6, we discuss how primates might adjust group size in response to mobile arthropods.

5.3.3.1 Physical deterrents to insect pests: fly-swatting

Animals can discourage insect pests by fly-swatting using their hands, ears, feet, and tails (Hart 1990, 1994). Many host species exhibit these behaviors, including cattle (Harris et al. 1987) and birds (Edman and Kale 1971). Tool use may even play a role in avoidance of flying arthropods, with elephants reported to use branches as "switches" to repel flying insects. Thus, in experiments that compared fly counts among elephants in two experimental treatments, Hart and Hart (1994) showed that elephants provided with a switch experienced a 43% decline in the number of flies on or near their bodies. On multiple occasions, the elephants modified the branches by shortening them or removing branches, possibly to maximize their efficiency as switches.

Among primates, Dudley and Milton (1990) provided fascinating details on fly-swatting behavior in mantled howling monkeys. In a population of howlers on Barro Colorado Island, Panama, monkeys performed slapping behaviors with hands and

tails at a rate of up to 20 times per minute. Based on a mean of 3.8 slaps (or other gestures) toward insect pests per minute, Dudley and Milton (1990) estimated that individual monkeys performed at least 1500 fly-avoidance actions per day. Remarkably, this activity consumed about 4.6% of the animals' metabolic costs (in excess of basal metabolism).

Wedge-capped capuchin monkeys (*Cebus olivaceous*) of Venezuela exhibit a remarkable behavior to reduce bites from mosquitoes and the parasites that they carry. Valderrama et al. (2000) reported that capuchins anoint their fur with secretions from millipedes (*Orthoporus dorsovittatus*), with many bouts involving sharing of a millipede in a "writhing cluster" (p. 2783) of up to four monkeys. The millipedes are known to contain benzoquinones, a chemical that repels mosquitoes (Weldon et al. 2003). This chemical defense also has costs because these substances are toxic and carcinogenic in rodents, yet capuchins presented with these substances in captivity readily exhibit self-anointing behavior (Weldon et al. 2003). Other potential repellents derived from insects or plants have been documented in a wide variety of primates, including owl monkeys (*Aotus* spp., Zito et al. 2003), red-bellied (*Eulemur rubriventer*) and rufous lemurs (*Eulemur fulvus rufous*, Overdorff 1993), spider monkeys (*Ateles geoffroyi*, Richard 1970), and in additional studies of capuchins (Baker 1996; see also Huffman in press). Similarly, white-nosed coatis (*Nasua narica*) in Panama use resin from the plant *Trattinnickia aspera* during grooming, possibly as repellent (Gompper and Hoylman 1993), although further study is needed to identify the benefits, if any, obtained from this behavior.

Several additional traits might influence avoidance of parasites in mammals and could apply to some species of primates. These include cooperative defenses, running from flying parasites, and (remarkably!) pelage coloration, such as the stripes of zebras (Duncan and Cowtan 1980; Waage 1981; Mooring and Hart 1992).

5.3.3.2 Use of closed sleep sites and containment of chemical attractants

Nunn and Heymann (2005) investigated host traits correlated with malaria prevalence in Neotropical primates, focusing on group size, body mass, and sleeping behavior. Anopheline mosquitoes transmit malaria to these monkeys and are attracted to body odorants and carbon dioxide emitted by hosts (Bock and Cardew 1996; Hallem et al. 2004). In comparative tests, the authors confirmed that malaria prevalence increases with group size in Neotropical primates, as suggested by a previous non-phylogenetic analysis (Davies et al. 1991). Sleeping in closed microhabitats, such as tree holes or tangles of vegetation, was also associated with a reduction in malaria (Fig 5.10, Nunn and Heymann 2005), possibly by limiting the ability of mosquitoes to locate hosts. This conclusion was based on only three evolutionary transitions in sleeping behavior, and animals probably obtain additional benefits from closed sites, such as thermoregulation or protection from predators (see Fig 5.8). Thus, further research, with larger datasets on vector-transmitted diseases and a larger number of primate species, should investigate whether use of closed sleeping reduces disease risk independently of other factors. In the field, it would be interesting to investigate whether

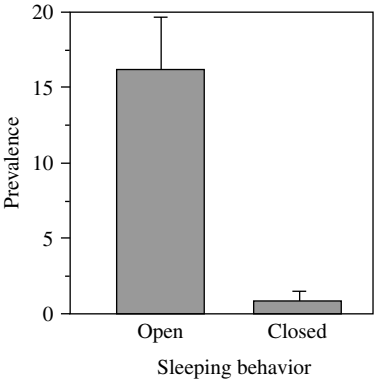


Fig. 5.10 Malaria prevalence in Neotropical primates in relation to sleeping behavior. Mean prevalence is lower among genera that sleep in closed microhabitats in non-phylogenetic tests (data from Nunn and Heymann 2005). Results were also significant in the majority of phylogenetic tests using independent contrasts, although analyses were based on only two or three evolutionary transitions depending on the phylogeny used.

primates prefer to sleep at heights above the ground that avoid overlap with vector foraging height preferences.

5.3.4 Parental care

In addition to providing resources and protection from predators, parents can help defend their offspring against infections and facilitate immune system development (Hart 1990). Mothers provide antibodies across the placenta or in milk, and they can be instrumental in exposing infants to sources of microorganisms that are essential for effective digestion and protection of the gut tissues (Hart 1990). Freeland (1976) and Hart (1990) proposed that parents regulate exposure to potential sources of parasites to stimulate immune system development in young animals. Altmann (1980) also proposed a role for parents in developing the immune defenses of their young, noting that she had "not seen mothers limit . . . the nonfood items that their infants mouth from the ground, especially in their first week" (p. 174). Freeland (1976) considered such exposure in the context of infant handling by non-mothers in primate groups, specifically proposing that handling exposes the infant to a wider range of group-specific microorganisms than if such handling did not occur. Freeland also acknowledged the disadvantages of this behavior, including exposure to more parasites in larger groups.

Primate infants obviously must suckle, and the mammary glands and surrounding skin and fur on mothers could harbor sources of infection. Mothers can provide a clean surface for nursing by self-grooming their mammary glands and nipples (Hart 1990). More speculatively, Hart (1990) proposed that mothers might protect

offspring by practicing infanticide to eliminate infants harboring contagious infections that could spread to litter-mates, although this seems unlikely in primates given their typically small litters. Finally, mothers can help offspring that are sick by allowing them to rest and recover from infection. The primatological literature provides several examples of mothers carrying sick or injured offspring (e.g. Altmann 1980; Goodall 1986).

5.3.5 Avoiding infected conspecifics

One obvious way to reduce the risk of directly transmitted parasites is to avoid contacting other hosts that express outward signs of infection (Freeland 1976; Borgia 1986; Loehle 1995). Experimental work on non-primates has shown that chemical or physical cues might limit interactions between diseased hosts and other animals. In tadpoles, for example, animals used chemical cues to avoid conspecifics infected with a fungal parasite (Kiesecker et al. 1999). Similarly, mice detected infection in conspecifics through cues excreted in urine, with subsequent effects on social interactions (Kavaliers and Colwell 1995a; Penn and Potts 1998; Penn et al. 1998). Among house finches, diseased birds with severe outward signs of mycoplasmal conjunctivitis, caused by a bacterial pathogen, were more likely to be seen foraging alone or in smaller flocks relative to birds that appeared healthy (Hotchkiss et al. 2004). However, "apparent isolation" of these diseased hosts could be caused by their reduced mobility rather than avoidance by flock mates (Kollias et al. 2004).

Anecdotal evidence suggests that nonhuman primates also can recognize sickness in conspecifics. Chimpanzees and baboons provide some intriguing, although speculative, examples. Thus, Goodall (1986) noted that "a change in the appearance or movements of an individual due to injury or ill health may affect the way he is treated by his fellows" (pp. 121–122), provoking fear or aggression in healthy chimpanzees. On the other hand, Huffman et al. (1997) described how individuals who were extremely sick continued to socialize with others, albeit at a reduced rate, and there was little convincing evidence to suggest that healthy animals actively avoided sick individuals (see also descriptions in Takasaki and Hunt 1987; Huffman and Seifu 1989; Wallis and Lee 1999; Boesch and Boesch-Achermann 2000). Reports from baboons also indicate that individuals might be capable of detecting sickness in conspecifics, including offspring (Altmann 1980). It remains unclear whether primates use behavioral, chemical, or physical cues to identify sick conspecifics.

Despite these intriguing examples, there is little support for the hypothesis that animals are shunned or quarantined based on infection status, even when trying to enter new groups. Freeland (1976) suggested that the stress and challenges of immigration should reveal latent infections, enabling resident animals to reject immigrants that carry infections. He noted that primates are "often conspicuous for the length of time that it takes for a new member to become completely assimilated into the group" (p. 14). In vervet monkeys, for example, the integration of a new

male took approximately 45 days (Struhsaker 1967), and ring-tailed lemurs drove away solitary males in over 90% of interactions at Berenty (Nakamichi and Koyama 1997). However, alternative hypotheses for this behavior have little to do with avoiding infection, and in many cases seem more plausible. For instance, opposition to immigrants is often greatest among like-sex members of the new group (Pusey and Packer 1987), suggesting that resistance to immigrants functions to minimize competition for mates or resources. Moreover, among 20 species of primates included in a review of female choice (Small 1989), females of nine species demonstrated a *preference* for strangers, such as extra-group males and recent immigrants.

It is important to bear in mind that reduced social activity of diseased hosts could occur as a byproduct of lethargy associated with illness (Hart 1990), with sick animals simply being unable to keep up with healthier members of the group (Huffman et al. 1997). It is also worth noting a more speculative benefit of identifying diseased individuals—*rather than avoiding these infected hosts, healthy animals might benefit from helping kin to recover* (Hart 1990). In this scenario, healthy animals could enable diseased relatives, mates, or allies to recover from illness, for example, by providing resources and medicinal plants that facilitate healing (dwarf mongooses, Rasa 1983). Thus, detecting behavioral cues could be driven by selection to help sick kin, especially in cases of infection with non-contact-borne infectious diseases such as malaria or schistosomiasis.

When individuals successfully avoid interacting with diseased animals, this breaks the links needed for directly transmitted parasites to spread through populations. From an evolutionary perspective, this could favor less pathogenic parasites that trigger fewer signs of infection in their hosts, an idea that has been investigated with both verbal models and in mathematically explicit epidemiological approaches (see Chapter 6 and Ewald 1994a; Møller and Saino 1994; Knell 1999). In other words, when animals can recognize and avoid contact with contagious hosts, this should select for parasites that most effectively hide their presence. Such an outcome could in fact benefit hosts, since parasites that produce fewer outward signs should be, on average, less virulent. But this scenario would also make it extremely difficult to document tangible benefits derived from behavioral avoidance of infected conspecifics at the population level.

Recognizing illness in conspecifics is a fascinating cognitive question (Heymann 1999), yet few investigators have directly examined this possibility in nonhuman primates. In future research, knowledge of the type of parasite and its transmission strategy could be integrated with understanding the benefits derived from identifying another animal's disease status. Thus, primates should most actively avoid contacting individuals that harbor highly contagious and debilitating diseases, whereas avoidance might not be observed for indirectly transmitted parasites. In addition, it would be useful to investigate the mechanisms used by primates to detect sickness in conspecifics. Human physicians and veterinarians have long used such cues, based on body smell or urine characteristics, for detecting infections (Hamilton and Zuk 1982; Penn and Potts 1998). Thus far, primatologists have focused on behavioral correlates of

illness, but hormonal variation or immune system activity, as signaled by chemical changes, might provide more convincing evidence that individuals can identify, and potentially avoid, sick animals.

5.4 Parasite pressure, mate choice, and sexual selection

Parasites play a prominent role in studies of sexual selection (Hamilton and Zuk 1982; Clayton 1991; Folstad and Karter 1992; Andersson 1994; Møller et al. 1999), and sexual selection also plays a central role in studies of primate sociality and evolution (Dunbar 1988; Jones 2003; van Schaik and Kappeler 2003). Indeed, a synthesis of individual-level host behavioral defenses would be incomplete without considering sexual selection as a response to infectious disease risk.

Sexual selection involves two processes: competition among individuals of the same sex for access to mates (intra-sexual competition), and preference for particular mating partners (mate choice, Andersson 1994). Most studies of parasite-mediated sexual selection center on mate choice, with three main benefits to the hosts (Read 1990; Møller and Saino 1994): (1) maximizing the quality of parental care by selecting uninfected partners (Milinski and Bakker 1990; Price et al. 1993), (2) avoiding contact with partners infected with contagious parasites spread through social contact (Price et al. 1993; Loehle 1995, 1997; Able 1996), and (3) choosing mates that will pass genetically based resistance to offspring (Hamilton and Zuk 1982). The first two cases provide *direct benefits* because the choosy individual benefits directly, that is, by avoiding contracting the parasite or obtaining better care for its offspring. The final hypothesis involves *indirect benefits*, with offspring acquiring genetic traits important to combating future infections (see Andersson 1994).

Several caveats should be noted when considering how mate choice might reduce the individual risk of infection. First, benefits acquired from mate choice typically focus on female preferences, but male primates could also be the choosy sex (Pagel 1994c; Paul 2002). Specifically, mate choice by males might be driven by parental care benefits, given that females are the primary caregivers in primates. Second, parasites could also affect the outcome of intersexual competition in addition to their effects on mate choice (Freeland 1976, 1981b; Howard and Minchella 1990). Third, remarkably few studies have been conducted in primates, leading Paul (2002) to note, "How the male mandrill, one of Darwin's famous examples, got his brightly colored face, is still unknown" (p. 877). This lack of evidence could partly reflect that females often mate promiscuously with many males, probably to reduce infanticide risk (Hrdy 1979; Schaik et al. 1999; Soltis 2002). Indeed, in surveys across primates, several experts have argued that evidence for female choice in primates is inconclusive (Small 1989) or "modest at best" (Keddy-Hector 1992, p. 65). Or, as stated by Small (1989), although "female primates are assertive sexual partners . . . they seem to be less discriminating than might be expected" (p. 124).

Finally, most hypotheses assume that sexually selected traits involved in mate choice, such as skin coloration or coat condition, have the potential to reveal an animal's infection status to potential mating partners. After reviewing three major

categories of benefits that primates might obtain from mate choice, we discuss possible signals used by primates to select healthy partners.

5.4.1 Direct benefits: selection of uninfected caregivers

Infected animals might provide poorer quality parental care, especially if they are unable to monitor their offspring or sequester sufficient resources for offspring growth and development. For example, Huffman and Seifu (1989) described how a sick female chimpanzee was unable to monitor her dependent infant, and in a separate study, an influenza-like sickness contributed to the separation of another mother–infant pair of chimpanzees (Uehara and Nyundo 1983). Based on these observations, animals should prefer uninfected partners that offer the best parental care, as potentially reflected by condition-dependent secondary sexual characteristics (Møller and Saino 1994). This hypothesis can apply to a wide range of parasites, regardless of whether or not they are contagious (i.e., spread through direct contact). The plausibility of this "caregiver" hypothesis has received little attention, however, and only a few studies have tested for benefits related to improved parental care (e.g. Milinski and Bakker 1990).

We can make predictions for when choosiness related to parental care is most likely to exist in primates and other animals. First, benefits should increase in populations or species that invest more in their offspring, a trait that can be quantified by the length of the juvenile period (age at sexual maturation) relative to body mass or other life history features. Second, the benefits of choosing healthy partners should be more important when hosts are faced with particularly virulent parasites that compromise the quantity and quality of parental care. Third, choice for healthy caregivers is expected to increase when mating is costly for the non-caring sex (in primates, these are generally males). When mating is not costly in terms of mate guarding, or risky in terms of STDs, males are expected to take advantage of all mating opportunities when they arise. Finally, a preference for healthy mates should be more likely under uniparental offspring care, since the other sex can do little to make up for lost parental care when a partner is infected with a debilitating parasite. Thus, benefits are most likely to accrue to male primates who choose uninfected females.

Future research on this subject will need to identify parasites that impact parental care in primates, and whether cues at the time of mating indicate future susceptibility to infection when offsping care is provided. In assessing the mechanisms used in mate choice, it is important to determine whether patterns of mating reflect deliberate mate choice by a healthy individual, versus a simpler explanation that infected individuals are less active and hence less interested in mating. For example, Edwards and Barnard (1987) found that infected female mice were more likely to avoid mating attempts by males, while Kaviliers et al. (1997) showed that infected males also expressed less interest in females, although this depended on the stage of infection.

5.4.2 Avoidance of directly transmitted parasites

Mating involves extremely close physical contact during which contagious parasites can be transmitted. Condition-dependent secondary sexual characteristics could

offer a means to identify healthy mating partners and hence avoid contacts with potentially infectious hosts (Freeland 1976; Price et al. 1993; Able 1996; Loehle 1997). In considering the direct benefits of parasite avoidance, the crucial assumptions are that at least one sex exhibits mate choice based on sexually selected ornaments, expression of the trait reflects current infection status, and a significant risk of infection occurs during courtship, mating and shared parental care. As noted in the previous section, tests of this hypothesis in the field and lab will need to control for the possibility that infected individuals may be less interested in mating.

Under this hypothesis, infections with parasites transmissible by direct contact should reduce mating success more so than infections by other parasite types. Able (1996) found support for this idea using a small dataset on parasitic infection and male mating success in vertebrate animals ($n = 15$ studies). Similarly, Walther et al. (1999) found that across 66 species of Peruvian passerines, male showiness correlated negatively with louse abundance, consistent with the hypothesis that females reduced their contact with infected males. Finally, Loehle (1997) developed a simulation model to investigate the plausibility of contagion avoidance as a driver of mate choice in a host population where the expression of showiness indicated lack of infection with an STD; he concluded that this mechanism provided a viable alternative to other models of sexual selection. However, one drawback of this general hypothesis is that it treats pathogens as evolutionary static entities, rather than considering a more dynamic model where parasite virulence and transmission can evolve. The assumption of fixed effects of infection on host mortality and sterility is violated if mate choice in fact selects for less virulent pathogens (Møller and Saino 1994; Knell 1999). Furthermore, rather than choosing mates based on ornaments or displays, female primates could instead mate with younger males, who are less likely to have contracted an STD simply because they have had fewer mating opportunities (discussed in Stumpf and Boesch 2005).

In summary, many animals can reduce disease risk through mate choice to avoid infected partners. Future experimental studies of primate mate choice in relation to host infection status can address whether or not the parasites in question can be transmitted by host contact. In addition to empirical studies, there is a need for coevolutionary models that allow both mate choice and pathogen virulence to evolve in order to understand the direct benefits of mate choice in terms of individual infection risk, parasite establishment in host populations, and evolution toward reduced parasite virulence (see Chapter 6 and Knell 1999).

5.4.3 Indirect benefits of mate choice

Indirect benefits of sexual selection in the form of "good genes" for parasite resistance have played a major role in sexual selection theory for several decades (Freeland 1976; Hamilton and Zuk 1982; Andersson 1994). But conflict remains over whether parasites actually generate fitness variation and whether they mediate honest signals for sexual selection (Read 1990). Hamilton and Zuk's (1982) classic argument is that animals (usually females) choose mates based on secondary sexual traits that signal resistance to parasite infection, thus indicating whether potential mates could pass resistance

traits on to their progeny. The hypothesis rests on three key premises: that host–parasite coevolution maintains heritable variation in parasite resistance, that parasites in question are debilitating in some way (but do not cause rapid host death), and that expression of secondary sexual traits is reduced in infected animals (Read 1990).

Researchers have investigated the Hamilton-Zuk hypothesis across a wide array of species with mixed results. An area particularly ripe for exploration in primates involves the role of hormones as mediators of immune responsiveness. Central to the good genes model is the requirement that sexually selected traits convey honest information about an individual's underlying genetic resistance to disease. Research on this topic has provided a conceptual framework for the "dual effects" of testosterone under the *immunocompetence handicap hypothesis* (Folstad and Karter 1992; Roberts et al. 2004). Under this hypothesis, testosterone is responsible for the expression of male sexual signals, but this hormone is also immunosuppressive. Thus, only those males that can withstand parasite pressure, possibly through "good genes," can afford to express traits used in female choice. With increasing understanding of hormones in primate behavior and sexuality (Dixson 1998), the interactions between hormones, sexually selected traits, and the immune system should receive greater investigation (Møller and Saino 1994). Hormones may also account for differences in patterns of infection between the sexes (see Fig. 3.10; Solomon 1969; Zuk and McKean 1996; Møller et al. 1998b; Moore and Wilson 2002).

5.4.4 Parasite status, resistance, and signals for choosing mates

Intriguing evidence from non-primates suggests that female mammals avoid mating with parasitized males. For example, one experimental study of mice indicated a preference by females for mating with un-parasitized males (Ehman and Scott 2002), and another study found that female meadow voles avoid nest materials used by parasitized males (Klein et al. 1999). In primates, too, a number of studies have identified links between parasitism and the expression of traits used in mate choice. Females can judge male health by examining their skin and coat condition, which is plausible in primates given the extent of inter-sexual grooming (e.g. Small 1989), and the large number of species with exposed, colorful skin (Dixson 1998). For ectoparasites, showy traits could allow females to discern infected males by providing a background that makes these parasites more visible to a potential mate (Borgia 1986; Able 1996).

Ayres (1986) proposed that the red and hairless head of the bald uakari (see Fig. 1.5) indicates health and plays a role in sexual selection. Indeed, bald uakaris appear to be ideal test case for the role of parasites in primate sexual selection for several reasons. First, the heads of captive bald uakaris fade when they become ill (Lasry and Sheridan 1965), suggesting that health status affects red coloration. Second, the red coloration of the uakari's bare facial skin probably depends on testosterone (Dixson 1998) and hence should be an "honest cue" of disease resistance, possibly driven by a tradeoff between testosterone and immune defenses (Folstad and Karter 1992). Finally, as compared to the black uakari (*Cacajao melanocephalus*), the bald uakari lives in "white water" forests where pH may be

more conducive to mosquito breeding. This is important because mosquito-borne diseases such as malaria can be debilitating and have figured prominently in previous studies of indirect benefits of parasite avoidance, particularly in birds (Hamilton and Zuk 1982; Yezerinac and Weatherhead 1995).

A recent study tested whether female rhesus macaques (*Macaca mulatta*) choose mates based on skin coloration. During the mating season, the facial skin of adult male rhesus monkeys becomes red. Using digitally altered images of males from Cayo Santiago, Waitt et al. (2003) tested whether captive females preferred males that displayed more red. In a video choice test, five out of six females exhibited a preference for the redder male, measured as gaze duration toward one male over the other. The results could support indirect or direct benefits of mate choice, but hormonal mediation of the signal (and thus its indication of overall male quality) could be a clue that indirect benefits play a role. Red coloration is commonly used in ornamental coloration and courtship displays across a wide range of species, and could also play a role in contests among males, as demonstrated by a recent study of humans using data from Olympic contests (Hill and Barton 2005). When contestants were randomly assigned red or blue outfits (or protectors) in four combat sports, the individual wearing red was significantly more likely to win!

Some studies in large mammals produced evidence for links between parasitism, body coloration and other traits in males and females, including one study showing that relatively parasite-free male Asian elephants (*Elephas maximus*) have longer tusks (after controlling for age, Watve and Sukumar 1997). As another example, parasite removal lead to more symmetrical antlers (but had no effect on size) in female reindeer (*Rangifer tarandus*, Folstad et al. 1996), suggesting that antler asymmetry may be important in assessing genetic resistance to parasites. In primates, Cheney (1988) reported that the coat color of vervet monkeys "changes from its usual olive gray to pale whitish" (p. 389) when they become ill, especially in infants. In another example, a Ph.D. study of semi-free-ranging brown lemurs (*Eulemur fulvus*) revealed a link between parasites and female appearance in the form of an association between worm burden and female body coloration (Regan 1998). A later study of the same species (Cooper and Hosey 2003) demonstrated that female brown lemurs preferred males with more colorful faces, suggesting that sexual selection could operate on both sexes in this species.

5.5 Summary and synthesis

The ubiquity of parasites and the pressures they exert on host fitness has favored a variety of resistance mechanisms to avoid, remove, limit, or clear infections, as illustrated by the multitude of defenses employed by wild primates. The strategies used will likely depend on the type of parasite, transmission mode, entry location, and site of infection, and whether the infectious agents are intra- or extra-cellular. Behaviorally avoiding encounters might be more important in reducing risks from macroparasites, in part because effects on host fitness depend on total parasite loads, and in turn parasite loads

for many macroparasites are directly related to the number of encounters (as most parasitic worms do not directly multiply within a single host animal, see Chapters 2 and 4). Conversely, microparasites can replicate quickly within the host, even following encounters with just a few infectious particles, and hence might select for a more efficient immune response to eliminate parasites following exposure.

Most host responses following pathogen invasion involve a combination of innate and adaptive immune defenses in addition to behaviors that actively counter infections. In the context of primate socioecology, immune defenses could lower disease risk when behavioral counterstrategies are unavailable or come with substantial costs in terms of other host activities. For example, animals could effectively avoid STDs through the behavioral strategy of lifetime monogamy (Loehle 1995), but this comes with its own costs, including lost reproductive opportunities and increased infanticide risk (Nunn 2003; Nunn and Altizer 2004). Similarly, mathematical models have shown that fitness advantages to multiple mating are so strong, at least among males, that they probably outweigh costs from STD infections under a wide range of scenarios (Thrall et al. 2000).

Immune responses can also be energetically costly and may divert resources away from basic maintenance and reproduction (Bonneaud et al. 2003), so that if the risk of infection and the virulence of the pathogen is low, hosts should invest in other activities. In general, optimal allocation to immune and behavioral defenses should depend on a balance between three key factors: (1) risks of encountering parasites and the fitness impacts of infection, (2) the effectiveness of a given strategy in light of parasite transmission and development within the host, and (3) the cost of the defense in terms of energy or lost opportunities for increased fitness. With this in mind, allocation to different types of defenses could vary among different primate species, and even among populations within a species.

The examples in this chapter highlight fascinating accounts of behavioral counterstrategies in wild primates, but simultaneously expose a need for experimental approaches and studies that control for other ecological forces, such as predation pressure. This is partly because many putative defenses likely provide multiple benefits. For example, sleeping in a closed site might reduce exposure to vectors (Heymann 1995, 2001; Nunn and Heymann 2005), but also could provide benefits involving predator-avoidance and thermoregulation (Kappeler 1998a). In addition, most behavioral defenses depend strongly on parasite transmission strategy, thus accounting for why behaviors to avoid STDs (Hart et al. 1987; Donovan 2000a, b; Nunn 2003) differ in fundamental ways from behavioral defenses to vector-borne parasites (Freeland 1977; Dudley and Milton 1990) or intestinal parasites (Hausfater and Meade 1982). Future research should focus on uncovering these defenses in greater detail, while also developing a cost-benefit framework for investigating why particular defenses are used against particular types of parasites. In the next chapter, we move beyond individual responses to infection and consider how social and mating systems might reflect both facultative and evolved strategies to counter disease risk and the ways in which hypotheses involving sociality can be tested.

6

Infectious disease and primate social systems

6.1 Introduction

Like other animals, primates gain many advantages from living in groups (Krause and Ruxton 2002). The main benefits of group living probably involve reduced predation risk (van Schaik 1983; van Schaik and van Hooff 1983), and possibly defense of food resources from neighboring groups in some species (Wrangham 1980). However, sociality also comes with costs, and one often-cited cost involves the spread of infectious disease (Alexander 1974; Freeland 1976; Møller et al. 1993; Krause and Ruxton 2002). This cost arises because social interactions provide an efficient network for the spread of directly transmitted parasites (Altizer et al. 2003b). Moreover, larger social groups could produce denser concentrations of chemical cues used by vectors to locate their hosts (Davies et al. 1991; Nunn and Heymann 2005). Thus, a major question is whether parasites represent a significant ecological force in primate mating and social systems.

In this chapter, we focus on whether social and mating systems are adjusted in response to parasite pressure—either as a plastic behavioral response, or genetically as a result of evolutionary change. We are stepping into an immense intellectual void by raising these questions, as most empirical and theoretical research on infectious disease and sociality in animals has focused on *opportunities* for transmission in different mating and social systems, whereas here we are considering the *effects* of disease on sociality and mating behavior. Examples of similar research on other animal species include studies of parasite dynamics and host evolution in social insects (Sherman et al. 1988; Schmid-Hempel 1998), and shifts in mammalian sociality in response to flying insects, especially in ungulates that form larger groups with increasing intensity of biting fly attacks (Rubenstein and Hohmann 1989; Mooring and Hart 1992). These studies demonstrate that parasitism can shape patterns of social interaction and evolution, but no studies have shown, for example, that individual primates adjust group size or restrict the entry of potential immigrants to minimize the spread of disease.

The idea that parasites are a potent force operating on sociality is not a new one. In pioneering papers, Freeland (1976) and Loehle (1995) forwarded the hypothesis that social behaviors have evolved to reduce the risks of acquiring new infectious diseases, and to reduce the spread of diseases that individuals already harbor (see Chapter 1). Also of historical significance are W.D. Hamilton's joint interests in

social interactions (e.g. Hamilton 1963, 1964) and the evolutionary arms race between hosts and parasites (Hamilton 1980; Seger and Hamilton 1988). Our goal in this chapter is to build on these conceptual frameworks to investigate how parasites influence primate sociality, and more generally, to identify approaches for studying the links between parasite pressure and animal social systems.

Three issues should be kept in mind when investigating the effects of infectious disease on social and mating systems. First, it is important to clarify the mechanisms that drive variation in social systems, and in this context to remember that social systems emerge from interactions among individuals (Chapter 1 and Hinde 1976; Kappeler and van Schaik 2002). Factors that influence costs and benefits to individual animals will determine, for example, whether they remain in a particular group, and which other animals they interact with in the group. Thus, questions aimed at mechanisms should primarily focus on selective pressures operating on individuals, rather than on groups.

A second issue is that parasite pressure could generate evolutionary changes in mating or social systems, or they could induce more facultative, short-term responses by individuals without necessarily producing evolutionary change. Many variables discussed in this chapter—such as group size, territoriality, and mating systems—show greater variation across primate species than within species; thus, much of the data needed to test hypotheses will come from comparative databases. However, differences in social parameters among primate species do not require that the behaviors in question are evolved (genetic) responses to selective pressures from parasites, as it could be that all host species exhibit the same potential for facultative responses to ecological conditions.

The final issue to keep in mind concerns responses by the parasite to host behavioral changes. When investigating the links between parasites and social systems, changes in host sociality induced by parasites are likely to result in reciprocal selection pressure on the parasites (coevolution), potentially causing the behavioral response of the host to become less effective. For example, increased resistance to immigration could select for parasites with longer incubation periods and reduced virulence, as diseased immigrants might otherwise die or recover before they enter new groups (Ewald 1994a; Boots and Sasaki 1999; Cross et al. 2005). This response by the parasite would therefore make resistance to immigrants less successful. Thus, the coevolutionary process makes it difficult to generate simple predictions, and through evolutionary responses, parasites could persist in the face of host social behaviors that would otherwise reduce infections, limiting potential benefits conferred by changes in host behavior.

Related concerns arise when attempting to identify causality in observed correlations between host behavioral traits and patterns of parasitism. By causality, we are referring to whether it is possible to show that parasites have actually impacted patterns of host sociality, versus an alternative scenario in which non-disease ecological forces determine social system characteristics, which then impact the establishment and spread of infectious diseases within those systems. To the extent that coevolutionary dynamics may obscure the effects of parasites on host sociality, this question

is unlikely to have a simple answer, and the most likely scenario is that parasite pressure and social systems are intertwined in complex ways and modified by ecological conditions.

In the face of these complications, the first step is to outline clear hypotheses, and that is the goal of this chapter. We review the potential interactions between infectious disease and primate sociality, specifically considering how parasites might influence group size and composition, interactions within groups, inter-group contact, and territorial defense. A major point is that increased group size and social contact are generally thought to increase disease risk—and hence hosts might become less social in the presence of harmful pathogens. However, some studies actually predict the opposite pattern, and parasites with different transmission modes could produce divergent effects on different social system parameters.

We begin with a brief review of the tremendous variation in sociality found among wild primates and the ways in which primate social systems provide networks for the spread of pathogens. We next consider more directly how parasites might generate pressure on host social and mating systems. We then explore how changing social systems can lead to evolutionary responses in the parasites themselves, thus drawing attention to coevolutionary dynamics and how this interplay complicates efforts to investigate the effects of parasites on host social systems. The chapter concludes by identifying methodological approaches for future research.

6.2 Variation in primate social systems

Primates are renowned for their incredibly diverse and complex social interactions, including grooming networks, sharing and cooperation, competitive interactions within and between groups, and the development of lasting social relationships between kin, mating partners, and even unrelated coalition partners. Primate species also show variation in group size, sex ratio, and mating system. Thus, if we look within a clade of primates, a remarkable diversity of social systems is captured (Fig. 6.1). In Asian primates, for example, the macaques (Fig. 6.2) generally live in large multimale–multifemale groups, with group sizes varying among species and ranging in size from 6 to more than 100 individuals (Melnick and Pearl 1987). In comparison, langurs (Fig. 6.3) often live in single-male mating systems and smaller group sizes (Struhsaker and Leland 1987). Primates of the genus *Rhinopithecus* (commonly called snub-nosed and golden monkeys, Fig. 6.4) exist in extremely large aggregations of hundreds of individuals (Bleisch et al. 1993; Kirkpatrick et al. 1998; Grüter and Zinner 2004). By comparison, proboscis monkeys in the genus *Nasalis* live in smaller, single-male groups at low altitudes along riverbanks in Borneo (Yeager 1990, 1991), and when they form aggregations, these gatherings are smaller than those found in *Rhinopithecus*.

These examples highlight that primate societies show variation with respect to many variables thought to influence variation in disease risk, with group size and rates of contact between groups especially relevant to the topics covered in this chapter. When considering variables such as group size, it is important to keep in

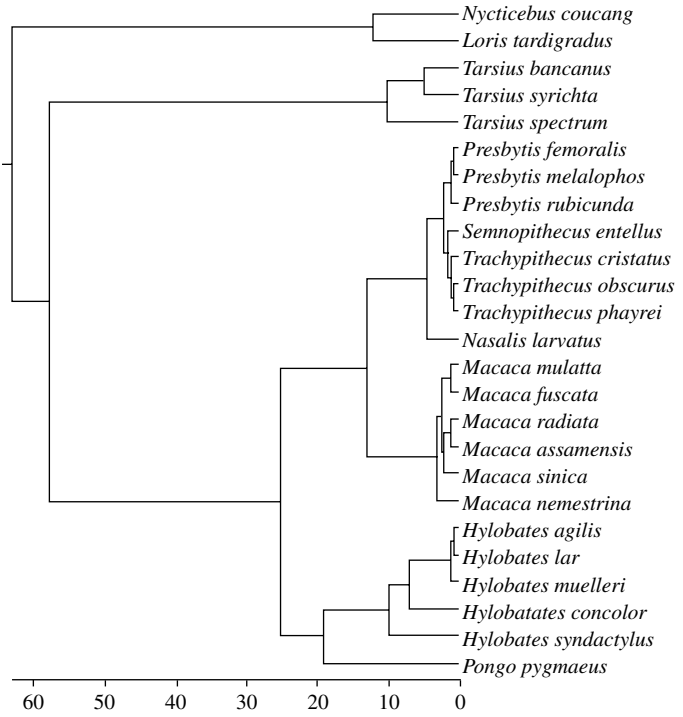


Fig. 6.1 Phylogenetic relationships among Asian primates. Branches are proportional to time, with scale bar in millions of years before present. This phylogeny includes most of the well studied primate lineages that are found in Asia. Taxonomic and phylogenetic information taken from Smith and Cheverud (2002).

mind that different types of grouping patterns can be found in primates, and that actual contact patterns within groups of the same size can vary greatly and may be crucial for understanding disease risk. In addition to the more common type of "stable" group, in which individuals forage, sleep, and move as a relatively cohesive unit, some primates exhibit more flexible arrangements, as just noted for *Nasalis* and *Rhinopithecus*, and also characteristic of hamadryas baboons and geladas. In these multi-level societies, units consisting of one male and several females are embedded hierarchically within a larger population (Stammbach 1987; Grüter and Zinner 2004). These units can forage individually or with other one-male units during the day, and commonly form larger groups at safe sleeping refuges at night. In fission–fusion societies, such as chimpanzees and spider monkeys, individuals also form subgroups within a larger community (Klein and Klein 1977; Nishida and Hiraiwa-Hasegawa 1987). Unlike the one-male units of hamadryas baboons and geladas, however, these subgroups show more flexible group composition, including all-male or all-female groups, and the subgroups rarely, if ever, fuse into one larger group that contains all individuals in the community.

Fig. 6.2 Long-tailed macaques (*Macaca fascicularis*) in a temple forest in Ubud, Bali. Photo courtesy of M. Huffman, Kyoto University.

Fig. 6.3 Hanuman langurs, *Presbytis entellus*, from Yala National Park, Sri Lanka. Photo courtesy of D. Behrens.

Group composition is another variable that is fundamental for understanding links between sociality and disease risk. Primatologists have a long-standing interest in the factors that influence the number of males and females in primate groups (Dunbar 1988). A combination of predation risks and resource availability are

Fig. 6.4 Golden snub-nosed monkeys (*Rhinopithecus roxellana*) inhabit high elevation forests in China. Photo courtesy of Zhang Peng, Primate Research Institute, Kyoto University.

thought to determine the distribution of females in space and time (Emlen and Oring 1977). Provided that resource availability permits larger groups, female group size will increase in diurnal primates when predation pressure increases, and when animals benefit from banding together to defend a resource from other groups. Males attempt to monopolize females, but their ability to do so is determined by the number of females in the group, the area over which those females are distributed, and overlap among their fertile (estrous) periods. In primates, it is now well established that the number of males in a group increases with the number of females, probably because it is more difficult for a single-male to monopolize a larger number of females, leading to multi-male groups (Andelman 1986; Altmann 1990; Mitani et al. 1996a; Nunn 1999). Similarly, greater mating synchrony explains additional variation in the number of males in a group, with groups of more synchronous females being more difficult to monopolize by one or a few males (Nunn 1999; Boesch et al. 2006). This general model of females having a causal effect on the number of males has been supported by findings that evolutionary changes in the number of males lag behind changes in the number of females (Lindenfors et al. 2004).

Researchers have long regarded resource competition and predation risk as two of the most important factors influencing primate social systems, with additional effects of inbreeding avoidance and intersexual conflict on patterns of grouping and dispersal. If infectious disease represents another ecological force that shapes patterns of sociality, we might expect individuals to live in smaller groups than predicted based on other environmental forces, to reduce their contact with

group-mates, or to show lower rates of dispersal between groups. Given the role of multiple factors in shaping both disease risk and primate social systems, it is important to bear in mind that considering the effects of other variables could be critical for making sense of the associations between sociality and parasite pressure. As compared to frugivores, for example, folivorous primates such as langurs might benefit to a greater extent from living in smaller groups to reduce disease risk, given that they probably face higher exposure to fecally transmitted parasites on leaves (Chapter 3). Substrate use can also influence exposure to parasite infectious stages, with terrestrial primate species encountering more parasites in the soil or water, resulting in stronger selection to reduce group sizes to minimize this risk. These potential effects of diet and substrate use illustrate that selection pressures arising from environmental forces could oppose or reinforce the effects of parasites on host social systems.

6.2.1 Chains of transmission within and among primate groups

An individual primate probably sheds countless numbers of parasite infectious stages into the environment over its lifetime. Some parasites are expelled with feces or urine, contaminating food, water or substrates used for locomotion. Animals in the same or overlapping social groups take in these parasites when they forage on material contaminated earlier by an infected host. Other parasites, such as the bacterium that causes tuberculosis, are ejected with microscopic droplets in the breath when an animal coughs or exhales forcefully; these bacteria must be inhaled by conspecifics in close proximity to generate a new infection. Still other parasites require close physical contact, such as occurs during mating, in aggressive encounters that involve biting or scratching, or through networks of grooming interactions when parasites are transmitted on the fur, mouth, or fingertips. Some of these directly transmitted parasites can spread from mother to offspring and will lower the mother's reproductive success when infections cause death, sterility, or developmental delays in offspring.

Within social groups, many individual primates interact most frequently with kin. As a result, directly transmitted infections are likely to move between networks of animals that are closely related to one other, and parasite transmission within groups could be highly detrimental to an individual's inclusive fitness. Primates can also transmit parasites to unrelated individuals within groups, as occurs when a male baboon grooms or mates with females from different matrilines, thus facilitating parasite transmission across kinship lines. A primate could accidentally infect an ally that could prove instrumental in attaining a top rank later in life. On the other hand, infections spread by aggressive encounters could infect a competitor within the group, thus indirectly improving the originally infected individual's reproductive success in a manner similar to parasite-mediated competition among species (Holt and Pickering 1985; Holt and Lawton 1994).

Less is known about how parasites move between groups, but individual dispersal and interactions among groups provide two major routes for parasites to spread through

Box 6.1 Pathogens as agents of selection on primate social behavior

Fluctuations in parasite pressure might induce phenotypically plastic changes in primate social systems, with individual animals adjusting their behaviors in response to factors linked with disease risk. Animal mating and social systems might also change over evolutionary time scales in response to parasite pressure. Parasites that increase host mortality or sterility will increase the relative fitness of resistant phenotypes; indeed, the evolution of host resistance traits in response to parasites is supported by an impressive number of positive associations between resistance measures and parasite exposure in natural populations, and parasites are known to drive rapid host evolution for traits that confer resistance in systems ranging from birds to mammals to insects (Van Riper et al. 1986; Dwyer et al. 1990; Altizer et al. 2003a). Yet despite their pervasiveness and impacts on host fitness, we know relatively little about the degree to which infectious diseases have caused evolutionary changes in the behaviors of wild animals, including social and mating contacts, patterns of dispersal, grooming rates, or levels of territoriality.

Researchers could demonstrate the evolution of host social or mating behavior in response to parasitism using information on (1) the genetic basis for host behavior and its underlying variation or heritability in the wild, (2) knowledge of how these behaviors influence disease risk, and (3) demonstrated effects of infection on host mortality or fecundity. For traits that show quantitative variation, including many behavioral characteristics, selection can be inferred by a relationship between measures of host fitness and measures of the trait in question (Lande and Arnold 1983; Endler 1986). For example, by regressing a measure of fitness (e.g. annual survival rate or lifetime reproductive success) on measures of the trait of interest (such as daily contact rates, lifetime mating partners, or group size), researchers can infer the potential strength of selection on these traits (Hoekstra et al. 2001).

Although the genetic basis for host susceptibility in the wild has been characterized in a variety of systems, we have little information about the rate at which hosts respond to parasite-mediated selection and how this compares to selection on other character types. Furthermore, most studies of the strength of phenotypic selection in the wild have focused on morphological rather than behavioral traits (Kingsolver et al. 2001), probably because morphological traits are easier to measure, especially in natural populations. More recently, breakthroughs in understanding the genetic, hormonal, and neurological bases for individual differences in social behavior have allowed researchers to examine components of host social behavior both within and among species, such as patterns of monogamy (Lim et al. 2004a,b).

Given that most parasites are likely to be endemic in populations and of low virulence, the spread of a single infection from one host to another probably has only a minor effect on an individual's short-term reproductive success. Over a lifetime, however, the cumulative effect of parasites is likely to be substantial, increasing mortality risk and decreasing individual reproductive success. For example, in the case of STDs, infection of a mating partner can cause long-term infertility or developmental defects in offspring (see Holmes et al. 1999). Depending on patterns of home range use, parasites might also re-infect the original host, with the result that once an individual is infected with a parasite, that infection can exert a chronic impact throughout the life of the animal and other animals in its group.

a population. Several studies have demonstrated the importance of immigrants for introducing novel pathogens (e.g. Freeland 1979; Barrett and Henzi 1998). Mobile arthropods could also move vector-borne parasites among individuals from different social groups, thus spreading the pathogen through socially structured host populations. Parasites can also invade a new group when infectious stages persist in areas of home range overlap, or at shared food and water sources. The ranging patterns of intermediate hosts, such as insects, can determine whether parasites move between groups, while flowing rivers provide a way for parasites such as schistosomes to infect individuals in another group. Finally, territorial encounters provide opportunities for the spread of disease when these activities are accompanied by physical contact, such as biting or scratching (Tutin 2000).

These scenarios emphasize how primate social interactions can influence disease spread across a wide range of parasite types. The role of host behavior in generating exposure to parasites, combined with parasite effects on primate survival and reproductive success, sets the stage for parasite-mediated changes in primate social systems. For such changes to occur, host behaviors must influence disease risk, and parasites must be costly in terms of individual survival, development, or reproduction. As noted above, these changes can be facultative behavioral responses or the result of evolutionary change. Demonstrating a potential for evolutionary response requires establishing a genetic basis for variation in host mating or social behavior (Box 6.1).

6.3 Disease risk and primate social systems

Infectious disease can potentially influence major axes of primate mating and social systems. Table 6.1 summarizes the key variables that are covered in greater depth in the text.

6.3.1 Group size and contagious infections

Many infectious diseases spread more rapidly in dense populations, and in some cases even appear to require a minimum host density to increase in prevalence or to persist in a population (reviewed in Chapters 3 and 4). Whether or not this occurs will depend on the transmission mode of the parasite and the biology of the host. In general, we expect that if close proximity or contact among individuals increases rates of parasite transmission, then greater levels of host sociality or gregariousness should lead to higher prevalence, intensity, and diversity of parasites, particularly for parasites transmitted by social contact. Based on this logic, more social hosts are predicted to suffer greater exposure to parasites (Brown and Brown 1986; Møller et al. 1993; Altizer et al. 2003b), to experience increased selection for innate or acquired immune defenses (Møller and Erritzoe 1996; Møller et al. 2001), and to be under greater pressure to evolve behavioral defenses against parasites (Freeland 1976; Loehle 1995).

Table 6.1 Social system variables potentially influenced by infectious disease

Category	Expected effects of increased parasite pressure
Group size and socially transmitted parasites (6.3.1)	Smaller groups, possibly driven by forced emigration, and more "floater" individuals that are unassociated with reproductive groups. Subordinate individuals of the dispersing sex are likely to experience the strongest negative effects.
Group size, flying arthropods, and vector-borne infections (6.3.2)	Larger, more cohesive groups, although may not operate with nocturnally active mosquitoes. Effects felt most strongly on less dominant individuals who are forced to remain on the edges of groups.
Group composition (6.3.3)	Fewer males per female in primate groups, including possibly more polygynous groups (although this may increase risk of STDs, see below).
Interactions within groups and group spread (6.3.4)	Increased inter-individual distance (group spread), and less grooming or more restricted grooming cliques.
Dispersal (6.3.5)	Behaviors that reduce immigration and lengthen the time required to enter groups, and a higher abundance of "floater" individuals who are unassociated with bisexual groups.
Territoriality (6.3.6)	Either increased or decreased territorial defense, reduced home range overlap or use of shared resources, and a reduced level of physical contact during intergroup encounters.
Sexual interactions, promiscuity, and mating system (6.4)	Reduced promiscuity and less reproductive (mating) skew, and a reduction in the number of sexual contacts (and contact duration) per partner. Benefits of promiscuity may outweigh the costs in some circumstances.

As reviewed in Chapter 3, few field studies of the links between group size and disease risk have been undertaken in primates, and comparative studies across a large number of primate species have generated mixed results. Important questions therefore remain about which parasites correlate most strongly with group size and their effects on primate sociality. It is also clear that an overly simplistic view of the relationship between group size and disease risk ignores other important variables, such as parasite transmission mode and actual patterns of contact within groups.

Primates could use several mechanisms to limit group size to reduce disease risk, most generally by increasing the rate at which animals leave groups (emigration) and reducing the rate at which they enter groups (immigration). Freeland (1976) proposed that parasites could drive primate hosts to leave larger groups for smaller ones, and that dominant animals could force subordinates to leave larger groups. He also argued that animals should be less likely to immigrate into larger groups, where infectious diseases should be more of a cost (see also Loehle 1995). Fission of large social groups into two or more smaller ones allows for more substantial and rapid reductions in group size; such fissions are common in primates, although these changes are not necessarily driven by the need to reduce disease risk (Cords and

Rowell 1986; Ménard and Vallet 1993). If parasite pressure leads to increased emigration from groups, the effects are likely to be felt most strongly on the sex class that disperses, and on younger, older, or less dominant individuals who are unable to retain a toehold in groups when pressure mounts from within to reduce group size. When parasite pressure increases at the population level, resistance to immigrants might also increase, leading to a larger number of dispersing or "floater" individuals who are unattached to reproductively active groups (see Section 6.3.5).

Few studies have directly examined primate dispersal and group size in the context of parasites, but available evidence suggests that primates probably do not commonly use this strategy to reduce disease risk, or at least that other benefits of living in larger groups erode the costs arising from increased disease risk. Thus, dispersing males prefer to move into groups with more females, rather than smaller groups, which probably reflects the importance of mating opportunities for male reproductive success. In baboons, for example, Alberts and Altmann (1995) found that males were more likely to emigrate from groups with an excess number of males and were more likely to join groups with a lower ratio of males to females. In females, dispersal decisions often are based on resource availability, predation risk, or protection offered by dominant males (e.g. Moore 1984; Watts 1990). The intensity of competition within groups over resources or mates (rather than effects of infectious disease) is probably a primary factor favoring dispersal in many species (e.g. howling monkeys, Crockett 1984; Glander 1992; see also Pusey and Packer 1987).

Introduction of an infectious disease could generate the appearance of smaller groups over time, but such patterns might arise from host mortality alone rather than behavioral mechanisms to reduce group size. An example of this comes from large-scale surveys of the abundance of wild house finches (*Carpodacus mexicanus*) before and after the introduction of a novel bacterial disease (*Mycoplasma gallisepticum*), which revealed that overall host abundance declined following pathogen establishment (Hochachka and Dhondt 2000). Although social aggregations (measured by flock sizes at bird feeding stations) also declined by a factor of two or more and remained low even a decade after establishment of the pathogen (Hochachka and Dhondt 2000), it is unclear to what degree this decline was driven by a behavioral tendency to avoid living in a group when parasite pressure increased, or whether the smaller flocks were due to increased host mortality.

Several approaches could be taken to assess whether infectious disease has shaped patterns of group size in primates. Using field protocols, researchers could examine whether changes in grouping patterns follow the introduction and spread of new pathogens in wild populations. For example, Carpenter (1964) documented a decline in mantled howler monkey group sizes following a yellow fever epidemic. This type of approach requires measuring group sizes before and after pathogen introductions, and it is necessary to discount the effects of disease-related mortality, that is, to show that reductions in group size are due to behavioral responses, rather than simply being the result of a death-related decline in population size.

An important caveat to the assumption that disease risk increases with group size has been noted in previous chapters but bears repeating: in some cases, group living might actually reduce parasite transmission at the population level, especially if groups are relatively isolated from one another (Watve and Jog 1997; Wilson et al. 2003). Thus, if hosts form groups with little dispersal or inter-group contact, then the risk of parasites entering new groups will be low, even if the potential for parasites to spread within groups following introduction is high. From a different perspective, a recent modeling study showed that optimal levels of host sociality might not necessarily decline in response to elevated disease risk (Bonds et al. 2005). In fact, when hosts benefit strongly from sociality and the prevalence of a communicable infectious disease is unusually high, then "the benefits of disease avoidance, in terms of decreased likelihood of acquiring the disease, are negated by the survival advantages conferred from higher contact rates" (Bonds et al. 2005, p. 1861). These theoretical insights are discussed further in Box 6.2 and show that assuming a reduction in sociality following increased disease pressures might be unjustified in some cases; scenarios could exist in which pathogens drive greater levels of sociality.

6.3.2 Group size, flying insects, and vector-borne infections

Based on theoretical studies of sociality and predation risk (Hamilton 1971; Turner and Pitcher 1986; Krause and Ruxton 2002), some authors proposed that gregariousness can reduce exposure to vector-borne parasites (Mooring and Hart 1992). As discussed in Chapter 3, the effect of grouping on rates of attack by vectors depends on the interaction between two processes: encounter and dilution effects. The encounter effect arises when the probability of locating a group increases more slowly than increases in group size, and the dilution effect occurs if vectors are satiated after visiting only one (or a few) hosts. Mooring and Hart (1992) refer to the combined process as the encounter-dilution effect.

In Chapter 3, we reviewed the evidence for and against the hypothesis that living in groups provides benefits against mobile parasites. A field study of polyspecific associations (Freeland 1977) and meta-analysis of previous studies (Côté and Poulin 1995) provided support for the hypothesis, but comparative research on malaria prevalence in New World primates suggested that rates of mosquito attack were higher in larger primate groups (Davies et al. 1991; Nunn and Heymann 2005). Thus, effects of flying insects on patterns of sociality in primates deserve a closer look, with different insect vectors, parasites, and host species potentially producing different patterns. Major biogeographic shifts in hosts or parasites could also be useful in testing for a link between vector-borne disease and group size. For example, several vector-borne diseases, such as yellow fever and malaria, have been introduced to the New World from the Old World. Thus, we expect the largest changes in group size among New World primates to occur in regions with the highest abundance of vectors that spread these diseases.

Box 6.2 Could infectious diseases favor increased host sociality?

Most studies of infectious disease risk in social animals assume that parasite pressure increases with greater rates of host social contact. Thus, social hosts should suffer to a greater extent from directly transmitted diseases, with greater parasitism favoring *reduced* sociality. On the other hand, some recent analytical and simulation-based modeling approaches indicate that parasites might favor the evolution of *increased* host sociality—either because host social organization actually slows pathogen spread, or because sociality confers other benefits that become more important than disease avoidance when parasite prevalence is high. We briefly explore these two ways that infectious disease could favor greater host sociality.

As discussed in Chapter 3, some authors argued that sociality should *reduce* disease risk by limiting random host mixing at the population level. One simulation model showed that increased aggregation could reduce pathogen spread and persistence when dispersal among groups was low (see Fig. 3.6, Wilson et al. 2003). In this study, social organization was captured by subdividing a larger population into smaller groups; within these subdivisions, contact rates were high, but among-group contact was restricted. As individuals become more tightly clumped into relatively permanent groups, infections were essentially "quarantined" into patches, and parasites were therefore less likely to establish in these structured meta-populations. A meta-population model by Hess (1996) similarly suggested that population sub-structuring and limited dispersal among patches could reduce the spread of disease at the population level. In this model, hosts divided into relatively discrete social groups might be somewhat protected from certain types of infections at the population level, although once a parasite invaded a group, greater host density or larger group sizes or contact rates would still increase parasite spread. Furthermore, other authors (Gog et al. 2002; McCallum and Dobson 2002) suggested that when disease risks arise from external sources, such as generalist parasites acquired from other species, greater movement of hosts among patches could prevent their population-wide extinction, even if disease prevalence is high.

From a different angle, Bonds et al. (2005) used an optimality model to show that even if greater rates of host social contact increase rates of parasite spread, other benefits conferred to hosts by sociality, such as reduced predation risk, can alter fundamental conclusions about the effects of parasite pressure on host social contacts. Using an approach whereby host fitness in the absence of infection was a positive function of contact rate (as a proxy for sociality and its benefits), Bonds et al. (2005) showed that when disease prevalence was low, the optimal host contact rate declined from its disease-free value with small increases in prevalence (see Fig. 6.5). However, when prevalence was intermediate or high, further increases in prevalence actually selected for hosts to maintain relatively high contact rates (near their disease-free level in Figure 6.5). This effect arises because, when prevalence is high at the population-level, even hosts with low contact rates have a relatively high probability of contracting the infection. It is important to note that this result was mainly true for highly transmissible pathogens of low to moderate virulence—and extremely virulent infections always selected for lower rates of host social contact.

Thus, counter to the conventional wisdom that hosts should become less social in the presence of infectious diseases, circumstances exist in which greater parasite pressure selects for increased levels of sociality that either make host populations more "viscous" and slow parasite spread at the population level, or allow hosts to realize the benefits of sociality when disease prevalence becomes high.

Box 6.2 (*Cont.*)

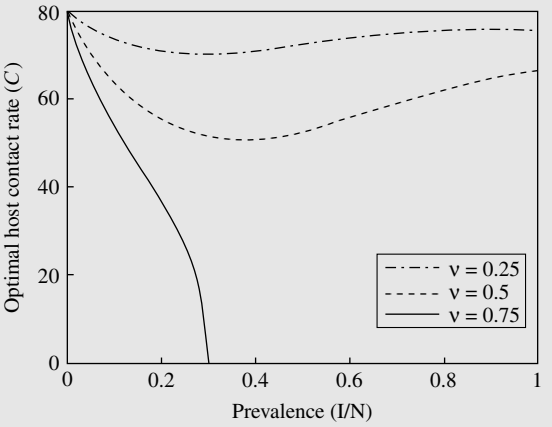


Fig. 6.5 Optimal rates of host social contact in response to parasite prevalence, where prevalence was "exogenously" determined as a fixed value of *I*/*N*, for three different values of pathogen virulence (v, the disease-induced death rate). When virulence is moderate to low, optimal host contact rates initially decrease with greater prevalence, but then further increases in prevalence cause optimal contact rates to rise. For virulent parasites, optimal host contact rates fall monotonically with increasing prevalence. Results are based on the output from a simple *S-I* (susceptible-infected) compartment model, where host contact rates (C) lower host mortality in the absence of disease, but also increase the rate of disease transmission. Copyright (2005) from "Higher disease prevalence can induce greater sociality; a game theoretic coevolutionary model," by M.H. Bonds, D.C. Keenan, A.J. Leinder and P. Rohani. *Evolution*, vol. 59, pp. 1859–1866. Reproduced with permission of the Society for the Study of Evolution.

In addition to influencing overall group size, attacks from flying insects could influence the behavior of animals within groups. In the presence of biting arthropods, for example, animals should seek the center of the group, since edge positions represent the attack zone for predators as well as for parasites (Mooring and Hart 1992). Hamilton (1971) termed this "the selfish herd effect" (see also Vine 1971, 1973). Mooring and Hart (1992) summarized studies documenting this behavior in response to both parasite and predator risk. They concluded that studies based on avoiding parasites provided stronger evidence for the selfish herd effect than studies of predator avoidance, and therefore proposed that protection from mobile parasites should be considered as one of the primary advantages of group-living in animals. This conclusion is strikingly divergent from the usual thinking in primate socioecology, which more often focuses on predation as the overriding force that drives the evolution of grouping behavior.

6.3.3 Group composition

We commonly think that group size is the key variable impacted by disease risk, but group composition (number of males and females) could also change in response to parasite pressure. For example, when disease risk from socially transmitted pathogens is high, we might expect to find fewer males per female (and thus smaller overall groups). The effect would be driven by females living in smaller groups or exhibiting less estrous synchrony, thus making it easier for a single male to monopolize all females and producing smaller mean group sizes. Increased parasite pressure might also lead to increased male emigration and an earlier emigration age. If this scenario is correct, the distribution of males could respond strongly to pressure from parasites, resulting in a large number of floater males in populations where disease risk is high. A prediction in this case is that greater risks from directly transmitted parasites should result in fewer males in a group, that is, a higher degree of polygyny, although this prediction might not be supported if other factors increase individual-level disease susceptibility in more polygynous systems, (for example due to stress from increased takeover attempts by floater males, or if diseases are introduced to groups during takeovers). More refined tests are discussed in Section 6.7.3.

Another important question involves identifying individuals within social groups that are at greatest risk of acquiring infections, as this could influence selection pressures acting on group composition. One host response to limiting disease spread in social groups might be to behaviorally exclude members of the most susceptible class(es) before they infect other members of the group. As noted in Chapter 3, parasitism is likely to correlate with dominance rank, age, and sex because these factors influence exposure to parasites through habitat use and the frequency of social contacts. Parasites could therefore drive pressures on age structure, kin structure, and patterns of host relatedness within groups.

6.3.4 Group spread and contact within groups

As noted in Chapter 5, animals can limit their individual risk of infection by avoiding conspecifics that show visible signs of disease, including behavioral, physical or even olfactory cues. An alternative to identifying infected individuals would be to reduce overall levels of interaction within groups. For example, a higher risk of acquiring socially transmitted diseases could lead to selection to increase the distance between individuals, a measure commonly referred to as "group spread." Or, there could be selective pressure to reduce grooming, or to avoid grooming outside of one's social clique. Because primates sleep in "huddles" (Anderson 1998, 2000), newly introduced communicable diseases could act as a pressure on individuals to sleep solitarily, or at least in smaller huddles.

Thus, the occurrence of socially transmitted infections should favor greater interindividual distances, reductions in grooming behavior, or an increased tendency for animals to sleep or rest in smaller subgroups. It should be possible to test these predictions comparatively or in the field. Following the logic used with hypotheses

involving group size and composition, for example, we expect that introductions of a new infectious disease will be followed by increases in group dispersion and more restricted grooming patterns. Despite the intuitive appeal of these predictions, however, they may not be supported in all cases. As noted in Section 6.3.1 and Box 6.2, for example, one recent modeling study showed that when hosts are infected with a moderately virulent pathogen but also benefit from social contacts, deaths could actually lead to increased attempts by hosts to locate other individuals (Bonds et al. 2005). Similarly, ecological factors such as resource competition could reinforce negative effects of contagious parasites on host contact rates, whereas other ecological forces, including predation pressure or selection from biting flies, could counteract the effects of socially transmitted parasites by selecting for more cohesive groups (Mooring and Hart 1992).

6.3.5 Dispersal among groups

As noted above and in Chapter 3, host movement between groups may be more important than group size for parasite establishment. Freeland (1976) and Hoogland (1979) suggested that contact with unfamiliar animals could be more critical for the spread of infectious diseases, as compared to contact with members of the same social unit. Effects of dispersal among groups should be more relevant for the spread of acute infections (i.e. those with a shorter infectious period), as these pathogens will have a narrower window of time for infected individuals to move among groups before the hosts die or clear the infection (Cross et al. 2005).

Group size and inter-group movement could be positively correlated, with larger numbers of individuals moving into and out of larger social groups. On the other hand, if smaller groups are composed of closely related individuals of the philopatric sex (e.g. Lukas et al. 2005), higher rates of dispersal could be favored to reduce inbreeding. These interacting factors could make it difficult to empirically disentangle the relative effects of group size and dispersal on patterns of disease risk and, conversely, the effects of parasitism on these host characteristics. As a case in point, in their classic paper on coloniality and ectoparasitism in cliff swallows, Brown and Brown (1986) noted that larger colonies also experienced more immigration, which could lead to increased introduction of swallow bug ectoparasites. In a more recent study, Brown and Brown (2004) found support for this possibility: immigration increased with group size, and these factors were positively correlated with parasite transmission among groups. Thus, it may be that social group size alone is not the critical factor, but rather overall levels of risk depend on a combination of group size, movement between groups, and the duration of the infectious period (Cross et al. 2005). From this perspective, we might expect to find a reduction in both sociality and immigration rates when disease risk increases, with a corresponding increase in the number of "floater" individuals (or the formation of new groups by floaters).

A major implication of this perspective for primates is that infectious disease should select for behaviors that reduce immigration of potentially infected hosts. Freeland (1976) made this point and followed it with support from a field study of mangabeys (Freeland 1979). He acknowledged that allowing new immigrants into groups provides

genetic advantages, but he proposed that risks associated with parasite introductions could outweigh these benefits. Freeland (1976) therefore suggested that disease-wary group members should inflict stress on potential immigrants to reveal their infection status and increase the time that it takes for immigrants to enter a new group. Given that emigrants in this situation will have more difficulty finding a new group, we should also find a higher abundance of floater animals in species or populations that experience pressure from socially transmitted parasites. Substantial variation in intergroup mixing exists among wild primate species. For example, some primates, such as muriquis (*Brachyteles arachnoides*), move easily between groups (Printes and Strier 1999), while others, such as baboons, undergo a lengthier and more competitive period of assimilation into new groups (Altmann and Altmann 1970).

Freeland's hypothesis may be supported in some cases, but many other factors could also account for resistance to immigrants in primate social groups. For example, females will benefit from preventing the entry of potential competitors for food, and males could benefit from excluding possible competitors over mates. Carefully designed tests will be needed to control for these factors, perhaps by developing experiments and by focusing on sex-related patterns of emigration and resistance. Testing these ideas across species is further complicated because we lack a quantitative measure of dispersal rates (e.g. frequency of immigration and emigration) to include in comparative tests, and we also lack comprehensive data on the time it takes for dispersal to occur (relative to the duration of infection). In constructing a measure of dispersal rate, immigration rates are probably more useful than emigration rates, as the latter often include disappearances caused by a variety of factors, including death. Unfortunately, however, immigration rates could be affected by the presence of researchers in ways that reduce the movement of less habituated animals into habituated groups that are observed by field biologists (E. Heymann, personal communication).

In summary, if infectious diseases are carried from group to group and have significant fitness costs for members of groups, we expect to find patterns similar to what Freeland (1976) envisioned: limits on immigration and the imposition of stressful situations to weed out immigrants who are likely to be infected. Thus, floater individuals that fail to enter a group should be carrying more parasites than those that successfully enter new groups. Experimental removal of infections from a subset of floaters might be feasible, providing an experimental approach to test whether treated individuals meet less resistance than untreated individuals during immigration into groups. Solitary floaters can exist outside of groups for long periods of time, and their survival goes against the notion that predation risk is important in primate socioecology. Thus, understanding how parasites impact behaviors that lead to floaters could provide new insights to primate behavior and ecology.

6.3.6 Territoriality and range overlap

Primates exhibit great variation in territorial behavior and parasite pressures could explain some of this variation (and resulting variation in home range overlap; see

Chapters 3 and 5). Physical separation of groups should prevent the spread of directly transmitted parasites and might therefore be under selection when this risk increases (Freeland 1979; Møller et al. 1993; Loehle 1995; Altizer et al. 2003b; Wilson et al. 2003). On the other hand, between-group interactions might also expose animals to new diseases when territorial defense involves physical contact (Loehle 1995; Nerrienet et al. 1998; Tutin 2000), potentially selecting for non-contact avoidance mechanisms involving visual or vocal displays (Loehle 1995, although of course other direct costs of fighting could also select for these signals). As noted in previous chapters, greater territoriality might also correlate with more intensive use of the home range (Mitani and Rodman 1979), elevating the exposure to, and re-infection with, fecally transmitted parasites already present among individuals in the group (Stoner 1996; Ezenwa 2004).

Thus, some aspects of territoriality are likely to increase disease risk, specifically when parasites spread through physical contact during inter-group encounters, and when animals become re-infected with fecally transmitted parasites that accumulate in the defended range. Other aspects of territoriality are likely to reduce disease risk, as might result from reduced home range overlap. Field tests in primates have not yet investigated these possibilities, but comparative tests provide some evidence linking territorial behavior and parasitism (Nunn and Dokey, in review). Causal links from parasite risk to territorial behavior remain to be studied in future research.

6.4 Mating systems, sexual behavior, and STDs

Primates exhibit an incredible diversity of mating behaviors (Hrdy and Whitten 1987; Dixson 1998; van Schaik et al. 1999). Some species, such as gibbons, are generally monogamous, with adults rarely changing mating partners throughout their lives (Leighton 1987). In other species, individuals mate promiscuously with multiple partners. For example, a Barbary macaque female in estrus may change partners up to ten times in a *single day* (Taub 1980), and female muriquis, who exhibit remarkable freedom in their ability to choose partners, generally mate with an average of eight males over a 5-year period, including extra-group males (Strier 1997). Females of supposedly monogamous species also engage in extra-pair copulations (e.g. *Hylobates syndactylus*, Palombit 1994; *Hylobates lar*, Reichard 1995; *Callicebus moloch*, Mason 1966).

Clearly, such variation in mating behavior should affect the spread of STDs (reviewed briefly in Box 4.5). A related and more challenging question that emerges is: how does variation in STD risk influence the evolution of primate mating systems and mating behavior? The most intuitive way that STDs could influence animal mating systems is through selection for lifetime monogamy (Freeland 1976; Sheldon 1993; Loehle 1995). In primates, Freeland (1976) argued for the importance of "sexual fidelity" of primate groups, focusing on the benefits of preventing both sexually and non-sexually transmitted infections. Similarly, Immmerman (1986) proposed that STDs are a key factor promoting human monogamy, a topic that we will return to in Chapter 8.

A fuller appreciation of the impact of STDs on primate mating behavior requires that we understand the contact structure of mating systems and how these networks facilitate the spread of disease. In what follows, we focus on two mating traits that are likely to shape STD risk. The first of these is mating promiscuity, defined primarily in terms of numbers of partners (or partner exchange rates) and also the number of copulations with each partner. The second trait is mating skew, defined as the distribution of copulations among individual males or females (Cowlishaw and Dunbar 1991; Kutsukake and Nunn, in review). We will focus in particular on mating skew among males, which we will assume is equivalent to reproduce skew. Throughout it is essential to keep in mind that dispersal, life history traits, and parasite characteristics will further influence the establishment of disease, including STDs (Thrall et al. 2000).

6.4.1 Mating promiscuity

Mating promiscuity has perhaps the most obvious implications for the spread of STDs (reviewed in Box 4.4). But should monogamy be the optimal mating strategy in the presence of a potentially sterilizing STD? Using a theoretical framework, Thrall et al. (1997) addressed this question by modelling mating events that were associated with both a per-contact disease transmission probability and a fertilization probability. Their results showed that STDs had the potential to influence differences in optimal mating strategies for males and females, but the outcome was sensitive to the parameters used, and monogamy was not always the optimal strategy. This study also confirmed that STDs spread more rapidly in promiscuous mating systems and that monogamy often resulted in lower disease prevalence.

In a subsequent study, Thrall et al. (2000) used an individual-based model to investigate the spread of an STD in polygynous mating systems. In addition to results involving reproductive skew (described in Box 4.5), the authors showed that increasing dispersal of females among single-male mating groups (which is equivalent to increased female promiscuity) tended to favor the establishment of an STD. At extremely high levels of dispersal, individuals effectively changed partners every mating season, resulting in high prevalence of infection in the simulated populations.

Given the risks of mating with multiple partners, why do individuals of so many primate species exhibit such high rates of promiscuity? The benefits of promiscuity are more obvious for males that do not exhibit parental care, since their reproductive success is usually more tightly linked to the number of partners they have. Although males could infect mating partners and thereby reduce their own reproductive success, the benefits of having more partners are likely to outweigh these costs in generally situations. Female primates probably mate with multiple males to confuse paternity and reduce the risk of infanticide (Hrdy and Whitten 1987; Schaik et al. 1999; Soltis 2002). One interpretation of these observations is that immediate reproductive benefits from multiple mating outweigh the costs of STD infection, even in generally monogamous species (Nunn and Altizer 2004).

6.4.2 Effect of reproductive skew

An important epidemiological consequence of heterogeneity in host sexual behavior is that more "attractive" males could experience a higher risk of STD infection (Graves and Duvall 1995; Thrall et al. 2000; Kokko et al. 2002). This effect could have major consequences for female mate choice and fecundity, as highly competitive or more preferred males may serve as super-spreaders, increasing the prevalence of infection in the population and potentially leading to higher rates of sterility. This pattern was nicely illustrated in Thrall et al.'s (2000) simulation study, in which they found that the prevalence of infection increased more rapidly for females than for males as sexual selection increased (see Box 4.5), and that a few males became the primary source of the infection for females. Because "successful" males had larger harems, they could infect more females, lowering female reproductive success in these groups. This effect could act as a "brake" on the evolution of extreme polygyny, depending on the details of host ecology, the mating system, and the effects of the pathogen on host reproduction (Thrall et al. 2000).

A more recent study also examined the effect of reproductive skew on the spread of STDs and the possible impact of these patterns on mating systems. Kokko et al. (2002) showed that female choice for particular males impacts the spread of STDs. They used two simple scenarios: one in which females could choose high-quality mating partners, and a second in which monogamous females paired with low-quality males could seek extra-pair copulations. In the first scenario, the simulations revealed that prevalence of infection increased to very high levels in attractive males when females were choosy, but declined to near zero when females were not choosy (Fig. 6.6). Similarly, extra-pair matings were not always advantageous, with an STD potentially selecting for greater mate fidelity by females, even when mated to an unattractive male. In a model in which female choosiness was allowed to evolve, a mixed ESS or polymorphism was favored, with perturbations from this equilibrium leading to a return to equilibrium levels of prevalence (center line in Fig. 6.6). From these results, the authors concluded that an STD could lower the preference by females for otherwise attractive males. Some studies have systematically examined patterns of mating skew in primates, and interest in this topic is increasing (Cowlishaw and Dunbar 1991; Hager 2003; Kutsukake and Nunn in review).

6.4.3 Testing effects of STD risk on primate mating systems

Comparative tests could help researchers understand the role of STDs in the evolution of primate mating systems. For example, species with longer durations of reproductive activity over their lifetimes could experience greater STD risk, predicting greater monogamy in these species (Loehle 1995). This prediction could be tested comparatively by examining how mating system correlates with the length of the lifetime reproductive period across species. Thus, Nunn (2003) tested whether monogamous species tend to be those that have longer lifetime reproductive activity or more reproductive events (expected number of births over a female's lifespan), but

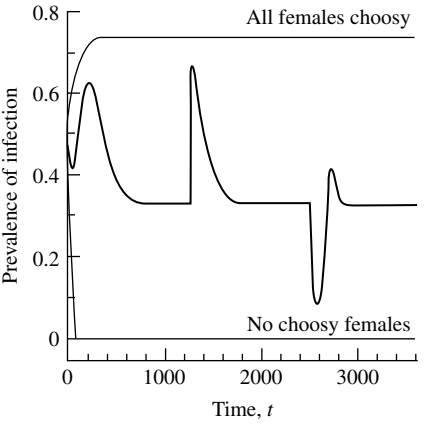


Fig. 6.6 Prevalence of infection in attractive males shown for the cases where only choosy females or non-choosy females are present in the population. Middle line shows the prevalence in situations in which female mating preferences were allowed to evolve, with perturbations producing a return to equilibrium values. The prevalence of infection always dropped to less than 0.015 in less-attractive males (not shown), regardless of the female strategy. Figure reproduced from H. Kokko, E. Ranta, G. Ruxton, P. Lundberg, "Sexually transmitted disease and the evolution of mating systems." *Evolution*, 56, 1091–1100. Copyright (2002) by The Society for the Study of Evolution.

found no support for greater STD risk in long-lived primates as a factor leading to monogamy.

For some species, researchers could assess the costs and benefits of promiscuity by using data on the duration of copulation events and the number of intromissions with each partner (Dixson 1998), as these variables should increase the risk of STD transmission on a per copulation basis. Thus, females that benefit from promiscuous mating but also suffer costs from STD transmission could offset this cost by reducing the duration of copulation, or they could have fewer mounts with the same male or different males. Genital morphology, such as the presence of penile "spines" (see Fig. 3.10, Dixson 1998), might increase the per mating probability of transmitting an STD by damaging the female genital tract, and hence might be selected against when the risk of infection is high, or could make promiscuity unsustainable when an STD is introduced to a population.

The models developed by Thrall et al. (2000) and Kokko et al. (2002) make predictions for mating patterns in primates that could be tested empirically. In polygynous groups, in which females are paired with a presumably high-quality male, more successful males are more likely to be infected with STDs, and prevalence should be higher in females than in males (Box 4.5). Similarly, females in populations where males represent a major source of STDs could be under pressure to leave

larger mating groups and to reduce mating skew. Nunn and Altizer (2004) tested the prediction that prevalence of STDs should be higher in females than in males, and they found support for this prediction (see Fig. 3.12). Other predictions involving STDs and primate mating systems have yet to be tested in the field or comparatively.

From a different perspective, studying host manipulation by STDs could provide insights to pressures favoring STD transmission. As mentioned in Section 2.6, one would expect that STDs benefit from manipulating hosts in ways that increase mating frequency, the attractiveness of infected hosts, or rates of partner exchange. Little is known about parasitic manipulation of vertebrate hosts, but a possible candidate for investigating these links involves herpes simplex virus 2 (HSV-2), which exists as latent infection of sensory nerves leading to sex organs (Hatalski and Lipkin 1997). STDs could also indirectly increase mating behavior in females through the effects of sterility, which would cause infected females to cycle repeatedly, and therefore to have more lifetime mating partners (Nunn et al. 2001; Nunn and Altizer 2004; Altizer et al. 2003b). Finally, theoretical models have shown that STDs may evolve to be inconspicuous in hosts (see Section 6.6.1 and Knell 1999).

6.5 Impacts of host behavior on pathogen evolution

Just as infectious diseases might influence variables linked with host sociality, host social behavior should also influence the evolution of parasites that depend on host contact for their spread. A major outstanding challenge in infectious disease research is to understand forces affecting variation in virulence among parasites in wild host populations. Modeling work has demonstrated that both parasite transmission and virulence can change in response to host social and mating behavior—sometimes in non-intuitive ways (Lipsitch and Nowak 1995; Bonds et al. 2005). Mathematical models combined with molecular phylogenies of hosts and parasites should provide new opportunities to study patterns of coevolution (Box 6.3), including investigating directional changes in traits associated with both long- and short-term host–parasite associations.

6.5.1 Evolution of virulence

Models of virulence evolution—where virulence is defined as disease-induced host mortality and/or reductions in fecundity—generally assume that there is an intermediate level of virulence that optimizes parasite fitness (Bull 1994, reviewed in Chapter 2). This intermediate level arises from the tradeoff between the benefits of within-host replication, leading to increased transmission, and the costs of killing a host (see Section 2.5 and Lenski and May 1994). How parasites are transmitted among hosts and the underlying rates of host contact are crucial to the balance of these benefits and costs (e.g. Fig. 2.13). In an oft-cited paper, Ewald (1983) proposed that parasites in which transmission is relatively independent of host activity (such as those spread by contaminated water or biting arthropods) should express higher levels of virulence,

because host death or morbidity represents a much lower cost in terms of lost transmission opportunities (see also Ewald 1994a). For directly transmitted diseases, greater rates of horizontal transmission are traditionally thought to select for higher levels of pathogen virulence (Ewald 1983, 1994a; Herre 1993, 1995; Fenner and Fantini 1999), in part because increased transmission compensates for the costs of virulence.

Recent theoretical work challenges these intuitive inferences about the evolution of pathogen virulence in response to host sociality on several grounds. First, in a model of virulence evolution for STDs, Lipsitch and Nowak (1995) showed that the effect of host contact rates on pathogen virulence depends critically on the stage of the epidemic and on the host population growth rates. Their results emphasized a difference between evolutionary pressures operating shortly after parasite invasion, versus those that affect the long-term success of parasite strains. When pathogens were newly introduced into a population in this model, increased partner exchange rates (which would increase the transmission of an STD) selected for more virulent strains. In contrast, at equilibrium when the disease is widespread and transmission opportunities are fewer, the parasite benefits more from host survival, thus favoring milder strains, and increasing rates of partner exchange could actually favor less virulent parasites. This counterintuitive effect arises because high rates of host contact will increase pathogen prevalence—and lower the numbers of susceptible hosts—hence favoring the less virulent strains (Lipsitch and Nowak 1995).

Second, when sociality provides benefits to hosts, for example through reduced predation, these benefits can affect the outcome of virulence evolution. In an optimality-based mathematical model, Bonds et al. (2005) showed that when host sociality lowers host death rates in the population, then higher host contact rates could select for reduced pathogen virulence. This relates to the more general phenomenon in which high host death rates will shorten the infectious period and favor more virulent pathogens that can replicate faster within hosts and achieve more rapid transmission. In the short-term, higher rates of host contact might sustain more virulent parasite strains, but in the long term, increasing rates of host social contact could in fact select for less virulent strains, if these contacts benefit hosts and increase survival in the absence of infection.

A third complicating factor relates to the ability of parasites to disperse through spatially structured populations. Most models assume that host populations are well mixed and average contact rates and transmission probabilities apply to all individuals. However, socially structured host populations are often also spatially structured, with higher rates of interaction within groups and less frequent mixing between groups. In general, mathematical models show that virulence evolves to lower levels when host populations are structured spatially (Van Baalen 2001; O'Keefe and Antonovics 2002; Haraguchi and Sasaki 2000). Boots and Sasaki (1999) modeled disease spread across a network of sites where new infections could arise from both local and global pathogen dispersal (as might be affected by host movement distances). They allowed pathogen transmission rate and virulence to evolve. When transmission events were highly local, as might be expected if

hosts interact predominantly within local groups and long-distance dispersal is rare, pathogens evolved to lower virulence. This effect arose because virulent pathogens in highly structured host populations tended to spread rapidly within local groups, but then local pockets of infection went extinct before the pathogen could disperse to a new group. When host populations exceeded a "critical connectivity" and new transmissions were widely distributed in space, pathogens evolved much higher virulence. These results suggested that greater connectivity and mixing among social groups would favor the evolution of more virulent pathogen strains (Boots and Sasaki 1999; O'Keefe and Antonovics 2002; Boots et al. 2004).

STD virulence is expected to be higher when extra-pair copulations are common, as compared to situations in which monogamy predominates. This idea has been discussed with respect to human sexual behavior and the evolution of HIV (Ewald 1994b) and is consistent with virulence increasing as host contact and transmission events increase (Lenski and May 1994). However, the results of Lipsitch and Nowak (1995) underscore the role of short-versus long-term selective pressures and suggest that higher contact rates might favor virulent strains in the short run, and less virulent strains (or no net change in virulence) in the long run.

Another complication for STDs is that selection could operate against parasites that "give away" their presence to potential mating partners, with animals avoiding sexual contact with infected individuals. A theoretical model by Knell (1999) investigated the links between STD virulence and host mating success (Fig. 6.7). In his model, virulence reflects the degree to which a parasite produces symptoms or outward signs of infection that results in reduced mating success. Knell's (1999) model showed that mate choice tends to reduce the optimal virulence for the pathogen, with the pathogen able to persist in a narrower range of virulence levels as mate choice increases. Similar principles should apply to other contagious pathogens when hosts avoid contacting infected individuals based on outward signs of infection.

An interesting case study for virulence evolution in human STDs involves syphilis, caused by the bacterium *Treponema pallidum*. Although the geographic origins of syphilis remain uncertain (see section 8.2), historical descriptions of the disease point to a rapid decline in virulence in just a few short years following the initial cases in Europe in 1495 (Knell 2004). Thus, initial reports of early syphilis included large (and often necrotic) pustules on the skin, a foul smell, and excruciating pain—effects that undoubtedly would have reduced sexual activity of affected individuals! Interestingly, a similar infection caused by another *Treponema*-like pathogen was reported to cause severe genital infections among baboons in Gombe, leading in some cases to genital mutilation and death (Wallis and Lee 1999, A. Collins, personal communication). Animals were treated with antibiotics to halt the outbreak, thus limiting any potential to observe evolution of the pathogen itself.

Although most models of virulence evolution assume that parasites lower host survival, virulence could also be expressed in the form of reduced host fecundity, as might be the case for a wide range of STDs (Lockhart et al. 1996). In this case,

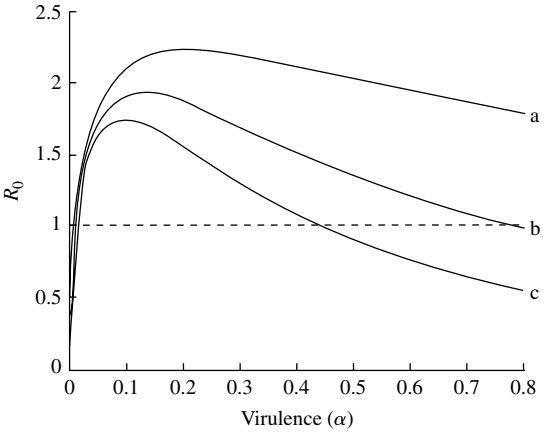


Fig. 6.7 The relationship between parasite fitness (R_0) and virulence for STDs in response to mate choice. Knell (1999) used a standard epidemiological model to investigate the how mate choice for uninfected hosts impacted pathogen virulence, based on the assumption that more virulent pathogens produce more obvious effects in infected hosts. This plot shows three scenarios: no sexual selection for healthy hosts (a), and two forms of sexual selection for healthy hosts (z=1 and 2 from Knell 1999). Dashed line indicates $R_0=1$. Redrawn based on parameters given in Knell (1999).

the self-limiting effects of increased virulence resulting in a shorter duration of infectiousness become irrelevant, and pathogens that sterilize their hosts can continue to be transmitted over relatively long time intervals. Using both individual-based simulation models and an analytical differential equation approach, O'Keefe and Antonovics (2002) showed that in a well-mixed host population, pathogens that cause varying degrees of reduced host fecundity should evolve to maximize their transmission, and hence sterilizing pathogens are favored, potentially leading to both host and parasite extinction. The simulation models further showed that in spatially structured host populations, less virulent parasite strains were favored, consistent with local infection and extinction events favoring lower levels of parasite virulence.

6.5.2 Evolution of transmission strategies

Transmission modes themselves could evolve in response to host social and mating behavior, and theoretical studies have provided some insights as to how this might occur. Using differential equation models, Thrall and Antonovics (1997) derived conditions under which an STD could invade an otherwise well mixed host population and displace a pathogen transmitted by non-sexual contacts. Invasion by the STD was easier when the equilibrium host population size was relatively small, whereas the non-STD could invade more easily if the equilibrium population size with an STD

was larger. Overall, these results reflect the general expectation that sexual transmission should be favored in lower density host populations (where social contact rates are generally lower), whereas non-sexual transmission should be favored at higher population densities with higher rates of social contact (Anderson and May 1991; Smith and Dobson 1992).

Based on more realistic assumptions related to the importance of host population density, Thrall et al. (1998) proposed the concept of a "social-sexual crossover point" (SSCP, see Fig. 4.5) for parasite transmission, focusing on the factors that lead to sexual versus non-sexual transmission. These formulations assumed that: (1) as population density increases, social and sexual contacts also increase, (2) the number of sexual contacts will initially increase more rapidly with density than the number of social contacts (at low population densities, individuals still seek mates), and (3) at higher densities, the number of sexual contacts will rapidly saturate, but the number of social contacts will continue to increase. Thus, the SSCP represents a critical host population density at which the number of social and sexual contacts is equal. Clearly, the host density at which the SSCP occurs can vary considerably depending on the details of host social and mating structure. Thrall et al.'s (1998) model predicted that increased sexual transmission will be favored if the equilibrium population size is less than the SSCP; otherwise, non-sexual transmission will be favored. This prediction could be tested using data from wild primates, based on the expectation that species characterized by living at high density should have more socially transmitted parasites, while those at low density should have more STDs.

6.5.3 Coevolution

A significant challenge to studying parasites and host social evolution is that both hosts and parasites will evolve in response to one another, reflecting reciprocal interactions between host and parasite lineages (Box 6.3). These evolutionary dynamics can happen on the order of a few host generations, or over millions of years—on the faster end, for example, consider the evolution of antibiotic resistance in response to drugs developed in the twentieth century (reviewed in Palumbi 2001). In this context, it is worthwhile to briefly return to the encounter and infection probabilities discussed in Chapter 2 and to consider how this framework informs the understanding of host-parasite dynamics. When encounters increase host exposure, we expect selection on parasites to exploit vulnerabilities in host defenses (i.e. increased infectiousness), and selection on hosts to reduce the likelihood of successful infection (increased resistance). Similarly, selection on host behavior should act to reduce the frequency and duration of encounters with parasites, whereas selection on parasite behavior should improve their ability to locate hosts. Finally, parasites have been shown to manipulate hosts (Moore 2002, section 2.6), and we expect hosts to respond evolutionarily to this manipulation when it is costly to their reproductive success (Poulin et al. 1994).

Box 6.3 Studying host–parasite coevolution

Coevolution can be broadly defined as the interdependent evolution of two or more species sharing any type of ecological relationship, including relationships that involve predation, competition, parasitism, and mutualism (Thompson 1989, 1994a). It is an alluring idea because it focuses our attention on the interactions between organisms as driving the reciprocal evolution of species, generating mutual adaptations, and preserving genetic diversity within species (Antonovics 1992). In the strictest sense, coevolution refers to the evolutionary changes in one population in response to a second species, followed by a reciprocal evolutionary change in the second species to changes in the first (Janzen 1980). On a large time scale, this could result in reciprocal adaptations of interacting lineages, possibly accompanied by cospeciation events (parallel cladogenesis) and genetic arms races (Moran and Baumann 1994; Clayton et al. 2003; Page 2003b). However, narrower views of coevolution should be buffered by the reality that most species interactions involve more than two partner species (diffuse coevolution, see text), that the strength of interactions can be asymmetrical or nonlinear, that partners might evolve at different rates and disperse over different spatial scales, and that environmental heterogeneity will play a crucial role in species abundances and the strength of species interactions (Thompson 2005).

Relative to other types of species interactions, the intimate associations between hosts and parasites offer many opportunities for observing coevolution on contemporary time scales—as well as investigating historical patterns of cospeciation and coadaptation. This intimate association is partly due to the fact that parasites live within their hosts, and that hosts and parasites have overlapping ecological dynamics and habitats, so that in many cases hosts and parasites do share a common and often ancient evolutionary history (Page and Holmes 1998). On relatively short (contemporary) time scales, studies of host–parasite systems emphasize a variety of processes that underlie host–parasite coevolution, including directional selection for greater host resistance and shifts in parasite virulence (Clayton and et al. 1999; Fenner and Fantini 1999), frequency-dependent selection leading to time-lagged cycles in host and parasite abundance and allelic frequencies (Dybdahl and Lively 1998; Lively and Dybdahl 2000), and genotype-specific interactions leading to the accumulation of a large number of resistance and virulence alleles through frequency-dependent and balancing selection (Nei and Hughes 1991; Hedrick and Kim 2000). These studies examine changes in host and parasite phenotypes or genotypes across multiple sites over time scales ranging from a few years to several decades, and they emphasize that evolutionary change in hosts and parasites can be extremely rapid. A classic example of selection operating on a wildlife–pathogen system over relatively short time scales is myxomatosis in Australian and European rabbit populations (Fenner and Fantini 1999).

On longer time scales (and larger geographic scales), interactions between hosts and parasites can lead not just to coadaptation but also to cospeciation (e.g. Fig. 6.8). Cospeciation is defined as the joint speciation of two or more lineages that are ecologically associated (Page and Charleston 1998; Page 2003b), and this process can generate congruent host and parasite phylogenies when interacting species diverge in parallel. Parasite traits that might favor cospeciation include chronic infections and limited dispersal or restricted transmission (i.e. vertical, sexual); host traits that favor cospeciation include a patchy distribution, limited dispersal, or other factors that lead to geographic isolation or limited contacts among species, and specific chemical or immune defenses against particular parasites (Hafner and Page 1995; Hafner et al. 1998; Clayton et al. 2003; Page 2003b). Several studies have demonstrated patterns consistent with host–parasite co-speciation, yet in general this should be relatively rare compared with other possible patterns, including host-shifting, parasite extinction, and a process called "missing the boat," whereby the host

Box 6.3 (*Cont.*)

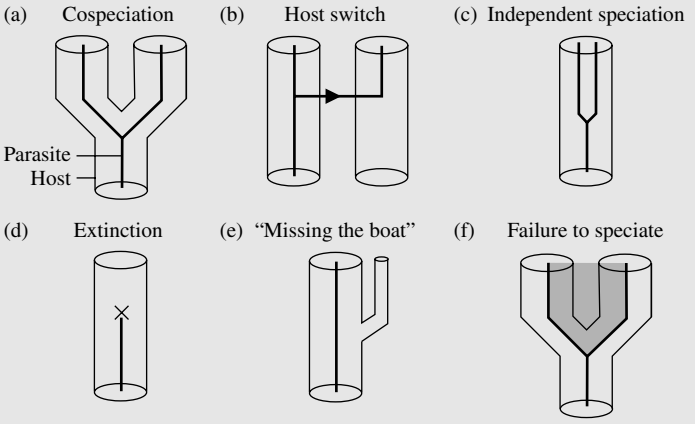


Fig 6.8 Example processes and evolutionary outcomes of host–parasite associations. Parasite lineages are drawn as black lines within host lineages (represented as "tubes"). Figures along the top row illustrate parasite divergence events that may or may not be associated with host evolutionary divergence, including: (a) hosts and parasites cospeciate, (b) parasites shift among unrelated host lineages (c) or speciate without its host. Along the bottom row are cases of parasite loss or host divergence in the absence of parasite divergence. (d) Hosts could persist while parasites go extinct and are lost from lineages, (e) hosts can speciate and parasites might be lost from one or more lineages, a phenomenon known as "missing the boat," or (f) the host might speciate but parasites do not, leading to the appearance of two or more host species "sharing" a parasite. Copyright (2003) from "Tangled Trees: Phylogeny, Cospeciation and Coevolution," by R. Page. Reproduced with permission of the University of Chicago Press.

splits into two or more lineages but the parasite remains in only one (see Fig. 6.8 and Page 2003b). Host-shifting is likely to be more common among parasites that can evolve rapidly relative to host generation times (due to high rates of mutation, recombination, large population sizes, frequent bottlenecks, and fast generation times), and for which transmission leads to frequent opportunities for cross-species transfer (see Section 2.4). It is important to note that although we usually think of phylogenetic patterns of coevolution involving assemblages of host and parasite species (such as pinworms in primates, Fig. 6.9), evidence for cospeciation could also include within-species phylogenies that show evidence for geographic variation and co-divergence among different populations (Biek et al. 2003).

Modern molecular tools allow researchers to examine the origins and longer-term coevolution of host–parasite associations as well as the relative rates of host and pathogen evolution (Holmes 2004). This can be achieved by comparing the relative genetic distances of host and parasite groups derived from phylogenies that include branch lengths (Nieberding et al. 2004). For most microparasites like viruses and bacteria that have fast generation times and large population sizes, we expect that parasites evolve much faster than their primate hosts and might frequently show evidence for rapid adaptation following shifts or jumps to new host species. Surprisingly, one study of cospeciation among

Box 6.3 (*Cont.*)

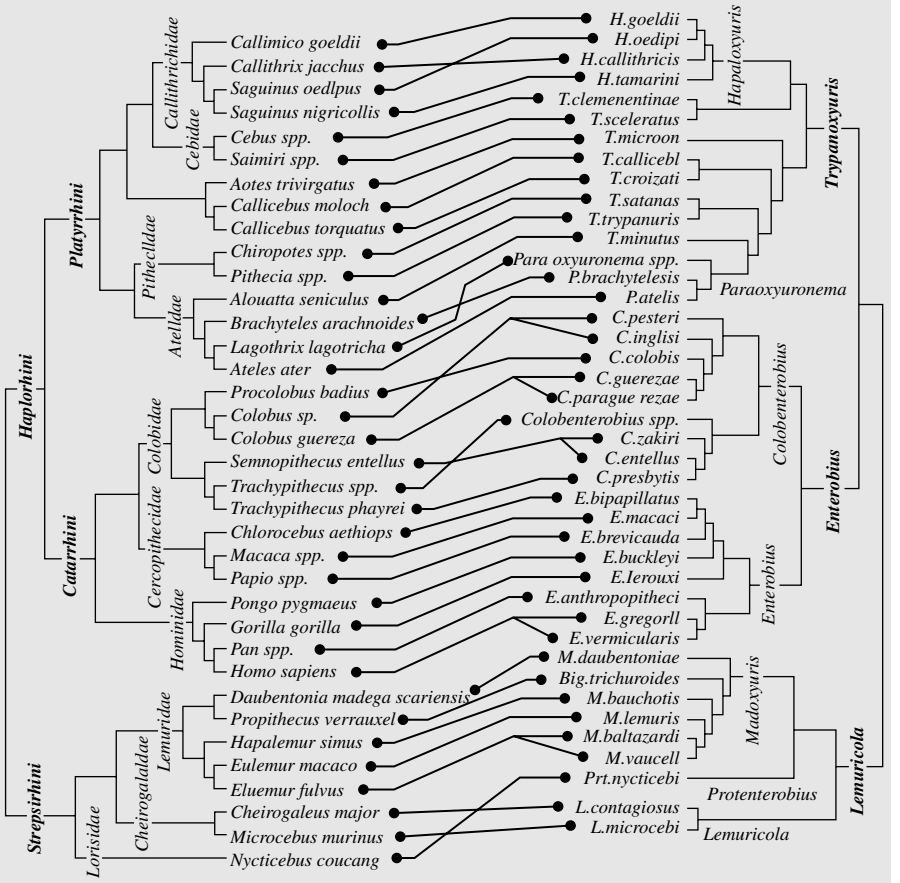


Fig. 6.9 Example of co-speciation between primates and their pinworm parasites. The parasite phylogeny (on right) is a morphologically based analysis of Enterobininae. The main genera of parasites fit major clades of primates and support the hypothesis that host and parasite lineages co-speciate. Despite generally high correspondence between host and parasite phylogenies, several discordances are also found, including possible host shifts from squirrel hosts. Copyright (1999) from "Primates and their pinworm parasites" by J. P. Hugot. *Systematic Biology*, Vol. 48, pp. 523–46. Reproduced by permission of Taylor and Francis Group, L.L.C.

strains of simian foamy viruses (SFVs, in the family Retroviridae) isolated from 44 species of Old World monkeys and apes provided evidence counter to this general expectation (Switzer et al. 2005). This study showed strong evidence for congruent primate and virus molecular phylogenies (albeit with evidence for a few "host jumps") and comparable divergence times and rates of nucleotide substitution for hosts and parasites, suggesting that primates and SFVs were evolving at similar rates (and documenting the lowest ever substitution rate reported for an RNA virus). Molecular phylogenies of hosts and

Box 6.3 (*Cont.*)

parasites can also be used to search for potential loci under selection (see Conway and Polley 2002; Anderson 2004).

As a final point, cospeciation is very suggestive of coevolution, but an adaptive basis for reciprocal interactions has to be established before it can be concluded that coevolution occurred. For example, recent studies of interactions between feral pigeons and feather lice demonstrated that selection in favor of host defenses for parasite removal was accompanied by parasite mechanisms to escape these host defenses (Clayton et al. 1999, 2003).

To identify coevolution requires evidence that two lineages have evolved together and exerted selective forces on one another (Clayton et al. 2003; Page 2003b). In the case of parasites and primates, we are often dealing with communities of multiple species of hosts and multiple species of parasites, a situation known as "diffuse" coevolution (see Ridley 1996 and Thompson 2005 for discussion of these and other topics). Coevolution can be contrasted with the alternative of non-reciprocal evolution, in which changes in one lineage impact the other lineage, but not vice versa. Predictions based on "coevolutionary equillibria" might be needed to evaluate empirically observed patterns of host social organization and parasite traits (e.g. Bonds et al. 2005), together with information on their history of evolutionary associations. Some tests could make use of non-reciprocal evolution, despite the fact that coevolutionary dynamics are likely to predominate. For example, in investigating the effects of parasites on host social systems, some signal of the effect of parasite introduction on the host lineage, such as smaller group sizes with fewer males, could remain even after counter-adaptations by the parasites—for example a longer incubation period—thus providing a means to detect a causal effect of the parasite on host behavior.

Coevolutionary studies of host–parasite interactions are challenging even in the most tractable biological systems, and studying coevolution in primates raises a number of challenges. In particular, we are dealing with long-lived, often highly endangered host species, where experiments that manipulate levels of disease risk are either impractical or unethical. To get around this problem, it would be possible to remove parasites in primate hosts and document the effects of removal on their behavior, provided that researchers are prepared to observe the animals over both the short term (to record plastic responses) and the long term (to record evolutionary responses over multiple generations). Alternatively, one can view primate evolutionary history as a "natural experiment" and use comparative methods to study coevolution of parasites and hosts. However, simply showing that a particular host trait, such as group size, is correlated with measures of parasite occurrence (or parasite characteristics) across species is not sufficient evidence for the hypothesis that disease has shaped the social system.

Another challenge arises if effects of parasites on selective pressures involving sociality are obscured by other, non-social host defenses. For example, if the probability of infection increases with group size or promiscuity, then highly

social or promiscuous hosts should experience more intense selection in favor of immunological defenses to limit transmission (Freeland 1976; Loehle 1995; Nunn et al. 2000). Ironically, if elaborate defenses act as effective barriers to parasite infection and impacts (e.g. Møller et al. 2001), this could eliminate expected correlations between parasitism and host sociality (the "ghost of parasitism past"). In other words, some host species might have few parasites or low infection rates despite living in groups with high rates of social contact. These same hosts might retain high measures of immune defenses or behavioral mechanisms to counter infections, indicating that they possibly experienced high parasite pressure at some point in the past.

6.6 Methodological approaches to study effects of parasites on host social systems

Researchers are just beginning to understand the many ways that host social and mating contacts influence disease risk—including the role of parasites as selective agents operating on host sociality, and how host and parasite traits might coevolve. Indeed, Janson (2000) and Kappeler and van Schaik (2002) identified infectious disease as a major frontier in our understanding of primate socioecology—an assessment with which we heartily agree! One major challenge is that in unmanaged wildlife populations, epidemiologically relevant data on social and mating contacts can be difficult to collect and often require long-term observational studies of individual animals. A related difficulty involves recognizing the critical temporal and spatial scales for analysis, as social contact patterns for many species will change seasonally, yearly and spatially. How and whether host contact patterns affect disease spread will further depend on the parasite's transmission strategy and on the duration of the infectious period. For chronic infections, effects of some social contact parameters might only become obvious at large spatial or temporal scales, whereas in other cases frequent host contacts at local scales could be crucial for parasite invasion and spread. With these challenges in mind, we return to the issue of "causality" raised in the Introduction to this chapter and identify four approaches to assessing whether and how parasites have impacted host behavior.

6.6.1 Fields studies

Observational and experimental field-based approaches require detailed data for demographic and social variables such as group size, local host population density, and social contacts both within and between groups. Observationally, if a parasite outbreak occurs in a group and animals subsequently splinter into smaller groups or reduce their social contacts with other individuals, this would provide circumstantial evidence for an effect of disease on social patterns. Evidence would be strengthened if the pattern were repeated as the infection spreads to additional social groups in the population. On the other hand, species in which individuals have experienced a long history of parasite exposure might already have evolved a variety of non-social

defenses to lower the prevalence of infection, including behavioral and immune defenses discussed in Chapter 5.

More research is needed on how and whether primates are cognitively aware of sickness in conspecifics, and whether they respond defensively to outbreaks of infectious disease, particularly for parasites that can spread via social contacts. We know remarkably little about whether primates recognize the infection status of conspecifics, and furthermore whether they use this information to modify their social interactions. As noted in the previous chapter, it may be that kin selection has tended to favor helping behavior rather than avoidance, especially if most diseases in primates are not highly contagious following direct host-to-host contact. Experimental tests could compare patterns of interaction among individuals, some of which are treated for infectious diseases while others are left untreated as controls. If disease status impacts levels of social contact, we expect that both treated and untreated individuals will preferentially interact with individuals who are uninfected (treated). Such tests would need to control for overall levels of activity, since infected animals may exhibit sickness behaviors (Hart 1990) that reduce their activity—an interesting question in its own right because these behaviors have been under-studied and rarely described in primates (Chapter 5).

Primatologists interested in behavior have collected data on pairwise interactions that could be used in social network based models, such as grooming matrices (see Chapter 4), similar to contact matrices and network graphs used to study pathogen outbreaks in human communities (Newman 2002; Ancel Meyers et al. 2003). These data can also reveal empirical variation in the level of heterogeneity in social and mating contacts (e.g. if most individuals have few contact partners whereas other have many)—leading to comparisons of social contacts in relation to individual infection risk (Ferrari et al. 2004), and pointing to selective forces operating on individual contact patterns before and after parasites are introduced naturally (or experimentally removed). At the population-level, social network models based on empirical data can indicate how temporal and spatial variability in contact structure influences rates of disease spread and prevalence. Such combined modeling and field approaches should be especially fruitful for exploring how host contact patterns affect disease dynamics over space and time for different pathogen types, and how pathogens change host behavior (Cross et al. 2004; Lloyd-Smith et al. 2004).

From the perspective of evolutionary responses to infection, studies that focus on shorter-lived hosts, such as social insects (Schmid-Hempel 1998), have some advantages over studying primates, including the possibility to run more invasive experiments. But the factors that play a role in insect societies are also likely to differ, for example with infanticide being more important in primates. Thus, while long generation times and low population sizes of many primate species make studying coevolution challenging, these challenges are not prohibitive. In fact, experimental studies of infectious diseases have been successfully performed in other large vertebrates, most notably Soay sheep (Gulland et al. 1993). Similarly, many "natural" experiments are available, as occurs through fragmentation and logging of forests (Gillespie et al. 2005; Chapman et al. 2005b).

6.6.2 Directional tests using comparative methods

Cross-species tests were discussed in the context of STDs (6.4.3). Phylogenetic comparative analyses also provide a means to investigate how parasites have influenced host social evolution more directly. If increased pressure from socially transmitted diseases generates selection for smaller social groups, we predict that evolutionary transitions to increased levels of parasitism will be associated with reductions in group size on a phylogenetic tree (Fig. 6.10). Harvey and Pagel (1991) term methods for testing whether one trait evolves before another "directional" approaches. One basic test uses parsimony to reconstruct ancestral states on a tree, then investigates whether one trait, for example increased richness of parasites, precedes reductions in measures of sociality (Maddison 1990). A more sophisticated approach uses maximum likelihood methods to test alternative evolutionary scenarios based on Markov models of trait change, including models that consider the temporal order of trait transitions (Pagel 1994). Other methods are useful for continuous characters (Deaner and Nunn 1999). For example, Lindenfors et al. (2004) used a method based on independent contrasts to test whether the number of males lags behind the number of females in primate social groups, as predicted if females determine the number of males in the group (Altmann 1990).

A related approach for studying host–parasite coevolution is to acquire phylogenetic information on co-occurring host and parasite lineages to examine the correlated evolution of host and parasite traits (Harvey and Keymer 1991; Morand et al. 2000). For example, Clayton et al. (2003) studied cospeciation and coadaptation among lice infecting multiple species of doves. High levels of specificity and cospeciation events among host and parasite lineages were supported by correlated host and parasite phylogenies. The authors also documented positive associations between host and parasite body sizes. In this case, experimental studies

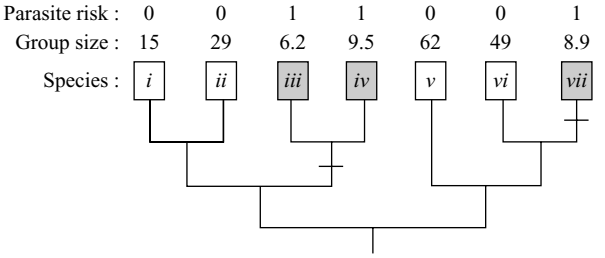


Fig. 6.10 Comparative tests of parasite-mediated selection on host social systems. Figure shows hypothetical data on group size for seven species, with parasite introductions (parasite = 1) into species iii, iv and vii. Evolutionary transitions over branches indicated by marks on the tree are associated with declines in group size. With more species, evidence for a chronological response to introduction of disease could provide evidence consistent with parasitism impacting social and mating systems.

further demonstrated that parasite adaptations to host body sizes resulted from host behavioral defenses, such that smaller parasites on smaller hosts were better able to avoid removal by host preening. Comprehensive parasite phylogenies have been compiled in relation to primate phylogeny (see Box 6.3, Hugot 1999; Switzer et al. 2005). These could be combined with infection characteristics to explore parasite adaptations to host behavioural traits.

6.6.3 Incorporating parasites in comparative studies of sociality

Comparative approaches could also be used to examine how patterns of parasitism alter well known functional relationships involving primate sociality. Some of the factors that influence male number are well established—for example, primate groups that contain more females also contain more males (Andelman 1986; Altmann 1990; Mitani et al. 1996a; Nunn 1999). As discussed above, evidence also suggests that females have the potential to manipulate the number of males in primate groups, specifically by increasing or decreasing the synchrony of their fertile (estrous) periods. More synchronous matings will tend to reduce the ability of any single male to defend access to females, leading to a greater frequency of multi-male groups (Dunbar 1988; Nunn 1999). Thus, if contagious parasites select for lower group sizes, levels of parasitism should explain additional variance in the association between the number of males and females across species, with female behavior favoring fewer males and reduced movement of males between groups when disease risk increases (see Section 6.3.3). By calculating residuals from the regression of the number of males on the number of females across species, negative residuals would be expected in species that experience greater pressures from directly transmitted parasites (Fig. 6.11).

In a pioneering study, Janson and Goldsmith (1995) investigated ecological traits, including proxy variables for feeding competition and predation risk, that influence primate group size. These authors did not include the costs of parasitism in larger groups because, at the time they were writing their paper, "there exist(ed) no broadly available indicators of different levels of exposure of primate species to parasites" (p. 331). Comprehensive data on primate infectious diseases are now available (Nunn and Altizer 2005), and it would be interesting to incorporate measures of parasite risk into such analyses to test whether group size is influenced by parasitism.

Finally, if biogeographic factors and climate play a role in determining disease risk, we might expect that social parameters show geographical variation associated with areas of high versus low parasite risk. Smaller groups might therefore be expected closer to the equator if contagious pathogens (or those spread by arthropod vectors that are attracted to larger groups) are more common at lower latitudes (Nunn et al. 2005).

6.6.4 Modelling approaches

Effects of parasites on host social evolution have been modeled explicitly, as described in several examples highlighted earlier in this chapter (Kokko et al. 2002; Bonds et al. 2005, see Box 6.2). A major challenge involves developing modelling

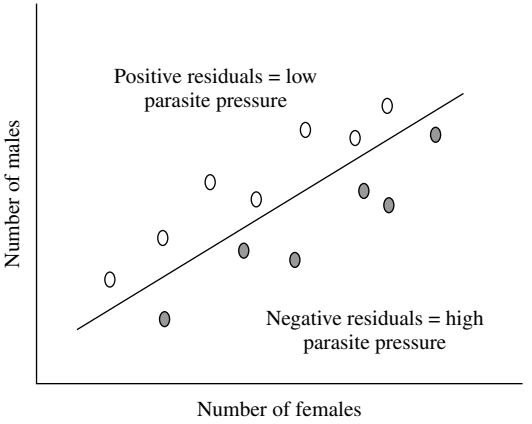


Fig. 6.11 Potential effects of parasites on group composition. Using the relationship between the number of males and the number of females in primate groups, one can make predictions for the effects of parasites on group composition. When parasite pressure is high and smaller groups can reduce that pressure, we expect negative residuals (filled circles) from the relationship shown here, under the assumption that females can control group composition by affecting male monopolization potential. Conversely, for relatively low parasite pressure, we expect positive residuals (open circles), with females potentially benefiting from male presence by reducing predation risk (van Schaik and Horstermann 1994). Examples of species with negative residuals include guenons, such as *Cercopithecus mitis, C. ascanius*, and *C. campbelli*, while positive residuals are found in multimale species such as *Pan paniscus*, *Macaca sylvanus* and *Cebus capucinus* (using data from Mitani et al. 1996b).

approaches to explore the joint coevolution of transmission characteristics, social systems, and pathogen virulence. In this case, researchers must decide how to represent variation in host behavior in a biologically realistic way that corresponds to observed social and mating systems. One possible approach would be to use contact networks or individual-based rules for association and dissociation of males and females to generate a wide range of social and mating structures (Cohen 1969; Thrall et al. 2000; Read and Keeling 2003). Behavioral ecologists have discussed verbal and optimality-based models extensively, but these approaches overlook the fact that it is unrealistic to describe selection on genes that directly translate to specific social systems. Rather, genetic effects will act on social systems by affecting individual behavior.

6.7 Summary and synthesis

Although researchers have long considered host social interactions to be important for parasite transmission dynamics and rates of disease spread, only recently have

studies of host social responses to parasite pressure emerged. In this chapter, we considered how parasites could impact group size and composition, contact among individuals within groups, movement of individuals between groups, and mating behavior. Given the increasing amount of data available on infectious diseases in primates (Nunn and Altizer 2005) and the development of models for parasite spread in animal mating and social systems (Hess et al. 2002), we are now in a position to begin addressing the role of parasitism as an ecological force in primate social systems. Theoretical models are revealing that the simplistic frameworks of the past may need to be discarded in favor of more sophisticated models that take into account contact patterns within and between groups (e.g. for STDs, Thrall et al. 1997, 2000; Kokko et al. 2002). Predictions will also hinge upon the transmission mode of the parasites themselves (Loehle 1995), an obvious point but one worth repeating because the importance of transmission mode is often overlooked.

Infectious disease has been considered a potent evolutionary force in primate social systems in several papers by Freeland (1976, 1979). But in the years since these papers were published, parasitism has been studied mainly within particular species and given less attention at broader scales. For example, in his remarkable synthesis of primate social systems, Dunbar (1988) mentioned infectious disease as a source of mortality, but he did not explore parasites as a major factor influencing variation in primate social systems. Other authors interested in social systems within particular primate host species have failed to distinguish between diseases caused by infectious agents and those caused by genes or environmental contaminants, lumping all of these together as "illnesses" (e.g. Goodall 1965; Cheney et al. 1988). This is not intended as criticism of previous work, but illustrates the difficulty of identifying causal agents of disease in the wild—a situation common even for human diseases in industrialized countries (Ewald 2000).

At present, we lack convincing evidence for the general effects of parasites on broad patterns of sociality and mating systems in primates. Such effects may not be there, or it could reflect a need to control for potentially correlated host and parasite traits and to better quantify host behavior and key parameters from epidemiological models. Furthermore, and somewhat ironically, if highly social hosts evolve more elaborate immune or behavioral defenses against parasites, this could virtually eliminate expected relationships between parasitism and host sociality, and would motivate further studies that controlled for the degree to which hosts invest in anti-parasite defenses (Nunn et al. 2000; Møller et al. 2001; Nunn 2002a; Wilson et al. 2003).

Finally, it is worth making a brief comparison of parasitism and predation, because the latter has featured so prominently in studies of primate socioecology (van Schaik 1983; Janson and Schaik 1993). Parasitism bears a superficial similarity to predation, but the effects of parasitism are usually more cryptic and less spectacular than an attack by a predator on a primate. Predation has received a great deal of attention despite its occurrence at a low rate, while parasitism has received less attention, and yet deaths or loss of reproduction due to disease probably occurs more frequently (Cheney et al. 1988). Like predators that use stealth or cooperative hunting to

acquire their prey, parasites exhibit a wide array of mechanisms to make use of hosts, including variation in transmission and manipulation of host behavior. Finally, anti-predator defenses are largely behavioral or involve anatomical adaptations, whereas mammals have an additional line of defense against parasites, namely the immune system, that could relieve pressure on primate behavior to be as tightly linked to parasite avoidance as it is to predation avoidance.

7

Parasites and primate conservation

7.1 Introduction

A paper published in *Nature* in 2003 captured headlines in newspapers around the world (Walsh et al. 2003b). "Gorillas and Chimps in Peril," proclaimed the *New York Times* (April 7, 2003), while the *Guardian* warned, "Wipe Out Warning on Great Apes" (April 7, 2003). In the paper that garnered this attention from the press, Peter Walsh and his colleagues compiled data on gorilla and chimpanzee nests in western equatorial Africa and compared the results to an earlier survey (Tutin and Fernandez 1984). They found that formerly healthy ape populations from relatively intact forests in Gabon declined by an average of 56% in the period from 1983 to 2000, with some populations falling by more than 90% (Fig. 7.1). A statistical model that included both distance from the nearest urban center and distance from the most recent Ebola virus outbreak explained 63% of the variation in ape density, suggesting that severe population declines were linked with a combination of bush meat hunting and Ebola infections. Additional research confirmed the presence of Ebola in ape carcasses (Leroy et al. 2004a), with antibodies to Ebola present in other primate species (Leroy et al. 2004b). Although details are still emerging on the mechanisms of the spread of Ebola in wild apes, Ebola poses a clear threat to wild apes (Morell

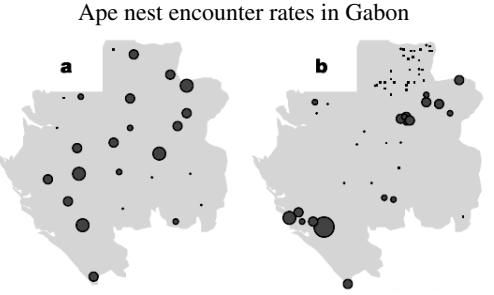


Fig. 7.1 Decline in ape populations in Gabon over a 17-year period. The relative size of circles indicates density of ape nests, with the smallest points showing sampling sites where no nests were found. Walsh et al. (2003) presented evidence showing that this decline was a function of both hunting and disease pressure. From P. Walsh et al., "Catastrophic ape decline in western equatorial Africa." *Nature*, vol. 422, pp. 611–61. Copyright (2003), reproduced with permission of P. Walsh and Macmillan Publishers Ltd.

1995; Formenty et al. 1999b; Walsh et al. 2003b, 2005; Leroy et al. 2004a; Karesh and Chapman 2005).

Primates are among the most threatened mammals worldwide, with over 60% of all species showing evidence for some degree of conservation concern (IUCN, Hilton-Taylor 2002). The two most widely acknowledged threats to wild primate populations are habitat loss and direct removal via hunting (Cowlishaw and Dunbar 2000; Chapman and Peres 2001). Surprisingly, no primate species had been formally listed as threatened as a direct result of infectious disease up through the release of the 2002 IUCN Red List (Hilton-Taylor 2002). By comparison, many examples of carnivores, artiodactyls, and marsupials have been identified as threatened due to parasitism (Fig. 7.2). It seems likely that parasites also have a role to play in primate extinction risk. Indeed, major epidemics in wild primates, such as those resulting from Ebola and examples highlighted in Table 1.2, have attracted worldwide

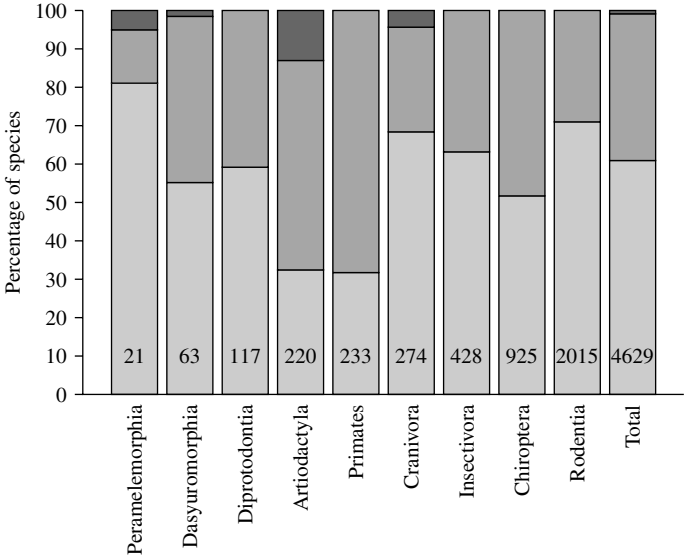


Fig. 7.2 The distribution of "threat due to disease" among mammalian taxonomic groups. Light gray represents the proportion of non-threatened species in each clade, medium-gray and dark-gray combined represent the proportion of threatened species (including species classified as extinct in the wild, critically endangered, endangered, vulnerable, lower risk-conservation dependent, and lower risk-near threatened), and dark gray only represents the proportion of species where infectious disease is identified as a threatening process. Numbers at the bottom of each bar refer to the number of species in each clade. Clade definitions follow Wilson and Reeder (1993) and threat data are from Hilton-Taylor (2000). Image courtesy of K. Jones, Zoological Society of London. Modified from S. Altizer et al., "Social organization and parasite risk in mammals: Integrating theory and empirical studies. "AREES Vol. 34, pp. 517–537. Copyright (2003), reproduced with permission of Annual Reviews.

attention and emphasize the potential negative consequences of infectious disease. More cryptic pathogens could go undetected for long time periods or persist in small and declining host populations, thus presenting more insidious obstacles for primate conservation, in part due to the challenges of convincing government organizations, conservation and management groups, and the general public that the impacts of less virulent pathogens warrant concern.

The goal of this chapter is to investigate the role of infectious diseases in primate conservation. We focus on two issues central to the conservation of primates—anthropogenic effects on disease risk in wild populations, including the emergence of new diseases, and the importance of considering parasites when planning conservation efforts (Fig. 7.3). Parasites can threaten biodiversity through a variety of processes, and several recent reviews have outlined a number of ecological and evolutionary drivers of disease emergence and disease-induced population declines in

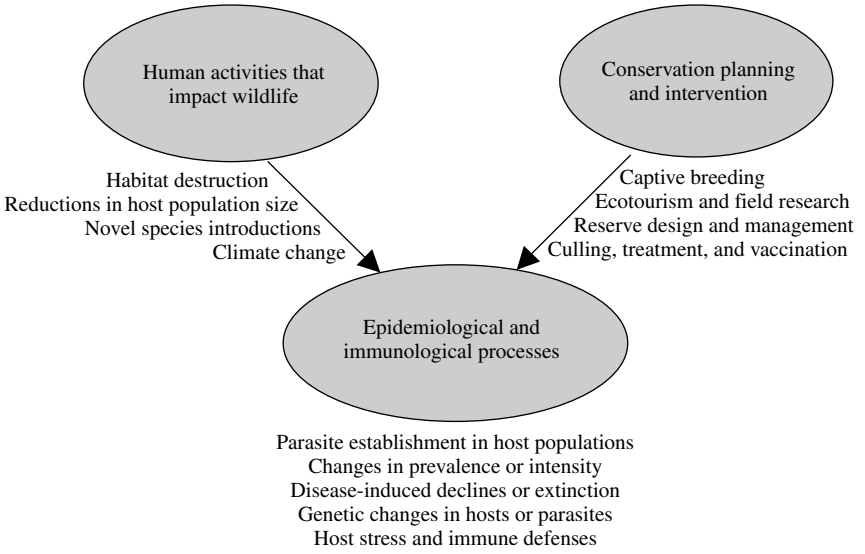


Fig. 7.3 Overview of the links between human activities, infectious diseases, and wildlife conservation. Habitat destruction concentrates animals into smaller areas and generates novel stressors that can negatively impact immunocompetence, while fragmentation can lead to food and social stress and new interactions among species that are usually separated. Reductions in host population size can reduce host potential to respond to disease by reducing genetic variation, while also increasing the risk of stochastic factors that drive host extinction. Human activities can also introduce novel pathogens directly or with the introduction of new host animals. Conservation planning involves a variety of activities in the field, lab, and captive breeding facilities. It is essential to have long-term monitoring of parasites in place as a means to identify outbreaks in primate populations and new threats arising from reservoir hosts.

humans and wildlife (Scott 1988; McCallum and Dobson 1995; Holmes 1996; Daszak et al. 2000; Taylor et al. 2001; Cleaveland et al. 2002; Lafferty and Gerber 2002; Altizer et al. 2003a; Chapman et al. 2005a). From this growing literature, we highlight mechanisms and issues most pertinent to primate conservation, including linking specific examples to more general principles in the emerging field of "conservation medicine," which aims to understand the connections between anthropogenic drivers, infectious disease risk, and wildlife health and conservation (Aguirre et al. 2002).

We begin by considering the direct effects of parasites on host population declines, focusing on emerging infectious diseases (EIDs) and impacts of humans on disease risk in wildlife. We then discuss how conservation efforts can become more effective by taking into account risks from infectious disease. Given the numerous examples of pathogen-driven wildlife declines, a need exists for wildlife managers to quantify parasite occurrence in primates to obtain baseline knowledge on the parasites that are present, to gain an understanding of transmission modes and impacts on individual hosts, and to identify potential "reservoirs" of infection in other hosts that might cross-infect primates. In the last section, we shift gears by considering the potential role of parasites in promoting biodiversity. If so, then conservation of parasites could be critical for maintaining existing host diversity now and in the future. The goal then would be to strike a balance between treating infectious disease as a natural process worthy of maintaining, and ameliorating the risks from new diseases entering natural systems.

7.2 Parasites as a cause of wildlife declines

Because of their ability to trigger sudden epidemics and their potential for rapid evolution, parasites represent a rising concern in conservation biology (Harvell et al. 1999; Dobson and Foufopoulos 2001; Lafferty and Gerber 2002). A growing list of disease outbreaks point to introduced pathogens as a cause of dramatic declines in previously thriving populations, or as threats to already declining species (Roelke-Parker et al. 1996; Hochachka and Dhondt 2000; Jensen et al. 2002). Although infectious disease theory predicts that parasite establishment and spread should be greater in larger host populations, smaller host populations might experience significant impacts from infectious diseases due to limited genetic variability or threats from generalist parasites (Lyles and Dobson 1993; Funk et al. 2001).

The example of Ebola in African apes provides sobering evidence that disease epidemics can decimate wild primate populations. The ultimate issue concerns whether parasites can drive hosts to extinction, either acting alone or in conjunction with other forces (de Castro and Bolker 2005). Multiple lines of evidence from non-primate species support this possibility (Sato et al. 1994; McCallum and Dobson 1995; Woodroffe 1999; Altizer et al. 2001; Boots and Sasaki 2002). In birds, for example, the introduction of avian malaria into Hawaii contributed to the extinction of several endemic forest species (Warner 1968; Van Riper et al. 1986). Several mammals have been driven to extinction (or the brink of extinction), in part due to

infectious disease. One of the best-known examples involves the precarious recovery of the black-footed ferret (*Mustela nigripes*, Thorne and Williams 1988), which is arguably the most endangered mammal in North America. In the mid-1980s, outbreaks of canine distemper and sylvatic plague effectively eliminated black-footed ferrets from the wild and severely threatened a captive breeding program, to the point that the entire species was reduced to fewer than 20 captive individuals (Dobson and Lyles 2000). Maclear's rat (*Rattus macleari*), once common on Christmas Island in the Indian Ocean, may have been driven to extinction by an infectious disease carried by ship rats (*Rattus rattus*) that were introduced to the island (Andrews 1909; Pickering and Norris 1996). Some scientists have even speculated that an unknown infectious disease was responsible for the extinction of the thylacine (*Thylacinus cynocephalus*)—the so-called "Tasmanian tiger"—from Australia (Guiler 1961).

Populations of howler monkeys appear to have been exterminated by yellow fever epidemics (Galindo and Srihongse 1967), and the recent outbreak of Ebola in Lossi Sanctuary eliminated an entire population of 143 gorillas (representing 8 social groups) that had been studied for 10 years (Leroy et al. 2004a). Remarkably, this gorilla population disappeared within a 4-month time period. Other cases where parasites appear to have caused substantial mortality or morbidity in wild primate populations were summarized in Chapter 1 (see Table 1.2). Similar effects span primate hosts from multiple continents and have been caused by vastly different types of parasites, including helminths, bacteria, arthropods, and viruses.

At a broader scale, MacPhee and Marx (1997) hypothesized that highly virulent generalist parasites were responsible for the extinction of large mammals during the last 40,000 years. Specifically, they proposed that cross-species transmission occurred during "first contact" episodes as humans and their domesticated animals expanded across the globe (see Van Blerkom 2003 for discussion of some of the viruses that could have been involved). While offering a provocative contrast to the alternative proposal that over-hunting contributed to faunal declines, the disease hypothesis cannot easily explain why large-bodied hosts were more susceptible to extinction (see Alroy 1999). In fact, because of the negative association between body mass and population density in mammals (Damuth 1981), smaller bodied hosts living at higher density would be more likely candidates for new pathogens to establish and spread (see Chapter 4 and De Leo and Dobson 1996 for conditions in which this is expected). Hunting pressure by humans would have further reduced the population densities of larger-bodied species, reducing the possibility of a sustained outbreak of a virulent pathogen. And once their numbers were reduced to low levels, recovery of larger-bodied hosts would be less probable, due to slower birth rates and longer generation times.

Regardless of whether it accounts for the megafaunal extinction that coincided with the spread of humans around the world, MacPhee and Marx's (1997) disease hypothesis does raise a key concept that will emerge repeatedly throughout this chapter: most attention should probably focus on generalist parasites as the primary

threat to biodiversity because these parasites can be maintained in high-density reservoir hosts (e.g. domesticated animals), and from these reservoirs, parasites can cross-infect threatened species that exist at lower population densities (and so cannot maintain the parasites on their own).

7.2.1 Emerging infectious diseases in primates and other wildlife

Concerns about direct threats from novel pathogen introductions have erupted over the past two decades as human populations gained intimate experience with AIDS, West Nile virus, sudden acute respiratory syndrome (SARS), Nipah virus, and threats of bioterrorism. The implications of these EIDs for humans have been discussed extensively in both scholarly and popular publications (Garrett 1995; Preston 1995; Morse 1996; Taylor et al. 2001, see Chapter 8). We follow other authors in defining EIDs as infections that either appear for the first time, or are increasing in prevalence or expanding their geographic ranges (Morse 1995; Daszak et al. 2000; Dobson and Foufopoulos 2001; Cleaveland et al. 2002; Wobeser 2002b).

In terms of wildlife populations, EIDs can undermine conservation efforts and pose significant threats to biodiversity (Harvell et al. 1999; Daszak et al. 2000). A growing number of emerging infections have been documented in mammals (Fig. 7.4), ranging from rabies and canine distemper viruses in African carnivores to rinderpest in ungulates (Scott 1981; Alexander et al. 1996; Roelke-Parker et al. 1996; Laurenson et al. 1998; Kock et al. 1999). Perhaps only amphibians have been studied more extensively than mammals in this regard, with great scientific effort focused on identifying the role of several parasitic agents in the global decline of amphibian populations (Berger et al. 1998; Daszak et al. 1999; 2003).

Three features characterize EIDs in humans and domesticated animals; these same three features are likely to play a similar role in pathogen emergence in wildlife. First, EIDs are usually caused by viruses, bacteria, or other microparasites that can evolve rapidly, rather than larger or more slowly reproducing parasites like arthropods and helminths (Cleaveland et al. 2001). Second, pathogens identified as EIDs can often infect a wide range of host species (i.e. multi-host or generalist pathogens, see Cleaveland et al. 2001; Woolhouse et al. 2001) or show evidence for recent cross-species transmission. Finally, anthropogenic effects on the environment—including habitat loss, pollution, and climate change—can trigger or enhance the emergence of novel infectious diseases in wildlife (Schrag and Wiener 1995; Daszak et al. 2000; Chapman et al. 2005a).

Bovine tuberculosis (caused by *Mycobacterium bovis*) is one example of an emerging pathogen that illustrates how infectious diseases can threaten wild primates and other mammals. This bacterium infects a wide array of mammals, including wild and captive ungulates, brush-tailed possums (*Trichosurus vulpecula*), and badgers (*Meles meles*, Hunter 1996; Clifton-Hadley et al. 2001). Bovine tuberculosis also poses concerns in captive settings, including zoological parks, farms and captive breeding facilities, in part because domesticated animals can serve as reservoirs of infection. Among primates, chacma baboons (*Papio ursinus*) are infected by *M. bovis* (Fig. 7.4.(d)), with rapid progression of disease (including the development of lung

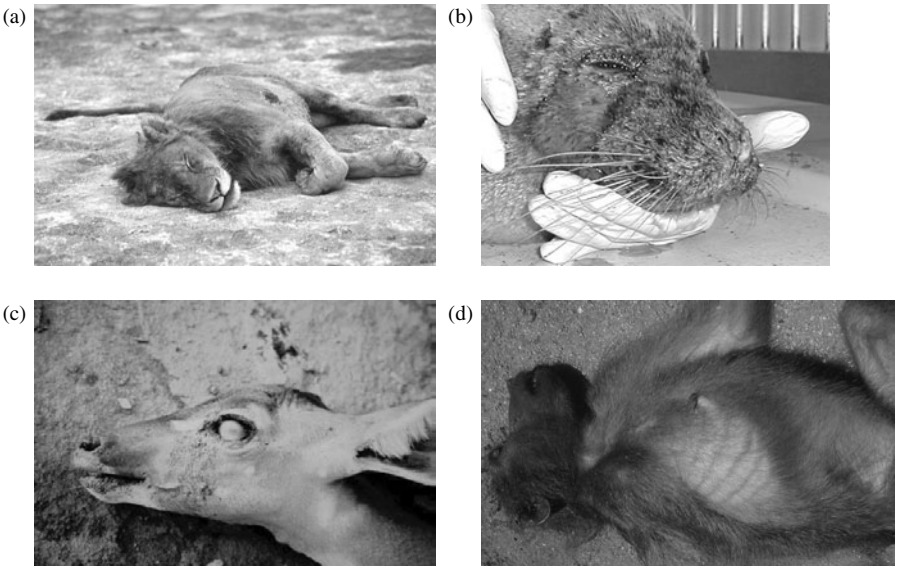


Fig. 7.4 Examples of emerging infectious diseases (EIDs) in wildlife. (a) Young male lion (*Panthera leo*) suffering from canine distemper virus. This individual was so lethargic that he made little effort to remove the biting flies from his body. Image taken in Ngorongoro Crater, Tanzania, Africa, 2001, courtesy of C. Packer, University of Minnesota. (b) This harbour seal (*Phoca vitulina*) died of phocine distemper virus (PDV) during an epidemic in northern Europe in 2002. This picture was taken at the Seal Rehabilitation and Research Centre, Pieterburen, the Netherlands, and provided by J. Philippa, Institute of Virology, Erasmus MC, Rotterdam. (c) Kudu (*Tragelaphus* sp.) with corneal opacity caused by rinderpest virus. This pathogen was introduced to wild African ungulates through domesticated cattle during the late 1880s. Image from Kenya, 1994, reproduced from FAO/EMPRES 2004. Image credit: P. B. Rossiter. (d) Emaciated chacma baboon (*Papio ursinus*) infected with bovine tuberculosis, caused by *Mycobacterium bovis*. Image courtesy of D. Keet, Kruger National Park.

nodules and emaciation). In one baboon troop in Kruger National Park, prevalence of bovine tuberculosis reached up to 50% (Keet et al. 1996; 2000). In this case, baboons probably became infected by feeding on infected buffalo carcasses, and subsequent rapid spread followed the use of a confined sleeping area that enhanced airborne and oral transmission among troop members (Keet et al. 2000).

The spread of bovine tuberculosis and other wildlife EIDs are consistent with the view that a major cause of disease emergence in threatened hosts relates to "pathogen pollution," namely the transmission of infectious agents from reservoir host species to more vulnerable wildlife populations (Daszak et al. 2000). In fact, the smaller population sizes of threatened species should be less able to support parasites on their own, particularly in fragmented host populations and when parasites are both directly transmitted and highly pathogenic (Lyles and Dobson 1993; Woodroffe 1999; de Castro and Bolker 2005). In many cases, an initial cross-species transmission event leads to some initial spread (but eventual fade-out) of the pathogen in a non-target

host population. But even for pathogens that can never spread directly within native wildlife populations, continual exposure from reservoir hosts can generate high prevalence in a vulnerable host species (Fenton and Pedersen 2005).

7.2.1.1 Epidemiology of emerging diseases

How do parasites establish in new host populations, and what factors influence the probability of parasite success? To further clarify the issues concerning EIDs, the process of disease emergence can be broken into two steps: (1) initial introduction of an agent into a novel host population, and (2) establishment and spread at the population-level (Morse 1995). Both epidemiological and evolutionary considerations become important during and following emergence (Schrag and Wiener 1995). Epidemiologically, parasites must meet the criterion of $R_0>1$ to establish and spread in a new host population (Chapter 4). Evolution could play a crucial role in the emergence process, as demonstrated by a modeling study by Antia et al. (2003). These authors used simulation and analytical approaches to show that for pathogens with R_0 just below the invasion threshold, evolution during initial introduction could allow parasites to increase in prevalence (Fig. 7.5). In this case, models demonstrated that novel infections are much more likely to establish in a host population if chains

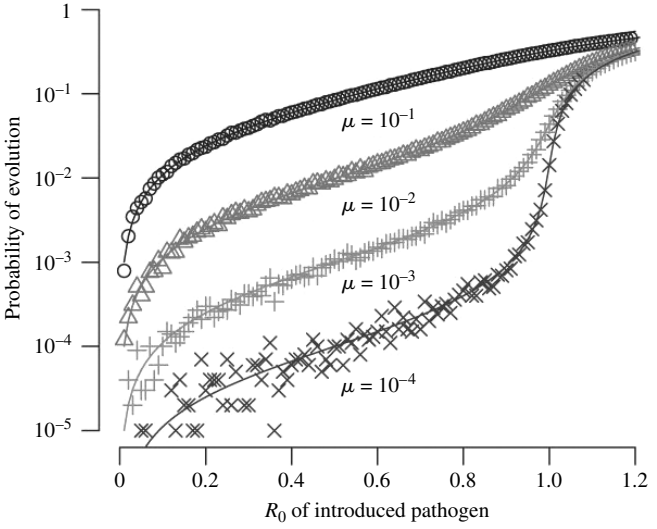


Fig. 7.5 Ecological and evolutionary considerations in the emergence of new diseases. Plot shows the probability of disease emergence for different pathogen mutation rates (μ) and reproductive number R_0 of the introduced pathogen. Even when $R_0<1$, evolution can facilitate disease emergence, and this is more likely closer to $R_0 = 1$ because the pathogen remains in the population for a longer period of time. From Antia, R., R. R. Regoes, J. C. Koella, and C. T. Bergstrom. 2003. The role of evolution in the emergence of infectious diseases. *Nature* 426:658–661 (Reproduced with permission from Nature Publishing Group).

of transmission are maintained long enough for new mutations to arise that increase the parasite's transmission in the new host, raising R_0 to greater than 1. Counter to the suggestion that ecology is more relevant than evolution in the emergence of infectious diseases (Schrag and Wiener 1995), this modeling effort revealed that ecological factors can provide a crucial platform for evolutionary changes leading to disease emergence.

A second important epidemiological question is, "can a novel parasite actually drive a host to extinction?" Indeed, standard compartment models for the dynamics of directly transmitted diseases in single host populations (see Chapter 4) lead to the expectation that all else being equal, pathogen fitness will decline as host population density falls. Thus, counter to the proposition of MacPhee and Marx (1997) discussed above, highly virulent EIDs should disappear from dwindling populations before their hosts go extinct, in part because infected hosts will die faster than new infections arise. A related point is that as parasites spread and diseased animals recover or die, the density of susceptible hosts will fall, leading to concurrent declines in parasite fitness. This is particularly true for directly transmitted parasites, where reductions in host density below the critical threshold population size (Chapter 4) will cause the parasite to go extinct (Anderson and May 1991; but see Lloyd-Smith et al. 2005).

Yet there are probable cases of disease-induced extinction, summarized in 7.2 and in de Castro and Bolker (2005). What are some of the conditions in which an EID might drive a host to extinction? First, directly transmitted parasites could drive host population sizes so low that extinction by stochastic factors becomes a concern, especially in host species with slow life histories in which populations require more time to recover. Second, pathogens transmitted sexually or by biting arthropods (i.e. with frequency-dependent transmission) should not suffer from reduced prevalence as host populations decline (reviewed in de Castro and Bolker 2005). Third, generalist parasites maintained in "reservoir" populations, particularly domesticated animals living at high density, can "spillover" to threatened species (as mentioned above and discussed further in the next section). Finally, spatially explicit models show that even if parasites do not cause global host extinction, they can certainly lead to local extinctions in many circumstances, in part because the parasites can be maintained in patches and cause large-scale density declines as the infection spreads to new patches (Sato et al. 1994; Haraguchi and Sasaki 2000; Boots and Sasaki 2002). Thus, a variety of disease-related mechanisms can drive host species to critically low abundance and even to extinction (Box 7.1).

7.2.1.2 Humans and domesticated animals as sources of infection for primates

Like other wild mammals, primates can be exposed to pathogens through contact with reservoir host species. In fact, humans and domesticated animals are probably important sources of infection for primates because they often exist at high density, can overlap in geographical range with wild primates, and because humans are relatively closely related to Old World monkeys and apes (Wolfe et al. 1998; Wallis

Box 7.1 Role of infectious disease in population viability analysis

Population viability analysis (PVA) is a conservation strategy aimed at estimating the relative extinction risk of populations given a variety of ecological scenarios; typically, the goal is to make conservation decisions in light of the probability that a population will persist over a set period of time (Boyce 1992; Beissinger and McCullough 2002; Morris and Doak 2002). PVA can involve one of several modeling approaches, incorporating information on key parameters like initial population size, age-specific birth and death rates, inbreeding depression, and the role of stochastic environmental forces (Morris et al. 1999; Gerber and VanBlaricom 2001). Within this framework, infectious diseases can be studied as a threat to population viability, especially when host populations are already small or when transmission occurs from reservoir hosts (Ballou 1993; Haydon et al. 2002b).

Use of PVA to study the impact of infectious disease requires information on pathogen biology and key social and life history variables of the host, particularly rates of dispersal between groups, social contact within groups, and host reproductive rates and lifespan. Several detailed PVA studies have been conducted on primates (see Cowlishaw and Dunbar 2000 for examples). Some of these models examined the potential for infectious disease to impact populations (as in the Barbary macaque, *Macaca sylvanus*: Fa and Lind 1996), but more work is needed to assess the threats of pathogens in different primate systems.

Haydon et al. (2002b) laid out a general procedure for integrating epidemiology and PVA, and they applied this framework to the case of rabies and canine distemper as threats to Ethiopian wolves (*Canis simensis*). Models predicted that introducing rabies from domesticated dogs sharply increased the extinction probability of the wolf population, particularly when the simulation was run with small numbers of individuals ($<$100 individuals), but that canine distemper had a weaker effect. Haydon et al. (2002b) used their simulation results to recommend actions to protect remaining populations at risk of rabies, including implementing vaccination programs aimed at wolves. In their models, vaccination of only 20–40% of the wolf population greatly improved the stability of the population in response to epidemics (Haydon et al. 2002b).

PVA can also be a useful tool for designing reserves of appropriate size and geometry to control infectious disease outbreaks. Indeed, future modeling and empirical studies that consider the spatial configuration of populations and contacts with reservoir species are needed to assess the effectiveness of reserve design and direct intervention methods for countering the harmful effects of disease (McCallum and Dobson 2002).

Although not strictly a PVA, a recent study of the spread of Ebola in African apes also is relevant to discussion of simulation models in assessing disease risk for primates. Using data on host characteristics from the field, Nunn et al. (in review) simulated the spread of an Ebola-like pathogen in chimpanzee and gorilla populations following a single introduction from an unknown reservoir (this model was discussed in Chapter 4, see Fig. 4.10). The simulations revealed that the pathogen spread to more groups when the simulation was parameterized using data from gorillas rather than chimpanzees, despite the typically larger social groups of chimpanzees (see Fig. 7.6). The key factor accounting for this difference involved the likelihood of female dispersal following the death of other group members. Female gorillas were in groups with only one or a few males; when these males died from disease, remaining females were more likely to disperse to neighboring groups, potentially carrying infections with them. In contrast, dispersal of females from infected chimpanzee groups was delayed by the presence of multiple males, as the model assumed that females would not disperse until most or all males had died. Because infected primates were assumed to die within 18 days post-exposure, reduced dispersal among groups

Box 7.1 (*Cont.*)

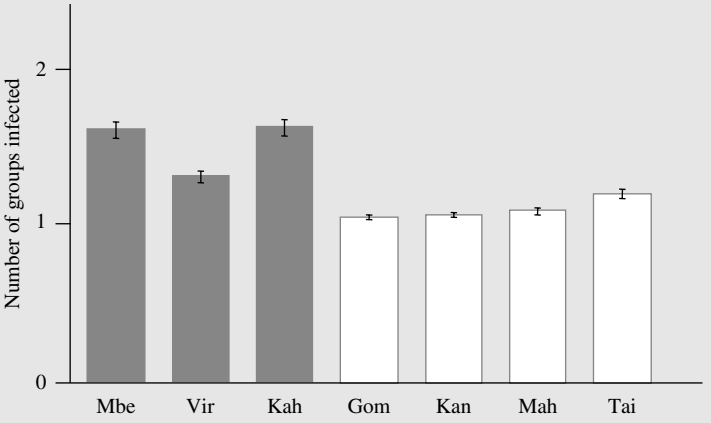


Fig. 7.6 Computer simulation of disease emergence in gorillas (gray bars) and chimpanzees (white bars). The simulation model used in Fig. 4.10 was initiated with a single case of Ebola in gorillas and chimpanzees using parameters from seven field sites, with an incubation period of eight days and a subsequent 10-day period over which the infection could be spread. The probability of death changed during the infectious period, followed a normal distribution, with a peak probability of death equal to 0.25 at the midpoint of infection. Plots show mean values +/- 1 SE. Population codes: Mbe: Mbeli; Vir: Virungas; Kah: Kahuzi; Gom: Gombe; Kan: Kanyawara; Mah: Mahale; Taï: Taï. From Nunn et al., in review.

greatly limited the wider spread of Ebola among chimpanzee populations in the simulations. Empirical data on the population-level impacts and rates of spread of Ebola in chimpanzee versus gorilla populations could be used to test the model assumptions and predictions.

and Lee 1999; Tutin 2000; Chapman et al. 2005a). Here we follow Haydon et al. (2002a) by defining a *reservoir host* as one or more populations that can maintain pathogens and transmit them to target hosts. This definition emphasizes that control strategies for limiting parasite effects on wildlife frequently require reference to a "target" host population—usually an at-risk population that cannot maintain the pathogen indefinitely without an outside source—and one or more reservoir species that serve as the primary sources of the infection.

Transmission of directly transmitted parasites from reservoir hosts to target hosts has been investigated using epidemiological models of multi-host systems (see Section 4.4.3 and Fenton and Pedersen 2005). Dobson (1995) provided one example involving the spread of rinderpest among eleven species of hoofed mammals in Ngorongoro Crater. Empirical data on nearest neighbor distances were used to estimate potential within- and cross-species transmission rates. A combined modeling and empirical approach showed that the vast majority of viral transmission probably

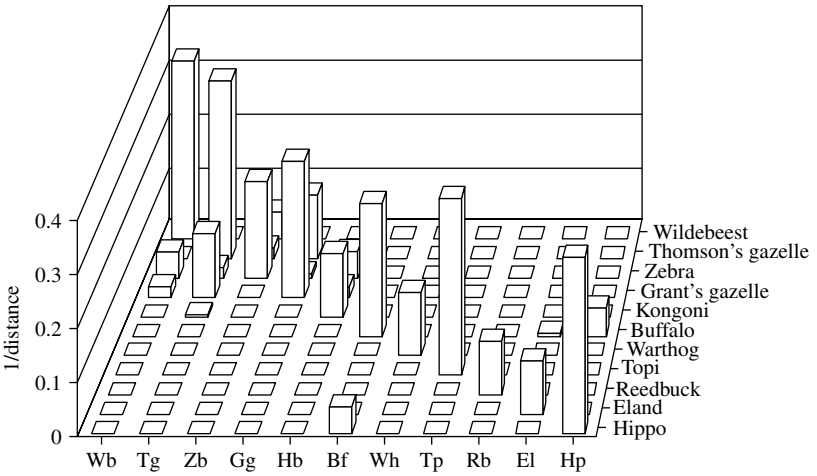


Fig. 7.7 Contact among hosts in a community of African mammals. Larger values on the vertical axis indicate closer proximity among a pair of species, predicting greater opportunity for the spread of directly transmitted parasites. The highest bars along the diagonal indicate intra-specific contact, showing that transmission within species is likely to be higher. Figure from Dobson, A. (1995). The ecology and epidemiology of rinderpest virus in Serengeti and Ngorongoro Conservation Area. In *Serengeti II: Dynamics, management, and conservation of an ecosystem* (eds. A. R. E. Sinclair, and P. Arcese), pp. 485–505. Permission to reprint granted from the University of Chicago Press.

occurs within species (Fig. 7.7), and that some pairs of species are likely to provide more opportunities for transmission (e.g. Thomson's and Grant's gazelles) than others (e.g. wildebeest and topi). A similar multi-host modeling approach examined the potential threat to wildlife from a pathogen harbored by a domesticated species (Foufopoulos et al. 2002). In this case, the shared pathogen had greater negative impacts on wild hosts when the domesticated animals were more abundant and when the total infectious period was greater (because animals could transmit disease for a longer period of time).

As reviewed in Chapter 4, researchers have developed multiple-host models for wildlife diseases, asking questions such as, "under what conditions can parasites generate 'apparent competition' between host species?" and "what role does host species diversity play in pathogen persistence?" (Begon et al. 1999; Gilbert et al. 2001; McCallum and Dobson 2002; Holt et al. 2003; Dobson 2004; Gandon 2004; Power and Mitchell 2004). From a management perspective, these models can inform intervention decisions when pathogens threaten wildlife through cross-species transmission, including whether control efforts should concentrate on threatened hosts or on the reservoir populations (Woodroffe 1999).

Our close phylogenetic relationship to wild primates, and especially apes, means that humans are likely to be an important reservoir host for wild primates (Wolfe et al. 1998; Wallis and Lee 1999; Tutin 2000; Chapman et al. 2005a). It has long been

known that nonhuman primates are susceptible to a wide range of human diseases (Kalter 1972a; Brack 1987; Chapman et al. 2005a), as evidenced by the widespread use of nonhuman primates as human models in biomedical research and the spread of pathogens between primates and humans. A recent survey found that nearly 25% of all micro- and macroparasites reported from free-living primate species were also reported to infect humans (119 out of 415 primate parasites, Pedersen et al. 2005).

Several prominent examples of infections that cross the boundaries between humans and wild primates are found in areas where human–primate contacts are common (Fig. 7.8). *Schistosoma mansoni* infections are frequently reported among baboon troops at Gombe, where animals commonly encounter humans (Müller-Graf et al. 1997; Murray et al. 2000). Similarly, a comparison of baboon populations at Gombe and Mt Assirik in Senegal showed higher levels of intestinal parasites at Gombe (McGrew et al. 1989a). In other populations, wild baboons likely contracted tuberculosis multiple times through contact with humans and domesticated animals (Tarara et al. 1985; Sapolsky and Else 1987; Keet et al. 1996; 2000). Gorillas in the Virunga Mountains are increasingly exposed to infectious material from humans, including food remains, fecal contamination, and even human corpses in the area around Karisoke; indeed, a measles outbreak in the area caused the death of six female gorillas before a vaccination program was implemented (Steklis et al. 1996/1997; Mudikikwa et al. 2001). Stuart et al. (1990) found evidence for infection with the human roundworm (*Ascaris lumbricoides*) in one howler monkey that lived in close proximity to humans, and an epidemic of paralysis in chimpanzees at Gombe might have been acquired from close contact with nearby humans infected with the polio virus (Goodall 1986; Wallis and Lee 1999).

Primates living in close proximity to humans have been observed to forage in garbage dumps, and this could expose them to infected meat or human fecal matter

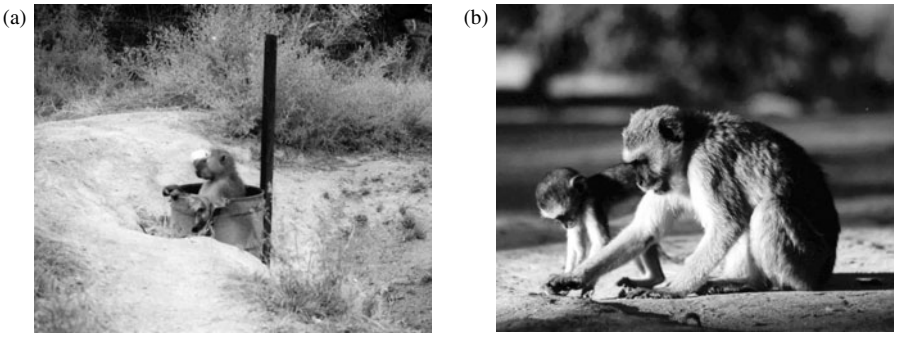


Fig. 7.8 Primates foraging near human settlements could be exposed to a number of zoonotic pathogens. (a) A male chacma baboon (*Papio ursinus*) emerging from a gargage can. This individual was observed eating waste material from inside the can. (b) Vervet monkeys (*Cercopithecus aethiops*) foraging near human dwellings. In many places throughout Africa, vervet monkeys and baboons live near tourist campus and forage at human waste dumps or by taking food directly from tourists. Images courtesy of D. Kitchen, The Ohio State University.

(e.g. Fig. 7.8(a)). Evidence is mixed as to whether using human garbage increases disease risk in these populations. In a study of the baboons at Amboseli, Hahn et al. (2003) found no evidence that one social group that forages daily in human garbage pits acquired parasites that exhibit high prevalence in local human populations, including roundworm infections. Similarly, Eley et al. (1989) did not find increased risk of acquiring gut parasites from foraging in garbage dumps. Other studies, however, have documented costs to baboons from foraging in human garbage dumps, including infection with antibiotic-resistant bacteria probably acquired from humans (Rolland et al. 1985; cf. Routman et al. 1985), infection with tuberculosis from eating contaminated meat (Keet et al. 2000; Sapolsky and Share 2004), and greater incidence of cavities and periodontal diseases (Phillips-Conroy et al. 1993).

This partial list of examples reveals the tremendous potential for transmission events from humans and domesticated animals to cause new infections in wild primate populations. These examples also point out that primate behavior itself can influence patterns of contact with humans. For instance, crop raiding by monkeys probably results in exposure to human wastes and increased contact with other crop-raiders, such as wild pigs or heterospecific primates. Some primates have been identified as pests or "weed species" that depend on and compete with humans, resulting in regular contact with humans and domesticated animals in the "urban matrix" (Richard et al. 1989; Cowlishaw and Dunbar 2000) and thereby provide more opportunities for disease spread to humans and domesticated animals (Jones 1982). These "weedy" primates include macaques, especially rhesus and bonnet macaques (*Macaca radiata*), some species of baboons, and Hanuman langurs (*Presbytis entellus*).

As human populations continue to expand, contact with wildlife, including nonhuman primates, is likely to increase (e.g. Cleaveland et al. 2002). Through habitat fragmentation, primates will encounter humans living in the surrounding habitat, while ecotourism and biological field research provide opportunities for pathogen "spillover" from international travelers that collectively carry a wide diversity of infectious diseases. Road-building increases the flow of humans into forests to extract resources or hunt primates, and political instability often leads to human migration, intensifying pressure on remaining forest fragments and increasing the probability of parasite transfer between humans, domesticated species, and wild primates.

In the future, it will be important to develop genetic approaches to determine whether cases of cross-species infection between humans and nonhuman primates have occurred. Thus, a number of studies that point to parasite transmission between humans and other primates are based on characteristics of parasite eggs (Muriuki et al. 1998; Jones-Engel et al. 2004; Legesse and Erko 2004), but combined genetic and morphological analysis are needed to determine whether or not parasites recovered from the dung of different host species are genetically indistinguishable. For example, recent genetic analyses have shown that *Oesophagostomum bifurcum* infections in human populations in Ghana were genetically distinct from those recovered from nonhuman primates in overlapping areas, suggesting that transmission is largely restricted to within single host species (De Gruijter et al. 2004, 2005).

7.3 Disease risk and anthropogenic change

It is well known that changes in pathogen incidence can result from natural processes, such as seasonal and longer-term climatic cycles and range expansions of hosts. In the present day, however, evidence for a human role in causing disease outbreaks has increased substantially, not only because humans directly introduce novel pathogens into wild host populations, but also because human activities alter environmental parameters in ways that increase the probability of disease emergence (Schrag and Wiener 1995; Holmes 1996; Daszak et al. 2000; Chapman et al. 2005a). Mechanisms such as habitat loss and climate warming can directly influence patterns of biodiversity, but little is known about their indirect consequences for host–pathogen dynamics.

In this section we explore how anthropogenic change could influence infectious disease risk in wild primates through habitat destruction and degradation, reductions in host population size, and human impacts on parasite biology. It is important to note that many of these ideas regarding anthropogenic drivers of infectious disease risk are based on theoretical models or speculation, supported in some cases by anecdotal evidence, but usually not investigated by quantitative field experiments or long-term monitoring. For example, most of what we know about habitat fragmentation and the mechanisms by which it influences disease risk in a metapopulation context is almost completely based on mathematical models, with only a few studies investigating how increased logging and fragmentation affects patterns of parasitism (Chapman et al. 2005a, c; Gillespie et al. 2005). Increased monitoring and field data are badly needed to evaluate the mechanisms by which human activity changes the dynamics of primate–parasite interactions.

7.3.1 Habitat destruction and degradation

Without question, disturbed and fragmented habitats lower the viability of primate populations in tropical forests (Cowlishaw and Dunbar 2000; Chapman and Peres 2001; Mittermeier et al. 2002). Land developed for agriculture in the tropics has overrun forested areas, and expanding human populations cause widespread habitat degradation as humans extract resources from forest fragments and introduce waste products and pollution. Because many tropical primates rely on forests for food and shelter, the destruction of rainforest generates dire consequences for many of these species (Cowlishaw and Dunbar 2000).

Habitat loss can also change the behavior and abundance of wildlife in ways that influence parasite spread, and human activities that crowd and subdivide populations should influence patterns of disease risk and host susceptibility (Chapman et al. 2005a, b, c). In the early stages of habitat destruction, the number of fragments increases and their size decreases (Fig. 7.9; Bascompte and Solé 1996), and this can result in both positive and negative outcomes for infectious disease risk. Positively, subdividing populations could slow epidemics in the same way that social clumping reduces the spread of disease at the population level (Watve and Jog 1997; Wilson et al. 2003), and smaller host populations within fragments might support fewer

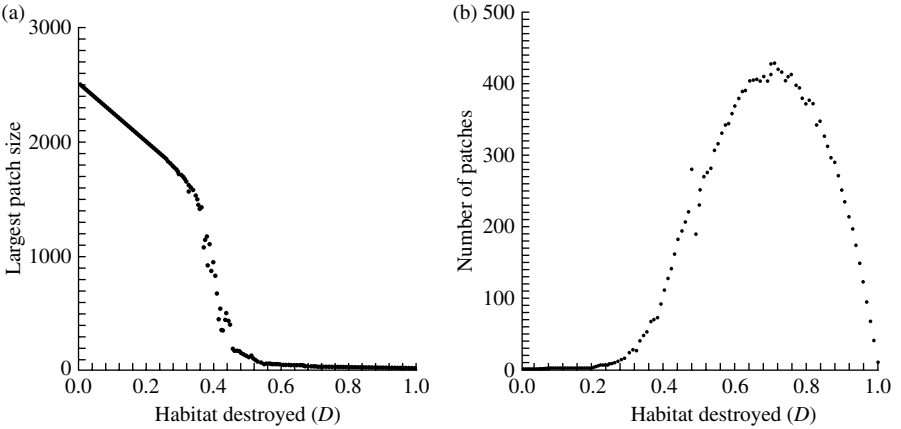


Fig. 7.9 Relationship between habitat destruction, patch size, and number of patches. Plots come from a spatially-explicit computer simulation model of random patches lost from a continuous habitat. As more patches are lost, the patch size declines, and the number of patches increases. Figures from Bascompte, J. and R. V. Solé, 1996. Habitat fragmentation and extinction thresholds in spatially explicit models. *Journal of Animal Ecology*, 65, 465–473. Reproduced with permission from Blackwell Scientific.

parasite species in those fragments. On the negative side, habitat fragmentation increases edge effects (Cowlishaw and Dunbar 2000), potentially exposing hosts to novel pathogens (see below). Indeed, a recent field study of two African colobines found that individuals on edges of forest fragments were more likely to be infected with multiple species of gut parasites, as compared with monkeys in the interior of these fragments (Chapman et al. 2005c). As habitat is destroyed and animals are displaced from their home ranges, they might crowd into the remaining habitat, resulting in increased population density (Diamond 1975), which could enhance the spread of directly transmitted parasites (Chapter 4). Over the longer term, densities decline in these fragments, either because the populations are not sustainable, or because individuals move to other habitats (Rylands and Keuroghlian 1988; Medley 1993).

By limiting pathways for travel and foraging, habitat loss further displaces primates and forces them into remaining forest, often concentrating animals into smaller areas of suitable habitat. More intense habitat use can cause build-up of fecal contaminants in the environment, leading to re-infection and greater parasite burdens (Chapter 3). For example, Stoner (1996) proposed that more intensive home range use (as might occur in shrinking habitats) could increase the risk of re-infection in the mantled howler monkeys that she studied. Among red-tailed guenons (*Cercopithecus ascanius*) in Uganda, Gillespie et al. (2005) showed that the number of intestinal parasites, including a debilitating nematode (*Oesophagostomum*), were higher among fecal samples from logged forests relative to undisturbed forest tracts. This pattern

could have resulted from several processes, including the effects of dietary stress on susceptibility to parasitism. From a different perspective, isolated populations characterized by small size and low inter-patch dispersal may ultimately lose all traces of an "immune class" of previously exposed animals. Ironically, this loss of new infections, and related loss of animals exposed to acute infections, creates a situation which would favor "virgin ground epidemics" when pathogens are reintroduced.

Crowding animals into smaller patches of habitat elevates stress levels and thereby can negatively impact immunocompetence, lowering resistance to infection and potentially intensifying the severity of disease (Coe 1993; Lyles and Dobson 1993; Lloyd 1995; Capitanio and Lerche 1998; Friedman and Lawrence 2002). This effect was highlighted in a recent comparative study of captive carnivores, in which carnivore species with the largest home ranges in the wild exhibited more stress-related behaviors, such as stereotypic pacing, when confined in captivity (Clubb and Mason 2003). Pollution and resource extraction as causes of habitat degradation could serve as additional sources of stress for wildlife. Crowding also increases rates of aggression, which has been shown to contribute to the spread of disease. In a semi-captive colony of mandrills, for example, researchers documented that simian immunodeficiency virus (SIV) spreads predominantly through male–male aggression (Nerrienet et al. 1998), whereas its spread through sexual transmission is probably more common in free-living populations (Phillips-Conroy et al. 1994).

7.3.2 Reductions in host population size

Declining population sizes are one major outcome of habitat loss, hunting, and other anthropogenic changes, particularly for rainforest animals such as primates that are sensitive to the destruction of primary habitat. Reductions in population size can further increase the risk of stochastic factors that drive populations toward extinction (Lyles and Dobson 1993; Dobson 1999). Of course, the introduction of a new pathogen threat itself can be a "random event" that pushes already depleted populations below a recovery threshold (Lafferty and Gerber 2002). Moreover, deaths caused by habitat loss (or any other process for that matter) can lead to social disruptions, with the magnitude of the effects depending on the social and mating system. For example, loss of males in a polygynous system could lead to greater movement of females among groups at the population level (see Fig. 4.10 and Box 7.1).

Small populations should harbor lower genetic diversity (Frankel and Soule 1981), and several examples point to the role of host genetic diversity in buffering populations against widespread epidemics (reviewed in Altizer et al. 2003a). Thus, inbred host populations will likely show limited ability to respond evolutionarily to new threats imposed by parasites and infectious diseases due to loss of allelic diversity or reduced heterozygosity. Although examples of disease-related problems arising from genetic bottlenecks are generally missing for primate systems, inbreeding in species such as lions and cheetahs has been linked with mortality caused by *Spirometra, Mycobacterium*, and a coronavirus (Heeney et al. 1990; Caro and Laurenson 1994; Müller-Graf et al. 1999). Evidence from California sea lions

showed that more inbred animals (as determined using microsatellite markers) were more likely to harbor helminth and bacterial infections, and were also more frequently afflicted by carcinoma linked with herpesvirus infection (Acevedo-Whitehouse et al. 2003).

It is also important to keep in mind that epidemics involving highly pathogenic diseases could themselves reduce genetic diversity and hence limit the ability of that host to respond to future outbreaks of disease (O'Brien and Evermann 1988). Thus, James et al. (1997) found a low level of genetic diversity in a population of black howler monkeys (*Alouatta pigra*) in Belize and proposed that past population bottlenecks from disease and natural disturbances (hurricanes) accounted for this low diversity. Similarly, low levels of polymorphism were found in several MHC Class I genes sequenced from wild and captive chimpanzees (de Groot et al. 2002). Because molecular evidence showed that this loss of variability did not affect other gene systems, the authors hypothesized that a selective sweep in the distant past coincided with a widespread pandemic caused by the original exposure to SIVcpz or a related retrovirus, much like the current emergence of the HIV pandemic in humans.

In addition to concerns regarding genetic diversity, smaller host populations should tend to support fewer species of parasites (Morand 2000); thus, threatened species might have fewer parasites simply because they cannot reach the threshold population size needed for some parasites to establish (Lyles and Dobson 1993). This effect should be most pronounced for directly transmitted parasites with narrow host ranges, as these parasites might depend most strongly on large populations for their maintenance in hosts. One comparative analysis provided evidence that host threat status correlates with parasitism using a dataset of 119 primates: host species classified as vulnerable, threatened, or endangered based on the IUCN Red List (Hilton-Taylor 2002) harbored fewer species of parasites than those listed as non-threatened (Altizer, S., C. Nunn and P. Lindenfors unpublished data). Counter to expectations, however, there was no indication that any single type of parasite, such as specialists or those transmitted by direct contact, was more likely to be missing from threatened primate species (Fig. 7.10).

When hosts go extinct, so do numerous host-specific parasites (Durden and Keirans 1996; Gompper and Williams 1998). An important question in a conservation context concerns whether the loss of parasites is beneficial or harmful to host populations. Put differently, would it be desirable to eliminate all naturally occurring parasites? One could argue that it is best to preserve intact communities that include predators and prey, competitors, and hosts and their parasites, thus leaving coevolutionary processes intact. This is especially true for host–parasite systems, as resistance-conferring host traits might be costly in terms of reducing other fitness components (reviewed in Altizer et al. 2003a). Hosts bred in captivity and protected from pathogenic agents may therefore experience increased susceptibility caused by relaxed selection and costs associated with immune defense (Lyles and Dobson 1993). Under this scenario, if pathogens are removed or lost from wild or captive hosts, resistance could decline over evolutionary time scales, potentially setting the stage for severe outbreaks in vulnerable hosts.

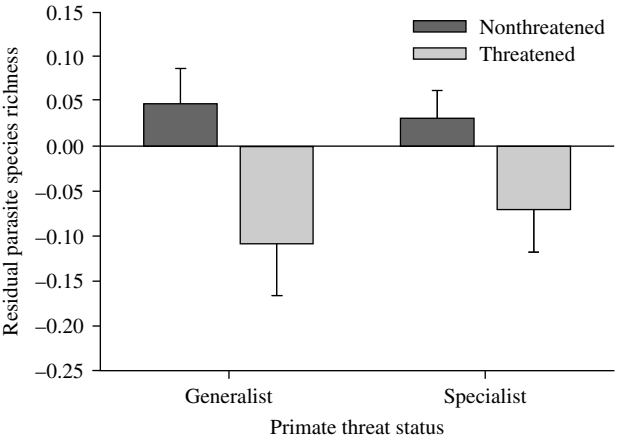


Fig. 7.10 Parasite diversity for generalist and specialist parasites in threatened (N = 36) and non-threatened (N = 83) primate species. Vertical axis represents least-squares residuals from the regression of parasite counts on sampling effort, and error bars indicate standard errors. From Altizer, S., C. Nunn, and P. Lindenfors, unpublished data.

7.3.3 Human impacts on parasite biology

In addition to affecting the biology of hosts, anthropogenic factors can also influence the development and survival of parasites (Altizer et al. 2001). Evidence from diverse parasite systems highlights the importance of human-induced climate change on parasite distributions and the behavior and ecology of vectors (Walther and Morand 1998; Harvell et al. 2002). Consider, for example, the effect of climate change on the distributions of biting arthropods that spread parasites to mammalian hosts. Rising temperatures and increased rainfall could increase vector abundance through greater reproduction or lower mortality rates, facilitating their expansion into new geographic regions (Dobson and Carper 1992); logging and other environmental impacts can increase mosquito abundance and shift the composition of mosquito communities and the pathogens they carry (Patz et al. 2000). Importantly, these alterations are unlikely to cause negative impacts in all host species at all localities, with some areas experiencing declines in risks from malaria. Multiple vector-borne pathogens of humans and wildlife recently have shifted their geographic ranges into higher latitudes and altitudes, probably due to the inter-related effects of human activity and climate change (Gratz 1999; Mellor et al. 2000), but closer monitoring will be required to understand the factors that lead to increased disease risk and whether this is a widespread outcome of climate change (Hay et al. 2002; Rogers et al. 2002).

In terrestrial systems, most attention related to environmental impacts on the distribution of disease has focused on vector-borne diseases, such as malaria, yellow fever, and dengue hemorrhagic fever. The focus on this group of pathogens may be

justified, given that many vector-borne parasites are highly pathogenic in human hosts (Ewald 1983). Moreover, many of the biodiversity hotspots where primates are in danger of extinction lie near the equator, such as the Atlantic coastal forest of Brazil (Myers et al. 2000). Given that the distribution of vectors is tightly linked to climatic variables involving rainfall, temperature, and humidity (Patz et al. 2000), latitude is likely to be an important factor influencing the distribution of disease risk. Thus, a recent study of human infectious diseases found a strong association between parasite diversity and latitude, driven by climatic variables involving precipitation and temperature (Guernier et al. 2004). Across species of nonhuman primates, Nunn et al. (2005) found that the diversity of vector-borne protozoa increases closer to the equator (see Fig. 3.14). Associations between climate, latitude, and vector-borne protozoa are pertinent to primate conservation, as these parasites have been documented in several threatened primate species (e.g. *Brachyteles arachnoides, Pan troglodytes*, Garnham 1966; Deane et al. 1969; Coatney et al. 1971).

Diarrheal diseases that spread through contaminated water, such as human cholera, could also respond to weather and rainfall patterns (Harvell et al. 2002). Many waterborne bacteria, for example *Leptospira* and *Shigella*, also occur in nonhuman primates (Minette 1966; Karesh et al. 1998; Kilbourn et al. 1998). Increased rainfall and humidity will plausibly produce some benefits for tropical primates, but could also increase the development rates of bacteria, protozoa, and helminths in the environment, resulting in greater transmission of these pathogens (McMichael et al. 2003). Similarly, these effects could improve conditions for reservoir hosts. For example, greater rainfall could increase rodent population density through resource augmentation, possibly leading to higher prevalence of infection and increasing the potential for cross-species transmission.

Schistosomiasis represents another parasitic disease relevant to primate conservation in the context of human-induced environmental change (Martens et al. 1995, 1997; Patz et al. 2000; Morgan et al. 2001). Reproduction and survival of this parasite in the environment, and the geographic range of snail intermediate hosts, depends on patterns of temperature and rainfall. Even Ebola outbreaks have been suggested to exhibit seasonal patterns in relation to temperature and rainfall, although associations with climate change have not been made explicit. Thus, Boesch and Boesch-Achermann (2000) suggested that Ebola outbreaks in Tai Forest occur more commonly during years with more dry months, as drier conditions might increase the density of the reservoir host that carries the infection naturally. Similar evidence from human cases corroborates this seasonal effect of outbreaks occurring during drier conditions at the end of the rainy season (Pinzon et al. 2004).

In summary, human impacts on parasite biology, particularly via climate change, pose increasing concerns for human health (McMichael et al. 2003) and should influence disease dynamics in nonhuman primates (Chapman et al. 2005a). This is particularly true for parasites transmitted by arthropod vectors, through contaminated water, or by stages that persist outside of their vertebrate hosts. Although the bulk of evidence cited here (and in several recent reviews) points to human-driven environmental changes as increasing the severity of pathogen-related threats (e.g. Harvell et al. 1999;

Patz 2002), it is important to keep in mind that climate warming and other components of global change could also reduce the risks from some pathogens and release their hosts from parasite pressure. Increased monitoring and comprehensive analyses that examine the mechanistic links between climate and disease risk are greatly needed to improve our ability to predict future risks to both humans and biodiversity, including better understanding of the diseases that are lost when climate changes.

7.4 Conservation efforts in response to infectious disease risk

Although infectious diseases can contribute to host population declines and push small populations closer to extinction, conservation managers often lack the information and tools needed to respond rapidly to disease risks in threatened species. Management strategies could be designed to mitigate the introduction of novel pathogens, to maintain genetic diversity, or to directly intervene to protect wildlife populations when necessary. Conservation planning strategies aimed at minimizing disease threats to nonhuman primates might focus on reserve design, maintaining wildlife corridors, captive breeding efforts, minimizing risks associated with ecotourism and scientific field research, and specific intervention strategies to limit the impact of parasites on threatened populations.

7.4.1 Monitoring parasites in wild populations

How much do we know about the occurrence and prevalence of primate parasites? At the present time, such data are rarely collected and published unless there is a direct implication for human health, livestock production, or other economically important activities (Cleaveland et al. 2002). With respect to wild primates, many studies have probed populations for pathogens that directly impact human health, such as arboviruses, retroviruses, malaria parasites, and schistosome infections (see Chapter 3). A smaller number of studies provide more exhaustive surveys of particular types of parasites (e.g. intestinal helminths) from single host species (e.g. Kuntz and Myers 1966; Myers and Kuntz 1967). Some of the best-studied primates with respect to parasites in the wild are baboons, chimpanzees, gorillas, and some macaques. Indeed, an online database for parasite reports from nonhuman primates (www.mammalparasites.org, Nunn and Altizer 2005) indicates that in some cases 50 or more different species of micro- and macroparasites have been reported from natural populations of a few primate host species, with over 400 parasite species in total reported across all wild primates. Despite these seemingly large numbers, data on parasites from wild primates lag far behind knowledge of parasites in domesticated animals and humans. For example, over 900 parasites have been reported to infect just seven species of domesticated animals (Cleaveland et al. 2001), and over 1400 parasites have been reported in humans (Taylor et al. 2001). This could indicate that humans and their domesticated animals harbor more parasite species than wildlife,

but also underscores that we have identified only a fraction of all parasite species that infect wild animals.

How is parasite surveillance best accomplished in threatened species like primates? As highlighted in Chapter 4, data can come from multiple sources, including noninvasive sampling of wild individuals, such as fecal sampling, which is already commonly used to assay hormones (Whitten et al. 1998; Hodges and Heistermann 2003). Blood, skin, or other samples could be taken from dead animals or from animals immobilized for other purposes, including for individual identification, vaccination, or treatment of existing health problems. Because of their close relationship to humans, primates have been used extensively in biomedical research (including studies of infectious disease), and up until recently, large numbers of primates were harvested from the wild for biomedical research (see Box 2.1). Some of these recently captured animals were examined for parasites prior to export to research laboratories, accounting for the high representation of baboons, macaques, and vervet monkeys in comparative data on primate parasites. More complete sampling of primates and other animals killed for food consumption (bushmeat) could provide critical information on pathogens found naturally in wild populations, as well as revealing the full spectrum of disease threats to humans from butchering and consuming wild primates (Hahn et al. 2000; Peeters et al. 2002; Wolfe et al. 2004).

At the present time, disease outbreaks are almost certainly poorly documented or remain unpublished, and even published data are not always rapidly accessible to the broader scientific community. Effective use of the knowledge gained from field studies further requires a storehouse of information that can be readily accessed by veterinarians, wildlife managers, zoo keepers, ecologists, and primatologists. Thus, a central repository is needed to aggregate data from historical surveys of parasite occurrence, museum collections for major parasite taxonomic groups, serological surveys of prevalence, and unpublished field records maintained by primate biologists. Several online databases currently exist that provide presence/absence data for different host–parasite species combinations (e.g. the *Host–Parasite Database* of the Natural History Museum, London, used by Vitone et al. 2004, and the *Global Mammal Parasite Database*, see Nunn and Altizer 2005).

Screening programs can provide information on the presence of particular pathogens in natural primate systems, but prevalence data alone cannot indicate population-level threats. Similarly, measures of pathogenicity or impacts on individual host fitness must be interpreted with caution. As described in Chapter 4, parasites with relatively low or moderate virulence can have surprisingly large impacts on host population size because infected hosts live long enough to transmit the parasites (Fig. 4.7; Anderson and May 1979; Anderson 1982b; McCallum 1994). In fact, infectious diseases with relatively small (but measurable) effects on host survival—and especially those that reduce host fecundity—may cause far greater conservation concerns and should not be overlooked when assessing potential threats to populations. Baseline studies of the occurrence and epidemiology of pathogens on wild animal hosts can also allow researchers to gain an understanding of how parasites are transmitted and to identify potential reservoirs within the target population and in peripheral regions (Salman 2003; Rouquet et al. 2005).

7.4.2 Reserve design and management

In the face of devastating habitat loss in the tropics, the most threatened primate species require aggressive protection of remaining patches (Cowlishaw and Dunbar 2000). Many factors go into designing reserves to protect threatened primates from poaching, environmental pollution, expanding human populations, and political instability, but infectious disease is less commonly considered among the suite of factors that threaten wild animals (Ballou 1993; Lyles and Dobson 1993; Woodroffe 1999). Examples of Ebola in apes, canine distemper in lions, and tuberculosis in baboons suggest that infectious disease should receive greater attention in conservation efforts. Disease processes relevant to reserve design include dispersal of infected animals between social groups or populations, changes in population densities of hosts in protected areas, and exposure to novel parasites through habitat use and inter-species contact.

Metapopulation models reveal that host dispersal among patches can be effective in reducing the extinction of populations and maintaining within-population genetic variation, and this modeling approach can play a critical role in conservation planning (Hanski and Simberloff 1997). Specifically, the metapopulation framework suggests that in sub-divided populations, migration of individuals between subpopulations can act as a buffer against stochastic and external factors that increase extinction risk. On the other hand, movement of infected hosts among subpopulations could also increase the spread of disease (Frankel and Soule 1981; Simberloff et al. 1992), and recent attention has focused on whether the costs of corridors connecting habitat patches outweigh the benefits (Hess 1996; Hess et al. 2002). Consistent with this finding, Ballou (1993) stated, "Perhaps the best strategy for reducing the probability of a single epidemic causing the extinction of an entire population is to locate subpopulations in geographically distinct areas" (p. 332). Such a strategy is implemented in some primate populations, although sometimes parasite risk reduction is an incidental benefit of habitat fragmentation. For example, in the Kahuzi-Biega National Park, the gorilla groups visited by tourists have been isolated from the rest of the population not intentionally, but through the effects of habitat destruction (Butynski and Kalina 1998). Thus, any outbreaks of disease in the populations visited by tourists would be less likely to spread to the larger population through natural host dispersal. Implementing "quarantines" is of course well known in human history and an active component of public health strategies to contain epidemics, including SARS in humans and foot and mouth disease in livestock. Installing fences, creating habitat breaks, or even active measures to drive animals away from foci of infection have been used to change patterns of animal movement and contain wildlife disease epidemics (Wobeser 2002a).

From simulations based on the spread of infectious disease in different spatial configurations of sub-populations, Hess (1996) found that some arrangements of populations could increase the spread of infections, and that quarantine can be an effective strategy in preventing the establishment of an infectious agent. However, several factors not considered in the model call for a more balanced view (McCallum

and Dobson 2002). This model was based on two classes of individuals, susceptible and infected hosts, without the possibility for recovery or immunity among infected individuals (an S-I model) and with no underlying variation in host resistance. These assumptions may not apply to viruses or other microparasites that induce lasting immunity among recovered hosts. The movement of animals between patches could also confer genetic benefits (e.g. increased movement of resistance alleles), even if humans physically transport individuals between patches (e.g. in black lion tamarins, *Leontopithecus chrysopygus*, Valladares-Padua et al. 2002). In more recent models that incorporated genetic processes (particularly with respect to resistance evolution), the benefits of developing corridors and other connections among populations outweighed the risks of disease spread (Carlsson-Graner and Thrall 2002; McCallum and Dobson 2002). That being said, under some conditions, the presence of a generalist infectious disease in a reservoir host can drive the threatened species to extinction in any configuration of habitat patches.

Creation of habitat "quarantines" will be most effective when paired with a deep understanding of how the pathogen spreads from host to host. The case of Ebola in African apes provides a striking example. Walsh et al. (2003b) described the epidemic as "gradually working its way south and west" (p. 613, actually should be east rather than west, P. Walsh, personal communication), based on geographical patterns suggesting that it was an epidemic moving through populations of gorillas (see also Walsh et al. 2005). Ebola could move between gorilla groups during direct interactions between groups, when females transfer due to the death of the male, and when individuals from different groups come into contact with gorilla carcasses or infectious stages of the virus in the soil, particularly around food resources (Walsh et al. unpublished manuscript). Leroy et al. (2004a) suggested that Ebola outbreaks in mammals are characterized by multiple strains of the pathogen, consistent with the hypothesis that Ebola outbreaks are driven mainly by transmission from an as-yet unknown reservoir and less by ape-to-ape transmission (see also Rouquet et al. 2005). Walsh et al. (2003b) also urged additional research on possible reservoirs, with the observed wave-like spread possibly occurring in the reservoir or through movements of the reservoir (see Walsh et al. 2005). The implications for control strategies may be profound if, for example, large expenditures of effort focused on halting the contact among individual apes failed to stop the spread of infections because animals continued to acquire new infections from reservoir hosts (see also Karesh and Chapman 2005). Indeed, a recent study found evidence that fruit bats harbor the virus (Leroy et al. 2005).

Ironically, reserves created to protect animals from habitat loss and poaching could carry costs of increased disease risk, in part because these reserves may maintain populations at higher densities, especially in the absence of top carnivores or hunting by humans. Crowding animals at higher densities could increase contact among hosts and facilitate the spread of disease. Park staff and tourists may inadvertently introduce infections into the reserve population, and mixing of host species not normally present in the same areas could increase opportunities for transmission of new infectious diseases. Corridors that facilitate movement between populations could represent poorer-quality habitats and might also expose animals to parasites

from domesticated animals, humans, and other wildlife species that also use the corridors. Thus, based on a study of mantled howler monkeys, Stoner (1996) recommended widening corridors and providing a greater diversity of arboreal pathways to reduce the risk of infection (or re-infection).

Based on these examples, a number of important tradeoffs exist when designing reserves in light of ways to reduce and control disease outbreaks. In this context, quarantines in continuous tropical forests will be more effective *between* reserves than *within* them, arguing for maintenance of threatened species in more than one spatially independent reserve (Frankel and Soule 1981). Reserve design requires that we improve our understanding of how edge effects, logging, and fragmentation impact patterns of parasitism (Gillespie et al. 2005; Chapman et al. 2005b, c). Animals in the surrounding areas should be fully evaluated for sources of infection, and appropriate buffers around reserves should be constructed to reduce the risk of pathogen transmission from animals that inhabit the edge areas or intervening matrix among reserves. Because many infections in wildlife involve a reservoir host, which in the case of nonhuman primates could be through contact with humans, it is also essential to consider the implications of reserve design for encounters with infectious agents in humans and domesticated animal populations.

7.4.3 Captive breeding and semi-free-ranging populations

In many cases, reserve design and implementation comes too late to save a species, or political instability disrupts protection of habitat critical for conservation of threatened species. In such cases, captive breeding (and restocking wild populations with captive-bred individuals) may be the last option to save a species from extinction. A variety of infectious disease issues arise in the context of captive breeding and management of mammals, with specifics depending on whether these facilities are zoological parks, breeding facilities, or free-ranging populations.

Surveillance and control of infectious disease should be an important component of captive management programs (Mikota and Aguilar 1996; Ryan and Thompson 2001), although not all captive or semi-free-ranging settings are breeding grounds for infectious disease, especially when veterinary and preventative care is readily available (Paul and Kuester 1988). Specific infectious disease threats in captive primates encompass many pathogens that can be transmitted between wild primates and humans, including tuberculosis, herpesviruses, hepatitis A infections, and a variety of pathogenic gut bacteria such as *Shigella* (Prier et al. 1964; Good 1984; Brack 1987; Brown 1997). Infectious diseases are likely to be a greater problem when animals are housed in close quarters and when contact occurs among different species. Captive primates, especially those exposed to outdoor settings, can also contact rodents or insects that serve as sources of infection (e.g. cockroaches, Brack 1996).

Understanding the transmission mode of different parasites is fundamental for controlling infectious diseases in managed semi-free populations—as a simple example, vector-borne diseases will be very difficult to eliminate without controlling the vectors! Technically, it should be easy to control parasites in captive animals by actively screening for parasites, separating young animals from adults at an early age to

prevent the spread of infections across generations, and administering anti-parasitic drugs (e.g. in bison, Nishi et al. 2002). Nevertheless, it is important to consider that long-term breeding of animals in the absence of their native parasite communities could lead to loss of resistance among captive individuals, limiting the ability of these animals to deal with new infections if released back into the wild.

A major risk is that the release of captive-bred animals will introduce new parasites into wild populations (Ballou 1993; Woodford and Rossiter 1994; Cunningham 1996; Wobeser 2002a). For example, a planned release of rehabilitated orangutans into Indonesia was aborted when human tuberculosis was discovered among them, potentially averting a major catastrophe if the disease had been introduced to the wild populations through release of infected animals (Jones 1982).

Many primate conservation programs involve translocations (e.g. Kleiman et al. 1986; Loftin 1995), defined as, "the movement of living organisms from one area with free release in another" (p. 1, International Union for Conservation 1987). The goals of translocations are to breed primates in captivity and release them in suitable habitat (introductions or re-introductions), or to transport animals from one area to another to increase the number of individuals in original habitat (re-stocking). Many primate translocations are actually rescues, implemented when habitat destruction is likely to lead to population extinction (e.g. Vie and Richard-Hansen 1997). These movements can be stressful for animals during and after transfer to a new range (Berman and Li 2002), potentially increasing their chances of developing infections. Parasites can be introduced to target populations along with the hosts, but the consequences can be different for parasites acquired in captivity, which may not be natural to the host, versus those that occur in wild populations.

A number of studies have discussed the elements of successful propagation of threatened species in captivity, often with an eye toward release in the wild (Conway 1980; Mikota and Aguilar 1996). The role of parasites in reintroduction and translocation programs is receiving greater attention in primates and other animals (Ballou 1993; Lyles and Dobson 1993; Stuart et al. 1993; Wolff and Seal 1993; Woodford and Rossiter 1994; Cunningham 1996; Mikota and Aguilar 1996). Specific recommendations to reduce disease risk include extensive parasite screening to identify infections in captive and wild animals, administering drugs to eliminate infections, vaccinating animals to prevent future infections, quarantining animals of uncertain infection status for at least 30 days, marking animals for identification after release, developing procedures to recapture released animals should disease or injury occur, and maintaining genetic diversity for successful immune defense. In the case of primates, human handlers at both donor and release sites should be screened for diseases transmissible to nonhuman primates, such as tuberculosis and a range of viral infections.

Infectious disease was an issue in the captive management and release of golden lion tamarins in Brazil, which included a 6-month quarantine (Kleiman et al. 1986). The concern over disease was justified because an infectious agent killed five animals following release, although the origin and identification of the parasite remains unknown (Kleiman et al. 1986). Similarly, screwworm larvae (*Cochliomyia hominivorax*)

became established under identification collars of several animals translocated during the building of a hydroelectric dam, leading to the deaths of three monkeys (Vie and Richard-Hansen 1997). As a third example, Kilbourn et al. (2003) performed parasitological surveys on orangutans involved in a translocation effort by comparing free-ranging with semi-captive animals at a rehabilitation center in Malaysia on the edge of a protected reserve. While some parasites were found in both categories of orangutans, differences also existed that probably reflected higher densities and more common contact with humans among the rehabilitated animals.

Researchers involved in a release of captive-born ruffed lemurs (*Varecia variegata*) in Madagascar took extraordinary (and exemplary!) steps to avoid introducing infectious disease to the natural populations of lemurs. In selecting individuals from the captive stock to be released in the wild, Britt et al. (2004) first conducted veterinary exams that tested for a wide array of viral, bacterial, helminthic, and protozoan parasites, as well as assessing overall health of individuals. These tests resulted in the rejection of some lemurs from the program due to infections with *Salmonella* and *Toxoplasma*. In addition to sampling parasites in the populations and facilities where potential release candidates were held, the authors also investigated the incidence of pathogens in the areas where the lemurs were to be released in Madagascar. Prior to release, the animals were held in quarantine for two weeks in the United States and 3 to 4 weeks in Madagascar, anti-parasitic drugs were administered during quarantine, and sampling for parasites continued after animals were released into the wild.

Behavior plays an important role in release programs, as animals should be allowed to range in a semi-free setting that provides experience in the use of substrates and foraging techniques needed for survival at the release site (e.g. see discussion of these issues in Kleiman et al. 1986; Beck 1995; Beck et al. 2002). For example, Britt et al. (2004) provided a "boot camp" for the captive ruffed lemurs to learn to use natural forest prior to release (see also Britt et al. 2003). This component of the release program also provided opportunities to train the animals for regular capture once the animals were released in the wild, for example to provide medical treatment if an animal became injured or diseased. Major risks from these training regimes are that animals can be exposed to novel parasites and transport them into wild populations (Woodford and Rossiter 1994), and habituated animals are more likely to contact humans once released, potentially increasing predation risk and contact with parasites from humans and domesticated animals. Moreover, through the lack of exposure to parasites, animals may fail to respond effectively—both behaviorally and immunologically—to parasite infection following release.

Genetic diversity is an important consideration in the management and breeding of captive populations (Seal 1986), in large part because genetic variation is important in the context of disease resistance (O'Brien et al. 1985; Lyles and Dobson 1993). With advances in reproductive technology, it is increasingly feasible to maintain genetic diversity in captive stocks through translocation of gametes and embryos. These new technologies, however, raise a number of disease-related issues involving the spread of pathogens during the transfer of reproductive materials (Woodford and Rossiter 1994).

In summary, a number of recommendations have been advanced for dealing with disease risk in captive breeding programs, including: maintaining a quarantine period sufficient to deal with specific disease risks to primates, such as tuberculosis; careful screening of parasites in the source and target populations; and behavioral training to ensure appropriate responses to resources, predators, and parasitic infections in the wild. Fewer captive management issues arise in translocation projects, provided that animals are released into the new habitat quickly after capture so that fewer opportunities for infection occur in captivity.

7.4.4 Ecotourism and scientific field research

Regrettably, the very individuals who are most concerned about conserving wild primates could put them at danger from infectious disease. Eco-tourists are typically strongly committed to conservation goals and spend extraordinary sums of money to view primates in their natural settings, yet these tourists often arrive from distant points on the globe and therefore can carry novel infectious diseases to endangered primate populations. Thus, Butynski and Kalina (1998) claimed that, "disease transmission appears to be the most serious threat that tourism provides for gorillas . . ." (p. 308). Similarly, field researchers who are committed to studying and preserving primates may introduce infections during habituation, capture, or simply by living in or near the reserve (Wallis and Lee 1999). In this context, wild animals face special risks from parasitic diseases that can be transmitted by momentary contact with humans. Specific examples include infectious agents transmitted through feces, droplets in air, water, or in the soil, such as *Shigella, Trichuris*, hepatitis A (HAV) and B (HBV) viruses, herpes simplex, scabies, a variety of intestinal worms, measles, and polio (Homsy 1999; Wallis and Lee 1999; Rothman and Bowman 2003).

Is there any evidence for the transfer of pathogens from tourists or researchers into wild primate populations? The answer is "yes," although details are often sketchy and the majority of cases probably remain uncounted. In primates, outbreaks of measles, human tuberculosis, and influenza probably resulted from contact with humans (Wallis and Lee 1999). "Tourist groups" of gorillas in the Volcanoes National Park, Rwanda, have been especially hard hit by respiratory illnesses (Sholley and Hastings 1989; Butynski and Kalina 1998). Chimpanzees at Gombe suffered from respiratory infections and a paralytic disease similar to polio in humans (Goodall 1986). Finally, animals could acquire infectious disease from feeding on human refuse at garbage dumps that are generated through tourist activities (see Fig. 7.8).

Feeding by tourists or researchers could further facilitate the spread of pathogens (Wallis and Lee 1999), and intentional provisioning might increase the risk of attacks by monkeys on humans. Such attacks have the potential to increase disease transmission between humans and nonhuman primates. Contacts between nonhuman primates and humans are remarkably common, even when authorities post warnings to avoid contact. For example, in a colony of Barbary macaques (*Macaca sylvanus*) in Gibraltar, tourists are advised to avoid direct contact with monkeys, but human-initiated contacts still occurred at a rate of 44 times *per hour* (!), and the majority of these involved

potentially close contact between humans and the monkeys (O'Leary and Fa 1993). These human–monkey interactions resulted in a substantial number of severe lacerations to humans (Fa 1992). Monkey-initiated interactions also involved sitting on tourists' shoulders and entering vehicles while searching for food (see also Clifford et al. 1972). A viral epidemic hit this macaque population in 1987, resulting in the deaths of all infants (O'Leary and Fa 1993).

In populations of primates under study by biologists, food is often provided to habituate wild animals (see examples in Fa and Southwick 1988). This activity has risks similar to those involving tourist activity (Wallis and Lee 1999). Moreover, when food is supplied in excess and then restricted (e.g. Japanese macaques on Koshima Island, see Watanabe et al. 1992), suddenly malnourished animals may become susceptible to disease (Beisel 2000). Indeed, provisioning can have a number of undesirable effects, including increased feeding competition, which might alter patterns of general health and infant mortality (Berman and Li 2002). On the other hand, carefully implemented provisioning can enhance the nutritional status of animals, and can be used to disseminate medications or oral vaccines should an outbreak occur.

A number of guidelines for ecotourism have been developed to reduce the spread of infectious disease (Butynski and Kalina 1998; Homsy 1999; Wallis and Lee 1999; Mudikikwa et al. 2001). These include the following six general strategies that are appropriate for most primate populations. (1) Restrict contact with humans by limiting the number of tourists and researchers that visit a group per day, enforcing a minimum distance that humans can approach the animals, and eliminating opportunities to feed the animals. (2) Prevent sick tourists and researchers from going into the field to view wild primates. (3) Provide emergency contingencies for disease outbreaks, including veterinary assistance and application of vaccines or medication to control epidemics initiated through human contact (see next section). (4) Eliminate contact between wild primates and human waste, refuse piles, and sleeping areas. (5) Provide a buffer between the groups visited by tourists and other social groups or populations. (6) Ensure that park staff enforces these rules, which can be a problem if the low pay of park personnel leads to temptations to accept financial rewards from wealthy tourists who wish to circumvent these rules.

7.4.5 Direct intervention to reduce the impact of disease

Despite the best plans to reduce disease risk, infectious disease outbreaks will continue to occur, leading to a series of difficult questions (Wobeser 2002a). Should humans intervene to contain the infection? What options for intervention are available, and what are the potential costs of different intervention strategies? What are the best ways to prevent transmission of infections across species boundaries, including minimizing risks to the humans who are providing assistance?

We can group the efforts to eliminate infections into three general approaches relevant to primates: care of individuals with potentially life-threatening infections or injuries, containment of the pathogen at the population level, and increased

knowledge of host–parasite interactions in wild populations. Many authors have addressed these issues at general and specific levels (e.g. Woodroffe 1999; Wobeser 2002a). Veterinary intervention probably plays a major role in conservation efforts to reduce the impact of infectious disease in wild populations, especially when veterinary medicine is practiced in a multidisciplinary framework that includes ecologists, epidemiologists, and evolutionary biologists (Hutchins et al. 1991; Cunningham 1996; Woodroffe 1999).

7.4.5.1 Providing care to infected animals

Field biologists who study primates have provided care to sick or injured individuals on numerous occasions. For example, Goodall (1986) described how researchers at Gombe medicated chimpanzees, including an animal with a fungal infection of the nose (see Roy and Cameron 1972). Similarly, when an outbreak of a sexually transmitted disease (STD) impacted the baboon population at Gombe, researchers provided treatment with antibiotics via syringe and food to halt the spread of the infection (A. Collins, personal communication and Wallis and Lee 1999). Direct intervention often requires safely capturing and handling animals. Primates are commonly captured using "darts" loaded with a general anesthetic (Glander et al. 1991; Sapolsky and Share 1998; Ancrenaz et al. 2003), for purposes of marking and sample collection and to provide medical intervention. At Karisoke, for example, Hastings (1991) described treating a laryngeal air sac infection in a free-ranging male mountain gorilla by darting the animal with penicillin and general anesthetic and performing surgery in the field. Similarly, Sleeman et al. (2000) summarized 26 surgical procedures performed on 24 gorillas over a nearly 10-year period to treat animals caught in snares. These authors describe the procedures that were most successful for field surgery, including maintaining distance from other members of the gorilla group during the operation, the specific drugs and doses used to anesthetize the animals, and "gorilla behaviors" performed by the human staff to comfort gorillas recovering from anesthesia (including grooming and giving grunt vocalizations to minimize the stress of the procedures). Additional examples of anesthesia used in field conditions are provided by Karesh et al. (1998) for black spider monkeys (*Ateles paniscus*) and Kilbourn et al. (2003) for orangutans.

7.4.5.2 Vaccination and culling

In recent decades, vaccination programs have targeted a variety of wild mammal hosts (Woodroffe 1999; Wobeser 2002a). Vaccination of wildlife works in part by increasing herd immunity, that is, by moving a proportion of individuals from susceptible to resistant classes, thus reducing the ability of a pathogen to become established and spread in the host population (see Box 4.2). Of course, vaccination is primarily an option for those viruses and bacteria that elicit lasting antibody-mediated immunity, and for which safe and effective vaccines have been developed. In primates, vaccination procedures have been undertaken for polio in chimpanzees (Goodall 1986) and measles in gorillas (Sholley and Hastings 1989). In other

wildlife systems, oral vaccines for rabies and anthrax show promise for successful disease control, since this eliminates the need to capture animals and administer injections (Cleaveland et al. 2002).

Vaccination strategies can be widespread across animal populations or applied in local "control zones" to slow or stop an advancing disease front with a strategically laid immune barrier. For example, to slow the spatial spread of rabies virus in raccoons in North America and foxes in Europe, and eradicate this infection from local areas, large amounts of oral rabies vaccine (mixed with bait and other ingredients) have been dropped from aircraft across large geographic regions (Rupprecht et al. 1986; Wandeler 1994; Russell et al. 2005). In some cases, vaccines can be applied to create *cordon sanitaires* for slowing viral spread, although such strategies might also be accomplished by culling susceptible hosts or through quarantine strategies applied over large areas. Vaccines might also be administered by targeting hosts that aggregate at local food sources or at watering holes. When harmful pathogens are transmitted to threatened hosts from a domesticated animal or a non-threatened reservoir host, vaccinating the reservoir should be considered as a means to contain the epidemic (Cleaveland and Dye 1995; Woodroffe 1999).

Regardless of the target, vaccination obviously should be implemented with great care and foresight, and cost–benefit analyses should include the risks of handling wild animals, including spread of diseases to wild populations (McCallum and Dobson 1995) and stress-related reductions in immunocompetence (Lloyd 1995). A study of wild dogs (*Lycaon pictus*) found, for example, that individuals experienced higher mortality when they were handled for radio-collaring and disease-related intervention, such as vaccination (Burrows et al. 1994), although this interpretation sparked considerable controversy (Burrows et al. 1995; Devilliers et al. 1995; Ginsberg et al. 1995). It is also essential to evaluate alternatives to vaccination, investigate the epidemiological implications of vaccinating threatened and reservoir populations at different spatial and temporal scales, and obtain sufficient funding to maintain the vaccination program for the period of time that is needed to make it effective (Lyles and Dobson 1993; Woodroffe 1999).

A final option involves culling diseased animals or reservoir hosts that might contact the target host population. Culling works by eliminating sources of new infections and reducing the ability of susceptible populations to maintain a pathogen. Culling is obviously less desirable for threatened species and has been the source of some controversy (Schiermeier 2003), but selective removal of diseased animals and maintenance of a smaller population size may be appropriate for some primate populations (Wobeser 2002a). Diseased primates removed from a population need not be killed, but could be treated in isolation and ultimately returned to the larger population. Similarly, reservoir animals could be vaccinated or treated for infections rather than being culled or permanently removed. These actions should be guided by knowledge of the biology of the infectious agent and host species, the risks of cross-species transmission, and evaluation of the benefits of removing infected animals versus reducing the size of reservoir populations (Cleaveland et al. 2002).

7.5 Evolutionary considerations and host–parasite biodiversity

Parasites are an integral part of life on earth, with parasite biodiversity exceeding the diversity of free-living hosts (Price 1980; Windsor 1998; Zimmer 2000). This simple fact led Windsor (1990, 1995) to the radical proclamation of "Equal rights for parasites!" And as noted earlier in this chapter, host-specific parasites will go extinct as host ranges contract. However, conservation of parasites has rarely been considered a primary goal of conservation strategies in primates or other animals (Freeland and Boulton 1992; Gompper and Williams 1998). From the perspective of host conservation, it is important to understand the links between infectious disease, extinction risk, and maintenance of genetic and species diversity, and also to investigate the degree to which co-extinctions of hosts and parasites will contribute to future biodiversity loss (Koh et al. 2004). Furthermore, keeping coevolutionary relationships intact requires conservation programs that operate at a landscape level, protecting resources, corridors, and networks of multiple habitat types important to a broad range of species.

Parasites are likely to be powerful selective agents in natural populations, and host species exposed to a diverse array of parasites should harbor a variety of resistance traits and inducible defenses (e.g. Chapter 5). Many studies have underscored the importance of genetic variation in host resistance in causing disease patterns in both field and experimental settings (examples provided earlier in this chapter, in Chapter 5, and reviewed in Altizer et al. 2003a). Evidence of microevolutionary processes important to host–pathogen coevolution is largely missing from primates (but see de Groot et al. 2002; Wooding et al. 2005). In terms of macroevolutionary studies of primates and parasites, Hugot (1999) found general support for cospeciation of primate hosts and their pinworms, and Switzer et al. (2005) showed molecular evidence in support of an ancient history of cospeciation between simian foamy viruses (SFVs) across more than 40 species of Old World monkeys and apes (see Box 6.3). In a broader comparative analysis that spanned host–parasite records across multiple parasite groups, Nunn et al. (2004) found that parasite diversity (species richness) across all primates was correlated positively with rates of primate host diversification (Box 7.2). From this perspective, pathogens could be one of the major factors promoting both genetic and species diversity in wild primate communities, and it might be this coevolutionary landscape that is at greatest risk and in most urgent need of protection.

7.6 Summary and synthesis

Nearly 90% of the world's primates inhabit forests in tropical regions, and many of these species occur in areas facing high rates of deforestation and extreme human population pressure (Mittermeier and Cheney 1987). Indeed, primates are among the world's most threatened mammals. At a global level, the amount of tropical forest

lost per year was estimated to support tens of millions of individual primates (Chapman and Peres 2001). Humans also hunt wild primates for a variety of purposes, including for food, use in traditional medicines, and live trade for the pet industry and for biomedical research. The bushmeat crisis in particular has caused devastating mortality in some wild primate species (Peres 1990a, 2000; Fa et al. 1995; Walsh et al. 2003b; Brashares et al. 2004), and it is not likely to cease in the immediate future (Wilkie and Carpenter 1999).

It would be impossible to dispute the importance of hunting and habitat loss for conservation of nonhuman primates; instead, we called attention to the ways that these anthropogenic effects influence disease risk, often through fundamental yet under-appreciated mechanisms that also impact primate populations. More generally, managing parasites and infectious disease represents a growing focus in wildlife conservation (Cleaveland et al. 2002; Lafferty and Gerber 2002), in part because parasites can threaten already-reduced populations, because infectious diseases can trigger catastrophic declines in otherwise robust host populations, and because human activities can drive both of these processes. In this chapter we reviewed plentiful examples that demonstrate the importance of parasites in planning and implementing primate conservation efforts. Probably the greatest threats will come from rapidly evolving pathogens such as viruses, generalist parasites that are maintained at high levels in reservoir hosts, and parasites that are most likely to emerge in wildlife through human activities, including deforestation and climate warming.

In the context of conservation and infectious disease, perhaps the greatest need is to increase our knowledge of host–parasite interactions in natural systems. In the case of EIDs, the identity of new pathogens causing population declines can remain uncertain for years, hindering effective management of the problem. This is illustrated vividly in many cases, including Ebola and the pathogen-driven declines of amphibian populations. Yet despite these high-profile examples, global assessments of extinction risk generally downplay the impact of parasites. Surprisingly, the 2002 IUCN Red List (Hilton-Taylor 2002) does not include a comprehensive list of parasites that threaten wild host species. Even among highly threatened mammals, such as primates, infectious diseases have only rarely been recognized as contributing to population declines. Thus, there is a need for conservation biologists to develop protocols for tracking parasites implicated in primate declines.

A final point highlighted by this chapter is that not all aspects of parasitism are necessarily negative; a strong argument can be made for conserving both hosts and their parasites, or at least for more balanced investigation of the importance of parasite conservation. Although the risks they pose to endangered species are apparent, infectious disease can play an important role in maintaining both genetic diversity within species and biodiversity at the community level. From a broader perspective, coevolution between hosts and parasites might be a major force determining global patterns of biodiversity, and conservation strategies that restrict disease spread might deprive host populations of the genetic diversity needed to respond to future ecological changes. As humans disturb natural balances, break transmission barriers among species, and reduce host population sizes, outbreaks of new or generalist pathogens

among rare or threatened host species, including a range of nonhuman primates, will continue to occur (Chapman et al. 2005a). Maintaining the ability of wild populations to respond evolutionarily to parasite-mediated selection could be one of the best long-term strategies for mitigating the risks of infectious diseases (Crandall et al. 2000; Stockwell et al. 2003).

Box 7.2 Parasites and the diversification of primate lineages

Parasites have been linked to the maintenance of host genetic variation (Hamilton 1982), and host–parasite coevolution can lead to surprisingly high levels of genetic diversity within and among interacting populations (Dybdahl and Lively 1998; Burdon and Thrall 1999; Altizer 2001). Species interactions involving predation, herbivory and parasitism have been proposed to drive major diversification events (Mitter et al. 1991; Farrell 1998; Percy et al. 2004). From a macroevolutionary perspective, theoretical work has shown that frequency dependent selection between prey and natural enemies can lead to evolutionary branching in both the host and enemy populations (Doebeli and Dieckmann 2000). Moreover, a recent empirical study of coevolution between bacteria and virulent phage in spatially structured environments demonstrated that parasites can drive allopatric divergence among host populations, increasing host diversification by selecting for anti-parasite defenses genetically linked to different host traits in different populations (Buckling and Rainey 2002).

Among primates, Nunn et al. (2004) used a phylogenetic comparative method to show that parasite diversity (species richness) was positively correlated with rates of primate host diversification (see Fig. 7.11). Thus, primate host species from more diverse lineages

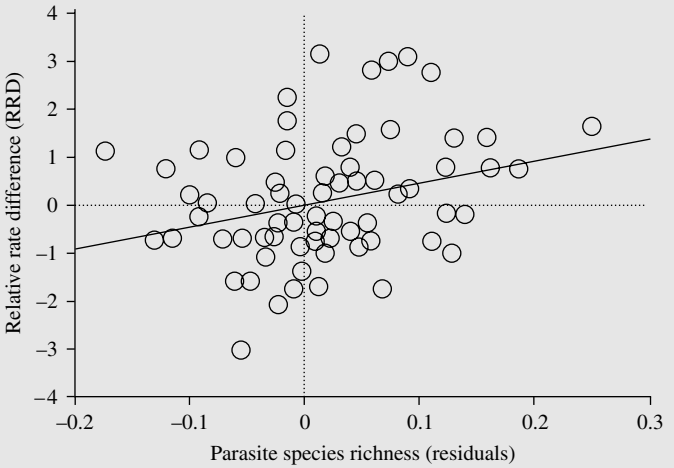


Fig. 7.11 Parasite species richness and diversification rates in primates. Host diversification (y-axis) was measured as the "relative rate difference" (RRD) after Isaac et al. (2003), with higher values indicating increased rate of diversification (Agapow and Isaac 2002). Parasite species richness reflects the total diversity of all parasites, including viruses, protozoa and helminths, on a per primate species basis, and controls for differences in sampling effort among primate hosts. Reprinted from Nunn et al., "Parasites and the evolutionary diversification of primate clades." *The American Naturalist*, vol. 164, pp. S90–S103. Copyright (2004) by The University of Chicago.

Box 7.2 (*Cont.*)

harbored a greater number of parasite species on a per host lineage basis. Results were most consistent in analyses of all parasites combined and for viruses and protozoa examined separately. The authors investigated two mechanisms that might underlie this significant positive association, namely that: (1) parasites increase the speciation rates of their hosts via a mechanism linked with sexual selection (Lande 1981; Barraclough et al. 1995; Gavrilets 2000; Panhuis et al. 2001; Turelli et al. 2001), and (2) parasites infecting hosts from more diverse lineages have greater opportunities for diversification through mechanisms involving host-shifting by specialist parasites or host-sharing by generalists (Raibaut et al. 1998; Combes 2001; Dobson and Foufopoulos 2001; Roy 2001; Taylor et al. 2001). Surprisingly, the authors failed to find consistent evidence for either mechanism, although measures of geographic range overlap were correlated with parasite richness in some tests, providing partial evidence for the second mechanism (host-shifting or -sharing).

Although a more general (and more difficult to detect) arms race between primate hosts and parasites could account for the pattern in the figure, an alternative explanation also exists. Rather than hosts and parasites diversifying collectively, the pattern could arise from processes linked with host and parasite extinction. Specifically, parasite lineages might be lost as their hosts decline in population size and ultimately go extinct. In other words, higher extinction rates in declining primate lineages could generally reduce parasite diversity, especially if parasites go extinct before their hosts (Koh et al. 2004). In another comparative study, we addressed this possibility by examining the diversity of parasites in both threatened and non-threatened primate hosts (Altizer, S., C. Nunn and P. Lindenfors unpublished data). We found that more threatened primate hosts harbored fewer parasite species (see Fig. 7.10), consistent with the idea that parasites go extinct in advance of their hosts (Gompper and Williams 1998).

Results of these comparative studies, although provocative, failed to reveal mechanisms that underlie associations between host and parasite diversification. Future research would therefore benefit from examining the geographic patterning of host-parasite interactions (Thompson 2005), incorporating information on parasite phylogeny (Hafner and Page 1995; Hugot 1999; Morand et al. 2000), and testing the possibility that parasites themselves have gone extinct along with their hosts (Gompper and Williams 1998). This final consideration raises the point that it might be important to consider the impacts of mammalian extinctions on the collective biodiversity represented by their parasites. Although it may seem heretical at first glance, efforts aimed at protecting mammalian diversity should perhaps consider pathogen biodiversity as an integral component of free-living host communities, particularly given their role in shaping variation within and among host species.

8

From nonhuman primates to human health and evolution

8.1 Introduction

Infectious diseases have exerted enormous impacts on human history and have carved deep marks on demographic patterns, causing more human deaths over time than all other sources of mortality combined (Oldstone 1998; Inhorn and Brown 1990; Anderson and May 1991). Historical records of human infectious diseases such as bubonic plague, smallpox, tuberculosis, cholera, and malaria date back many centuries (Barrett et al. 1998; Oldstone 1998). Infectious diseases also changed patterns of human migrations, shaped the outcomes of wars, and had tremendous impacts on the fates of civilizations (Diamond 1997). One intriguing example involves the death of Alexander the Great, who died after two weeks of illness that included fever and possibly encephalitis. Although previous authors attributed his death to poisoning or to more commonly recognized infectious diseases such as malaria or typhoid fever, Marr and Calisher (2003) suggested a new and provocative hypothesis that Alexander the Great died of West Nile fever, which is common in the Middle East in the present day and causes deaths in humans. Moreover, they found the following passage, written by Plutarch, concerning Alexander's entry to Babylon, "when he arrived before the walls of the city he saw a large number of ravens flying about and pecking one another, and some of them fell dead in front of him" (p. 1601). This is strikingly similar to the observation of dead crows in the wake of the introduction of West Nile virus to the United States (Hochachka et al. 2004).

Despite major advances during the past century in understanding the origins and epidemiology of infectious diseases, parasites continue to have a massive impact on human health around the world. More than 1.4 billion humans are infected with roundworms, *Ascaris lumbricoides* (Crompton 1999), a nematode that lives in the small intestine and leads to significant pathology, including reduced growth, lower activity levels, and learning disabilities among children (O'Lorcain and Holland 2000). Cholera, *Shigella*, and rotavirus infections trigger over a billion cases of diarrhea each year, primarily in developing countries, where they pose critical threats to childhood survival and development (Guerrant et al. 2002; Kosek et al. 2003). At the same time, vector-borne diseases such as malaria and dengue fever

cause millions of deaths annually, and over 40% of the world's human population inhabits malaria-endemic regions (CDC 2004b). Infectious diseases pose new concerns for human health in the twenty-first century, in part due to technological advances that elevate public concerns about how microbes might be used in warfare and terrorism.

In this chapter, we consider how knowledge of parasites in nonhuman primates can broaden our understanding of factors that affect human exposure to infectious diseases and associated cultural and evolutionary responses. At the outset, we acknowledge that *Homo sapiens* is by far the best studied of all primate species, and knowledge of human–parasite interactions more commonly inform and motivate primate–parasite studies than vice versa. For example, field sampling data of parasite occurrence in wild primates are often targeted toward infectious diseases of concern to human health (see Box 2.1 and Nelson 1965; Nelson et al. 1965; Legesse and Erko 2004), and nonhuman primates have been used as experimental models for vaccine development and the treatment of many human pathogens (Voss and Hunsmann 1993; Amaral et al. 1996; Misra et al. 1997). But beyond their obvious biomedical importance, studies of parasite infections in wild primates can also introduce new questions for human disease research—for example, what is the role of basal immunity in mediating resistance to different types of pathogens (see Box 5.1), and can behavioral responses to diseases in nonhuman primates point to novel strategies for countering human pathogens?

We begin from the perspective that humans share a common evolutionary history with the many nonhuman primate species that were discussed in earlier chapters. Thus, understanding parasite community assemblages in contemporary primates offers a useful starting point for reconstructing ancestral parasite communities in early humans, and also underscores the striking differences between infectious disease dynamics in humans and nonhuman primates. These differences are represented historically by "epidemiological transitions" that characterized the evolution of human societies but have few, if any, parallels in other primate lineages. Second, we consider how approaches for studying primate evolution and behavior can shed light on human *responses* to infectious diseases, including physical and immunological adaptations and cultural practices that alter parasite transmission. From a cultural perspective, parasites are probably responsible for human social customs ranging from methods of preparing food to cultural taboos involving use of one hand for hygienic functions (McNeill 1977, 1997). Comparative approaches that have generated interesting and valuable insights when applied to nonhuman primates might also hold promise for understanding factors that influence the global distributions of human infectious diseases. Finally, examining contemporary patterns and transmission of pathogens in wild primates can inform public health strategies, particularly in terms of risk factors for human disease emergence. We therefore conclude by considering the exchange of pathogens between humans and wild primates, identifying routes by which some new pathogens might enter human populations (Wolfe et al. 1998).

8.2 Origins and early history of infectious disease in humans

Where do most human infectious diseases originate, and how long have they persisted in human populations? Parasites and microbes repeatedly evolved ways to exploit changes in human behavior and demography, with evidence suggesting that the types and total diversity of human pathogens have shifted over time with changing social structures, lifestyles, political factors, and ecological conditions (Barrett et al. 1998; Lederberg 2000; Weiss 2001). Some viruses, for example, show evidence of an ancient relationship with humans and other nonhuman primates (Van Blerkom 2003), whereas other pathogens appeared after humans developed technologies for living at higher densities, or modified their environments in ways that increased transmission. The development of agriculture probably provided new selection pressures for many pathogens to shift from wild animals to humans and their domesticated livestock (Edman 1988), and to evolve in response to new transmission opportunities (Su 2003).

8.2.1 Infectious agents in early human societies

The majority of human pathogens either coevolved in primate lineages leading to *Homo sapiens* or were acquired through host shifts following the domestication of livestock and carnivores (Inhorn and Brown 1990; Diamond 1997; Barrett et al. 1998; Weiss 2001). Scientists have partially reconstructed the community of infectious diseases in early human societies using a combination of genetic analyses of parasite lineages, fossil evidence based on human bones and fecal material (i.e. coprolites), and "ethnographic analogy" informed by disease patterns in modern-day hunter–gatherer groups (e.g. Inhorn and Brown 1990; Weiss 2001). Some parasites have an ancient coevolutionary history with humans, with examples including herpesviruses, papovaviruses, pinworms, and ectoparasitic lice (Weiss 2001; Van Blerkom 2003; Ashford 2000; Hugot 1999; Table 8.1). On the other hand, contemporary assemblages of human parasites probably bear little resemblance to those that existed in early hominids. This divergence likely arose as a result of three major processes, including (1) animal domestication and the transfer of pathogens from livestock and pets, (2) lifestyle shifts toward greater population density, more permanent settlements, and trade routes that enabled the spread and persistence of acute infections, and (3) environmental modifications such as irrigation and dam-building that favored some pathogens and led to declines in others.

For the greater part of human evolution, bands of hunter–gatherers lived in relatively small foraging groups (Barrett et al. 1998). In these groups, many directly transmitted acute infections, including influenza, smallpox, and measles, would have been unable to establish and persist due to the small size of bands and, relative to modern humans, their isolation from one another (Dobson and Carper 1996). Instead, parasites infecting early humans most likely caused chronic infections, had

Table 8.1 Examples of human infectious diseases, including those that have likely had a long coevolutionary history with humans and those with more recent origins, particularly following contact with domesticated animals or wild primates. Possible ancestral host species that might have served as sources for human infections are shown, including the possibility that the parasite was present in early hominids, although many of these remain speculative or are based on anecdotal evidence. The approximate duration of association with humans is based on paleoanthropological data, molecular evidence, and recorded historical notes. The final column indicates whether or not the pathogens themselves or close relatives are present in modern-day populations of nonhuman primates. Information compiled from Diamond (1997), Barrett et al. (1998), Ashford (2000), Weiss (2001), Joy et al. (2003), and Van Blerkom (2003)

Disease	Parasite name	Type	Ancestral host	Association with humans	Present in nonhuman primates?
Pinworms	*Enterobius vermicularis*	Nematode	Early hominids	> 10,000 yrs	Genus common in wild primates
Lice	*Pediculus humanus*	Arthropod	Early hominids	> 10,000 yrs	Genus common in wild primates
Herpesvirus	*Simplexvirus*, *Varicellovirus*	Virus	Early hominids	> 10,000 yrs	Related viruses in wild primates
Malaria	*Plasmodium falciparum*	Protozoan	Early hominids or African primates	> 10,000 yrs	Genus common in wild primates
Measles	*Morbillivirus—Measles virus*	Virus	Sheep or goats	8000 yrs	Infrequent reports from humans to nonhuman primates
Syphilis (also yaws, bejel)	*Treponema pallidum*	Bacterium	Uncertain	2000–8000 yrs	Yes, occasional reports
Smallpox	*Orthopoxvirus—Variola virus*	Virus	Uncertain, possibly cows or rodents	3000–4000 yrs	No, occasional monkeypox reports but mainly from wild rodents
Rabies	*Lyssavirus—Rabies virus*	Virus	Dogs	3000–4000 yrs	No
Tuberculosis	*Mycobacterium tuberculosis*	Bacterium	Possibly cows or other ruminants	3000 yrs	No, infrequent *M. bovis* infections
Schistosomiasis	Five spp. of *Schisotosoma*	Trematode	Uncertain	3000 yrs	Common in several Old World primates, including some parasite species that can infect humans
Typhus	*Rickettsia typhi*	Bacterium	Rodents	2000 yrs	No
Plague	*Yersinia pestis*	Bacterium	Rodents	1500 yrs	No
Yellow fever	*Flavivirus—Yellow fever virus*	Virus	Old and New World monkeys	1000 yrs	Common in many wild primates
Cholera	*Vibrio cholerae*	Bacterium	Probably evolved from free-living ocean dwelling bacterium	1000 yrs	No
AIDS	*HIV (Human Immunodeficiency Virus*)	Virus	Old World monkeys and apes	70 yrs	Related viruses in African primates

long latent phases, or caused sub-clinical effects with relatively low virulence—and were probably similar to infectious agents reported from contemporary populations of many nonhuman primates.

Helminth infections such as pinworms and tapeworms that could be transmitted through encounters with contaminated substrates and by eating unwashed food or uncooked meat were probably common in pre-agricultural human groups, as were ectoparasitic infections caused by lice and mites (Barrett et al. 1998; Ashford 2000). Phylogenetic analysis of primate malaria parasites supports an African origin for *Plasmodium falciparum*, with this parasite present in humans for at least the past 10,000 years (see Box 8.1 and Escalante et al. 1998; Joy et al. 2003). A study of human remains in the New World revealed long-term human association with another vector-borne protozoan also found in New World monkeys (Chagas' disease, caused by *Trypanosoma cruzi*), with infections dating back to at least 7000 BC (Aufderheide et al. 2004). Remarkably, the prevalence of infection exceeded 40% in some remains of pre-contact populations. In terms of viral infections, Van Blerkom (2003) used a combination of molecular evidence and pathogen biology to suggest that directly transmitted viruses in early humans likely included endogenous retroviruses, sexually- or vertically-transmitted papilloma- and herpesviruses, and those that had persistent latent stages, such as varicella zoster virus, which causes chickenpox in children but also flares up later in adult life as shingles (Weiss 2001).

Some human diseases leave marks on skeletal material in the form of scarring, lesions, and bone deformations, often included in the catch-all term spondyloarthropathy, which involves joint erosion, tendon ossification, and, in many cases, spine and sacroiliac fusion (Rothschild and Woods 1991b). Human populations have probably experienced a long association with these debilitating conditions, which might be caused by several infectious agents, possibly including sexually transmitted and fecal-borne pathogens (Rothschild et al. 1993; Rice and Handsfield 1999). Skeletal malformations consistent with spondyloarthropathy have also been documented in a wide range of nonhuman primates (Rothschild and Woods 1989, 1991a, 1992, 1993, 1996). Understanding variation in the patterns of infection within and among primate species could provide new insights to the causes and consequences of these arthritic conditions in humans, particularly with regard to the predominant transmission mode or the ecological characteristics that lead to development of spondyloarthropathy. For example, in a comparative study of primates and carnivores, the primary predictor of spondyloarthropathy was body mass, suggesting that larger bodied species are more frequently exposed to infectious agents of this disease, or perhaps due to the physical stresses on joints in large-bodied animals (Nunn et al. in review b).

As one example of how ancient human remains might inform studies of infectious disease origins, researchers have used bone signatures of syphilis (caused by *Treponema pallidum pallidum*) and related non-sexually transmitted diseases (STDs) (yaws, bejel) to propose that a yaws-like bacterium probably spread from East Africa across Asia and into North American human populations many thousands of years

Box 8.1 Diversity of the primate malarias and origins of human parasites

Malaria parasites in the genus *Plasmodium* are a leading cause of human death worldwide, with nearly half of the world's population inhabiting malaria-endemic regions in Africa, Asia, and Latin America (CDC 2004b). Human infections are largely caused by two common and widespread species, *P. falciparum* and *P. vivax*, in addition to *P. ovale* and *P. malariae* (Coatney et al. 1971). Malaria parasites are reported to infect a large number of vertebrate host species including reptiles, birds, and mammals, where they are transmitted by blood-sucking dipterans, primarily mosquitoes in the genus *Anopheles* for mammalian parasites. Primates harbor an unusually high diversity—at least 24 species—of *Plasmodium* parasites, with the greatest diversity among parasites reported from Asian monkeys (especially macaques) and African apes (Table 8.2, Coatney et al. 1971). At a global level, *Plasmodium* has been reported to infect over 45 species of wild primate hosts from free-living populations in Africa, Asia, and Latin America (Nunn and Altizer, unpublished data).

The life cycle of malaria is similar across many vertebrates and alternates between insects and vertebrate hosts (summarized in Coatney et al. 1971 and most parasitological texts). Primate malarias have had a long evolutionary history, as evidenced by their diversity and range of host species affected (Table 8.2). However, existing studies do not provide strong evidence for concordant phylogenies with their primate hosts (Coatney et al. 1971). Multiple studies using molecular genetic approaches have shown that each of the four malaria parasites infecting humans has a unique origin and arose independently as human parasites. Counter to earlier ideas suggesting an origin of falciparum malaria ca. 5000 years ago from an avian host, current evidence shows that the closest relative to *P. falciparum* is *P. reichenowi*, which infects chimpanzees (Fig. 8.1), and that the timing of divergence between avian lineages and the lineage giving rise to *P. falciparum* and *P. reichenowi* was quite ancient, possibly coinciding with the divergence of human lineages from apes (Escalante and Ayala 1994; Escalante et al. 1998). Further evidence suggests that despite recent expansions in population size and geographic range, *P. falciparum* originated in Africa, where strains are also genetically most diverse (Joy et al. 2003).

The high prevalence of a mutation that confers resistance to *P. vivax* among humans in sub-Saharan Africa (called "Duffy negativity," or lack of a Duffy blood group antigen) led some researchers to postulate an African origin for this human parasite (Carter 2003).

Table 8.2 Malaria parasites (in the genus *Plasmodium*) described from wild primates, including their approximate geographic location and examples of primate hosts affected. Information summarized from Coatney 1971; Escalante et al. 1998, 2005

Parasites species	Geographic location	Primate hosts
P. faliciparum, P. vivax, P. malariae, *P. ovale*	Tropical and subtropical regions including Latin America, Asia, Africa	Humans
P. fieldi, P. simiovale	Maylasia, Sri Lanka	Asian macaques
P. cynomolgi, P. knowlesi, P. coatneyi, P. fragile, P. inui	Southeast Asia and neighboring areas	Asian macaques
P. hylobati, P. eylesi, P. jefferyi, P. youngi	Indonesia, Malaysia	Asian gibbons
P. pitheci	Borneo	Orangutans
P. gonderi	Africa	African monkeys
P. schwetzi, P. rodhaini, P. reichenowi	Africa	African apes (gorillas, chimpanzees)
P. simium, P. brasilianum	Latin America	New World monkeys
P. girardi, P. lemuris	Madagascar	Prosimians

Box 8.1 (*Cont.*)

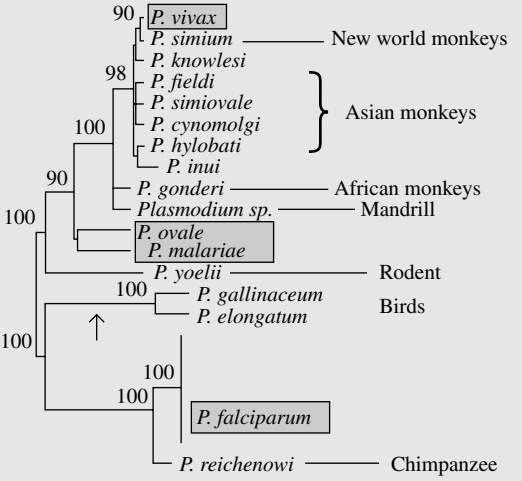


Fig. 8.1 Inferred phylogenetic relationship among 17 *Plasmodium* species from humans and nonhuman primates as inferred from the gene encoding cytochrome *b*. Bootstrap values for each node are indicated as percents over 1000 replications. Human parasites are indicated with shaded boxes. Note that *P. vivax* clusters with a number of parasites from Asian macaques (Table 8.3) rather than with the two parasite species from African primates (*P. gonderi, P. reichenowi*). Also note that *P. yoelii* is a parasite of rodents, and *P. gallinaceum* and *P. elongatum* are avian parasites. Image modified from "The evolution of primate malaria parasites based on the gene encoding cytochrome *b* from the linear mitochondrial genome" by A. A. Escalante, D. E. Freehand, W. E. Collins and A. A. Lal. *Proceedings of the National Academy of Sciences USA*, vol. 95, pp. 8124–8129. Copyright (1998) by The National Academy of Sciences, USA.

However, analysis of multiple genes provides strong evidence that *P. vivax* arose from a more recent host switch involving malaria parasites transmitted from macaques to humans in Southeast Asia (see Fig. 8.1 and Escalante et al. 1998, 2005). Furthermore, molecular data indicate that the *Plasmodium* species that radiated among Asian monkeys share an ancient African origin, and that *P. gonderi* (the only malaria parasite to infect African monkeys) is basal to the large Asian parasite clade (Escalante et al. 1998). Among the two major *Plasmodium* lineages from New World monkeys, *P. simium* is virtually identical to human *P. vivax* isolates, suggesting that humans introduced this parasite into monkeys in the Americas (Escalante et al. 1998). Similarly, *P. brasilianum*, a parasite reported from a wide range of New World monkey hosts, is genetically indistinguishable from the human parasite *P. malariae*, and both of these parasites form a group with *P. ovale* (also from humans) that is basal to the parasite clade from Asian primates (see Fig. 8.1 and Escalante et al. 1998).

Studies of the origins and radiation of primate malarias and their adaptive evolution in primate hosts will no doubt be improved by greater sampling of parasite strains from more wild primate populations and species (Wolfe et al. 1998; Escalante et al. 2005). Understanding of the length of associations between wild primates and *Plasmodium* species, biological traits of the parasites themselves, and immunological or resistance traits among wild primate hosts could generate insights for managing malaria infections in humans, and could help researchers understand how these parasites have radiated among and adapted to a large number of primate hosts.

ago (reviewed in Rothschild 2005). The sexually transmitted form of this disease might have been acquired by Columbus' exploratory crew in the Dominican Republic and subsequently introduced to Europe (Knell 2004). Despite population-based methods for discerning between yaws and syphilis, the historical scenario supported by skeletal studies of human treponemal diseases is controversial, with some paleopathologists suggesting that only non-venereal treponemal disease was present in the New World prior to Columbus's arrival (or that venereal syphilis was present in Europe before 1492, reviewed in Powell and Cook 2005). Interestingly, baboons and other nonhuman primates are also known to suffer from treponemal disease, leading some researchers to propose the exchange of infections between wild primates and humans—but aside from several decades-old seroepidemiological surveys (Fribourg-Blanc et al. 1966; Fribourg-Blanc and Mollareet 1969; Baylet et al. 1971; Felsenfeld and Wolf 1971), very little is known about the ecology of treponemal diseases in nonhuman hosts.

Perhaps not surprisingly, the current distribution of agents that infect humans appears to have diverged dramatically from those that probably infected early human societies. Indeed, contemporary human populations harbor a much greater diversity of infectious agents relative to those reported from wild primates. Of the roughly 1400+ species of parasites and pathogens reported to infect humans at a global level (Taylor et al. 2001; Ashford and Crewe 1998), the vast majority (60% or more) are known to be zoonotic—yet only a small fraction of modern-day human pathogens are documented to infect wild nonhuman primates (Pedersen et al. 2005). Even those primate species that have been particularly well-studied in terms of infectious diseases (including several species of baboons, macaques, chimpanzees, gorillas, vervet monkeys, and howler monkeys) reportedly harbor only a tiny fraction of the diversity of parasites infecting contemporary human populations. Furthermore, whereas the greatest diversity of parasites reported from wild primates is captured by helminths and protozoa, which are commonly linked with chronic infections and vector- or fecal-oral transmission (see Fig. 2.3), the majority of modern-day human pathogens are bacteria, viruses, and fungi, many of which cause acute infections and are often associated with contact-based transmission.

Much of the disparity between parasites reported from humans and wild primates could reflect the intensity with which human diseases have been studied, and the types of infections recorded in the medical literature. Many bacteria and fungi reported to infect humans are associated with secondary infections or abscesses of tissues or organs, and their prevalence and transmission strategies remain uncertain, whereas other microbes are common in humans but only rarely cause pathology. These types of organisms are unlikely to be reported as parasites in wild primate populations, although reporting biases alone probably do not explain all of the differences in parasites described from humans and wild primate populations. Indeed, it is also likely that behavioral and ecological changes (many of which are described in the next section) exposed developing human societies to new and varied sources of infections relative to other primate hosts (Diamond 1997).

8.2.2 Epidemiological transitions and the rise of human pathogens

Very recently in human evolutionary history, a major shift in infectious diseases followed the rise of agriculture, animal domestication, and greater human population densities as permanent settlements formed (Inhorn and Brown 1990; Dobson and Carper 1996; Diamond 1997). This was described by Barrett et al. (1998) as the first of three "epidemiological transitions" reflecting major changes in human–parasite interactions, and leading to the proliferation of many human diseases that are rarely documented in wild primates (see also McNeill 1977; Diamond 1997; McMichael 2004). The first transition occurred approximately 10,000 years ago and accompanied the development of food production and a more sedentary lifestyle, leading to higher birth rates and more abundant populations of humans and domesticated animals. Human and animal wastes probably accumulated around these settlements, contaminating food and water supplies and attracting rodent reservoir hosts for diseases such as typhus and plague. Simultaneously, humans experienced greater contacts with domesticated animals and their fur, milk, meat, and waste products, particularly from sheep, goats, cattle, pigs, and dogs.

8.2.2.1 Animal domestication as a source of new infections

Evidence suggests that several pathogens were transferred to humans from domesticated animals between 5,000 and 10,000 years ago (Table 8.1), including measles, caused by a morbillivirus which is similar to the rinderpest virus of hoofed mammals. Similar origins had been proposed for tuberculosis, caused by *Mycobacterium tuberculosis*, a bacterium closely related to *M. bovis* (the agent of bovine tuberculosis). More recent phylogenetic analyses indicate that modern-day *M. bovis* isolates arose from an ancestor of *M. tuberculosis*, making the directionality of transfer among species uncertain (Brosch et al. 2001; Mostowy et al. 2002). Rabies is another prominent disease triggered by contact between humans and domesticated animals. Although rabies cannot be sustained in human populations alone, human cases probably increased dramatically following the domestication of dogs, with evidence of human cases of rabies dating back at least 4000 years (Weiss 2001).

Animal domestication not only provided opportunities for host shifts to humans and increased exposure to zoonotic agents, but also favored new transmission strategies, as exemplified by *Toxoplasma gondii*, the pathogen responsible for toxoplasmosis infections in humans and other mammalian hosts. This parasite originally had a complex life cycle with transmission alternating between two hosts—a definitive carnivore host and an intermediate herbivore host (Sibley 2003). A recent genetic analysis suggested that the origins of a second, direct transmission strategy (via a fecal-oral route) occurred around the same time as agricultural expansion (ca.10,000 year ago), providing support for the hypothesis that this parasite evolved rapidly in response to selection driven by agrarian lifestyles (Su 2003).

8.2.2.2 Urbanization and parasite transmission

During the early stages of civilization, growing human populations provided larger numbers of susceptible hosts that were aggregated around cities or other relatively permanent settlements, with significant consequences for sustaining many of the contact-borne pathogens that are well known to modern humans (McNeill 1977). Crowding of humans into urban centers probably intensified outbreaks of infectious diseases, and cities fostered infections as centers for trade and via contaminated water supplies and poor sanitation (Diamond 1997). In Chapter 4, we discussed the concept of a "critical community size" for infectious diseases, defined as the population threshold below which infections cannot persist. Measles infections in human populations show one of the clearest examples of such a population threshold, with cities of less than 250,000 people unable to support continued measles cases without periodic reintroduction (Bartlett 1960a; Keeling and Grenfell 1997a). The local population sizes of most wild primates probably rarely, if ever, exceed the size needed to sustain acute, contact-transmitted infections, such as measles, influenza, and rubella.

Infectious diseases associated with urban centers also include cholera, transmitted by contaminated drinking water, and typhus and plague, endemic in rodents and transmitted to humans following contact with their fleas or lice (Table 8.1). Again, these infections appear to be largely absent from wild primate populations, either because primate groups do not commonly associate with rodent reservoirs, or because waste accumulation in primate societies rarely reaches the levels seen in human settlements. Human cases of cholera, a diarrheal disease spread by fecal-oral transmission and caused by the bacterium *Vibrio cholerae*, can occur following contact with aquatic reservoirs, while "secondary" or "human-to-human" transmission occurs via shared food and water resources (Colwell 1996). The build-up of wastes around permanent settlements and contamination of drinking water necessary for widespread cholera epidemics occur more commonly around cities, although patterns of rainfall and temperature also play crucial roles (Pascual et al. 2002). Other pathogens associated with diarrheal diseases (e.g. *Shigella* and *Salmonella*) have been occasionally reported from wild primate populations (Kourany and Porter 1969; Nizeyi et al. 2001). Whether these infections are caused by contact with humans or wild animals remains unknown.

Plague, a bacterial disease caused by *Yersinia pestis*, was responsible for some of the most devastating epidemics in human history (McNeill 1977). Plague bacteria can be harbored by rats and are vectored by fleas to nonhuman hosts. In humans, *Y. pestis* is associated with plague following contact with infectious fleas, and can also cause another form of plague where transmission occurs by direct inhalation. All forms of plague are highly virulent in humans, causing 75–100% mortality in the absence of medical treatment. Plague likely affected humans throughout ancient times, but the most severe epidemic, commonly known as the "Black Death", occurred in Europe during the 1300s (Ziegler 1969). This epidemic originated in India and spread along trade routes to China, ultimately reaching Europe via rats

that were transported on Italian ships. In total, an astonishing 25–30% of the European population perished from the Black Death between 1346 and 1352 (Ziegler 1969). Recurrent outbreaks followed until the late 1600s, when black rats were overtaken by Norwegian rats (an inferior reservoir host), and changes in housing construction limited human contact with rats (Weiss 2001). Plague is now a rare disease in humans and isolated outbreaks mainly occur following contact with rodents harboring the bacterium. Not surprisingly, cases of plague in wild nonhuman primates are not generally known, probably because sustained outbreaks require a close association with rodents and are favored by conditions in crowded urban centers.

8.2.2.3 Human movements and disease introductions

Also important during the first epidemiological transmission was greater human mobility, both among local communities and also through long-distance trade routes, which increased the ease with which parasites could be maintained in human populations and enabled the long-distance transfer of parasites and pathogens between settlements (Diamond 1997). Indeed, as human populations expanded in places like Europe and Asia, isolated communities that could not sustain prolonged outbreaks of "human specialist" pathogens probably became connected by networks of local and long-distance dispersal.

Smallpox is one example of a viral disease that achieved a nearly worldwide distribution following the rise of urban centers and global colonization by Western societies (see Box 8.2). Specializing exclusively on humans and spread through direct contact, this pathogen might have evolved from an ancestral rodent or cow virus, although its origins remain uncertain (Table 8.1). Smallpox changed the course of human history in multiple ways, most notably by making the colonization of the New World easier for Europeans (Oldstone 1998). Although Aztecs vastly outnumbered Spanish forces in the early 1500s, smallpox spread so rapidly among the Aztec troops, noblepersons, and the general population that their armies were readily conquered by Cortés' forces (Diamond 1997). A similar scenario ensued in North America when British forces deliberately "donated" blankets contaminated with smallpox virus to Native American tribes in the 1700s (Oldstone 1998). Thus, the spread of smallpox in Native Americans vividly illustrates the devastating effects that can result when a pathogen is introduced into a previously unexposed host population.

Unlike many bird species and some large mammals, wild primates are not known for long-distance migration. Thus, compared to humans, pathogen exchanges at a continental or global level are almost certainly rare among nonhuman primates. Furthermore, although cross-populational and cross-species transmission could occur among primate species sharing the same habitats, such biogeographic shifts probably occurred more slowly, possibly allowing time for hosts to evolve adaptations that defend against new pathogens.

8.2.2.4 Loss of parasites in developing civilizations

Not all changes associated with developing human civilizations increased our exposure to infectious diseases; some parasites were lost over time, particularly those for which changes in human diets and hygiene interrupted transmission opportunities. For example, practices associated with washing and cooking of foods, especially meat, probably reduced the transmission of many intestinal parasites, such as tapeworms with complex life cycles. In Chapter 3, we argued that wild primates are often exposed to parasites encountered in their environments while foraging, sleeping, or locating new resources. Food production probably narrowed the diets of many human societies from a wide range of resources obtained through hunting and gathering, to a relatively small number of livestock species and crops. By limiting encounters with parasites in the environment and via food items, the rise of agricultural production and sedentary human populations probably reduced the diversity of parasites transmitted by intermediate hosts and contact with infectious stages in the environment.

In Western societies, a second epidemiological transition coincided with the Industrial Revolution in the middle of the nineteenth century. Although this historical period could have increased the prevalence of some diseases following rural-to-urban migrations, concomitant scientific progress allowed humans to treat and prevent infections by parasitic organisms. Key advances involved better understanding of how pathogens spread and enter hosts, and improved hygiene, sanitation, and health care practices (reviewed in Barrett et al. 1998). The prevalence of many infectious agents and levels of disease-induced mortality were lowered by public health control strategies, with notable outcomes in the twentieth century involving the eradication of smallpox as a global threat (Box 8.2) and the widespread use of DDT to limit the spread of malaria and other insect-borne diseases. In Western societies where drinking water is sanitized and human contacts with rodent reservoirs are minimized, diseases such as cholera, typhoid fever, typhus, and plague have been nearly eliminated. As briefly discussed in Section 8.3.2, several lines of evidence suggest that the loss of parasites for which humans have evolved immune defenses could have some unexpected consequences, particularly in terms of the expression of allergies among both children and adults. With the lengthening of human life spans due to reductions in parasitic infections in industrialized nations, the so-called "diseases of civilization," particularly heart disease and cancer, surpassed infectious diseases as important causes of mortality.

Barrett et al. (1998) argued that humans are in the midst of a third epidemiological transition, marked by the emergence of new diseases in an ever more globally connected world, as well as the evolution of antibiotic resistance among some of our more ancient killers (see also McMichael 2004). Although it is tempting to focus on disease emergence as a modern phenomenon, the large number of infectious agents transferred from animals to humans during the last several thousand years emphasizes that new infectious diseases have appeared repeatedly throughout human history (Lederberg 2000; Weiss 2001). Comparing modern human parasite

Box 8.2 Smallpox, vaccination, and the eradication of a human disease

One of the world's most notorious pathogens is the *Variola* virus in the family Poxviridae—the causative agent of smallpox. This highly virulent disease is the only pathogen known to have been intentionally driven "extinct in the wild" by humans (Fenner et al. 1988). Although the evolutionary origins of smallpox are uncertain, evidence for this virus dates back over several thousand years and includes blisters preserved on the mummy of the Egyptian Pharoh Ramses V, who died in 1157 BC (Behebani 1983). Smallpox continued to cause human suffering throughout recorded history until its eradication in the 1970s. Eradication was accomplished largely through (1) development of a highly effective vaccination campaign, aided in part by smallpox's telltale signs of infection (Fig. 8.2(a)), (2) its exclusive specialization on humans, and (3) the slow rate of spread relative to other contagious diseases, such as measles and influenza.

The term "vaccination" was coined in the early 1800s following reports that dairy maids with cowpox appeared to resist smallpox infection. The doctor and scientist William Jenner discovered that injecting patients with cowpox virus conferred immunity to smallpox (the Latin root word for vaccination, "vacca", refers to cows, and the term *Vaccinia* refers to the cowpox virus; Fig. 8.2(b)). This highly effective practice resulted in lasting immunity in immunized patients (Friedman and Friedland 1998). Even before this discovery, however, injection of fluid from smallpox scabs was used in Europe in the 1700s; it caused a mild form of smallpox with much lower mortality than typical infections. In fact, exposing humans to attenuated virus as a means to prevent new infections can be traced back over 1000 years ago, when Asian cultures inhaled dried material from smallpox lesions or scabs of infected individuals (Behebani 1983). One particularly intriguing historical footnote is the role of Lady Mary Wortley Montagu in bringing this practice of "variolation" to England. After becoming familiar with the practice while in Turkey (where her husband was an ambassador), she later had her children immunized during the early 1700s and helped to gain acceptance of the procedure in her homeland (Behebani 1983).

The World Health Organization launched a global campaign in the 1960s and 1970s to vaccinate humans worldwide, as by that time the disease had been largely eliminated from industrialized nations (Behebani 1983). Smallpox has an R_0 of about 3 to 5, so in theory it should have been driven to extinction in many places by immunizing two-thirds to

(a) (b)

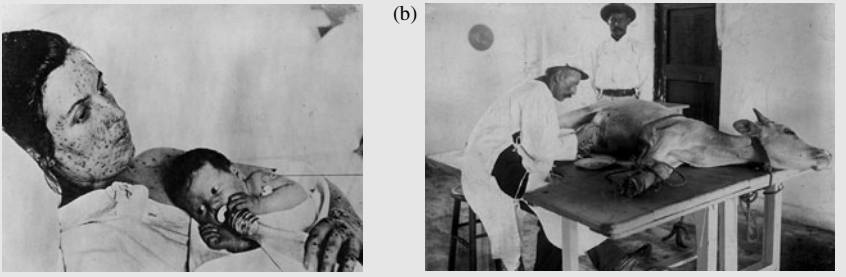


Fig. 8.2 (a) A woman with smallpox holding her vaccinated infant, (b) Cowpox fluid being harvested from an infected cow to be used in vaccinations. Images reproduced from the National Museum of Health and Medicine Gallery (photo credits Reeve 32486 and CP 2611, respectively).

Box 8.2 (*Cont.*)

three-quarters of the population (Anderson and May 1991). By the early 1970s, success had been achieved nearly worldwide, but more intensive efforts were needed to eradicate the disease from the final few remaining countries, including India, Pakistan, Nepal, Bangladesh, and Somalia, where smallpox remained in remote settlements. Thus, even though the critical vaccination threshold for disease elimination had been met at a global level, isolated populations still existed for which few or no individuals had been immunized (Fenner et al. 1988). To achieve final eradication, a search and containment strategy identified areas with remaining cases, and local vaccination of everyone in affected villages and neighboring areas served to eliminate these pockets of disease. The last cases of endemic smallpox were reported in Bangladesh and Somalia in 1975–1977 (Fenner et al. 1988b). By the 1980s, smallpox was considered to be eradicated and vaccination efforts disbanded, with routine vaccination ending earlier (around 1972) in some countries, such as the United States. In the decades since vaccination ended, more susceptible hosts have been recruited into the population through births. For example, nearly half of all US citizens are potentially unprotected against smallpox, which has generated concerns about global smallpox stocks and calls to develop vaccination strategies to respond to potential attacks from biological weapons (Henderson 1998).

assemblages to those from wild primates emphasizes how many pathogens have been acquired by humans over time, and points to several mechanisms—including animal domestication and the growth of large, globally connected populations—that have allowed pathogens to shift into humans and adapt to new transmission opportunities.

8.3 Human responses to infectious diseases: from Darwinian medicine to public health

Because wild primates share a close evolutionary relationship with humans and can harbor many of the same infections (Brack 1987; Chapman et al. 2005a), they are extensively used in biomedical research aimed at understanding how pathogens invade host cells and tissues, how disease develops, and the efficacy of vaccines and drugs used for control measures. Macaques, baboons, chimpanzees and owl monkeys are among the primate species most commonly used to develop new treatments and vaccines for infectious diseases, including research on HIV/AIDS, leishmaniasis, and malaria. Far fewer studies have investigated how free-living primates respond to infectious diseases, both behaviorally and through immune defenses, yet these studies could point to novel strategies for countering infectious diseases in humans, including low-cost approaches for discovering new medicinal plants and behavioral strategies for avoiding infections. Examining parallels in the responses of humans and wild primates to infectious diseases—including dietary and cultural practices, patterns of mate choice, and evolutionary shifts in major histocompatibility

complex (MHC) genes and other genetic responses—could provide a deeper understanding of the ways that infectious diseases have shaped human lifestyles and evolution.

Recent interest in evolutionary medicine, in which human health is viewed in a broad evolutionary framework (Ewald 1980; Nesse and Williams 1996; Stearns 1999; Trevathan et al. 1999), has focused attention on mechanisms underlying the causes of disease, including the adaptive significance of fever, the origins of host immunity, and medical problems not commonly thought to arise from infectious agents (Cochran et al. 2000; Ewald 2000). A particularly striking example involves a possible link between toxoplasmosis and the development of schizophrenia and personality traits, considered in the context of how parasite-induced changes in host behavior might enhance transmission (see Section 2.6 and Box 8.3). These and other examples illustrate how establishing links between infectious agents and human disorders could lead to new approaches to treatment and prevention, as well as general understanding of human cultural practices and physiological responses to disease.

Box 8.3 Evolutionary medicine and human health

The emerging field of evolutionary (or Darwinian) medicine views human health and disease in an evolutionary context (Ewald 1980; Nesse and Williams 1996; Stearns 1999; Trevathan et al. 1999). Examples of research questions that fall under this area include understanding the adaptive function of human physiological responses to infection, such as fever (Nesse and Williams 1996), and the degree to which classical signs and symptoms of infectious disease are a product of pathogen activity versus the host's own response to infection. Researchers have considered the ways that human behavior can modify the evolution of pathogen virulence, primarily by affecting opportunities for parasite transmission (Ewald 1993, 1994a). Other studies consider the ways that life in the modern world produce "diseases of civilization," in part because the environments to which humans might have adapted during the long Paleolithic period are probably very different from the world in which we live today (Barratt et al. 2002). Many researchers who study evolutionary medicine aim to develop clinical applications of their research; in the case of infant health, for example, clinical applications include solutions to deal with colic (Barr 1999) or sudden infant death syndrome (McKenna et al. 1999).

Comparative primate socioecology provides a further evolutionary framework to improve understanding of human responses to infectious disease, the origins of some non-infectious diseases, and behavioral defenses. One striking example involves the evolutionary roots of alcoholism, which although not infectious, does have serious implications for human health. Over 17 million Americans suffer from the effects of alcohol abuse and dependence (Grant et al. 2004), with economic consequences in excess of $180 billion per year in the United States (Harwood 2000). Could understanding selective pressures involving ethanol in the lives of nonhuman primates provide insights to this modern epidemic? Dudley (2000, 2002, 2004) has drawn such a link, based on the importance of fruit in the primate diet and the historical legacy of fruit-eating in humans. Specifically, he proposed that primates could use "ethanol plumes" to locate fruit patches, and may therefore have

Box 8.3 (*Cont.*)

acquired a preference for ethanol as a feeding stimulant. Because ethanol provides nearly two times the caloric value as other carbohydrates, animals could also gain energetically from locating ethanol-rich food sources (Dudley 2000). In nature, the yeast that produces alcohol in decaying fruit would have been unlikely to produce a yield of greater than 5 or 10% ethanol, and relatively few fruits would be likely to contain even these levels. With the development of technology to produce higher alcohol content relatively inexpensively, humans may be capitalizing on an evolutionary legacy, resulting in negative effects on human health. In other words, alcoholism could be seen as an example of nutritional excess (Nesse and Williams 1996), similar to hypotheses for the preference for fatty and high carbohydrate foods in human diets in the modern world.

Another area of research related to evolutionary medicine involves identifying associations between parasites and host responses to infection in ways that provide new insights to the development of disease. A notable example here involves a possible link between toxoplasmosis and the development of personality traits or psychological disorders, including schizophrenia. *Toxoplasma gondii*, the causative agent of toxoplasmosis, typically infects small prey, such as mice, with cats serving as the definitive host. Humans may acquire the intermediate stage of this protozoan by eating infected meat or through exposure to cats and their feces. Studies of toxoplasmosis in rats reveal a reduction in risk aversion (Berdoy et al. 2000), which could increase their chances of becoming prey for a definitive host. Recent studies in humans show that toxoplasmosis might also affect human personality traits by increasing risk-taking behavior (Flegr et al. 1996). Furthermore, by delaying locomotor reaction times (Havlicek et al. 2001), toxoplasmosis is associated with greater risks of being in a traffic accident (among drivers and pedestrians, Flegr et al. 2002a). Studies also showed statistical links between severe infections with *T. gondii* and psychotic symptoms similar to schizophrenia, and exposure to cats during childhood was positively related to the risk of developing schizophrenia later in life (Torrey and Yolken 2003). Given that the prevalence of infection in human populations can reach 60% (Flegr et al. 2002a), a large number of us might be unknowingly behaving in ways that reflect manipulation by this parasite.

Comparative studies of cross-cultural variation in human behavior, such as the use of spices (see Section 8.4, Billing and Sherman 1998), could provide novel insights into how humans manage health and disease risk in an evolutionary and cultural context. Another comprehensive study across human societies pointed to an adaptive role of morning sickness for lowering the risk from infectious diseases and harmful phytochemicals to the fetus during a crucial phase of development. Specifically, Flaxman and Sherman (2000) showed that in cultures where meat or animal products are not "staple food items," there was little or no frequency of morning sickness, whereas in Western societies in which there is a longer history of consuming animal foods, the most common aversion among pregnant women was to meat, fish, poultry, and eggs. These are exactly the items that pose a greater risk of transmitting food-borne illnesses, especially prior to the advent of modern food handling and refrigeration. Examples such as these cast new light on human behaviors that might otherwise appear maladaptive or inexplicable. More generally, evolutionary medicine proposes that knowledge of evolutionary history and ecology can provide insights to human health, while also pointing toward new tools for combating infections, including ways that humans might change their behavior to reduce the transmission and severity of infectious diseases over longer timescales.

8.3.1 Behavioral responses to infectious diseases

Just as nonhuman primates exhibit a variety of behaviors to limit their exposure to infectious disease (Chapter 5), humans employ many behavioral defenses to avoid or eliminate infections. These include dietary customs, religious rituals, agricultural techniques, and methods for childcare and traditional medicine (Inhoof and Brown 1990). Simple actions such as washing hands after using the toilet play a substantial role in limiting the spread of fecally transmitted diseases, and condom-use has slowed the spread of HIV in western societies. To reduce contact with insect vectors that transmit debilitating diseases, people in the tropics commonly sleep in rooms with screens on the windows, or use mosquito nets when screens are unavailable (e.g. Pålsson et al. 2004). These human behaviors have their parallels in nonhuman primates; for example, New World primates use "closed" sleep sites that potentially reduce their risk of acquiring malaria (Nunn and Heymann 2005, see Fig. 5.10).

Some primates even show evidence for cultural transmission of food-washing behaviors (McGrew 1998), exemplified by Japanese macaques that dip potatoes in the ocean, possibly for adding a salty flavor to food (Watanabe 1994), but perhaps also for hygienic purposes, as macaques living farther from the sea washed food items in a stream (Nakamichi et al. 1998). Chapter 5 revealed other behavioral defenses used by nonhuman primates, including the ways in which primates use medicinal plants. Humans in non-Western societies use a similar variety of medicinal treatments, and in industrialized societies we are bombarded with new remedies for a wide range of ailments and infections, with plant-derived compounds representing potential sources of new drugs that remain under-explored by contemporary pharmaceutical companies (Farnsworth 1988). In what follows, we highlight a few examples to illustrate how comparisons with nonhuman primates provide insights into human behavioral defenses to disease.

8.3.1.1 Behavioral defenses to sexually transmitted diseases

An interesting place to start is with human STDs. Across cultures, Donovan (2000b) described the fascinating diversity of behaviors that modern humans use to reduce the risk of contracting STDs, including urinating after "risky" sex, and even drinking large quantities of beer! (Neither of which, we should add, have been shown to be effective preventative measures.) Humans in modern times can use condoms as a physical barrier to prevent the spread of STDs, but this option is clearly not available (and unlikely to be developed!) for nonhuman primates. And of course condoms were similarly unavailable throughout most of human history and evolution.

Other options for behaviorally avoiding STDs likely arose throughout primate evolution, with humans developing additional solutions. Thus, Donovan (2000a, b) documented that in some cultures, people inspect the genitals of potential mating partners, and that individuals wash their own genitals after sex. Many potentially similar behaviors are found in nonhuman primates, including manual and oral genital self-grooming after mating, pre-copulatory inspection of a partner's genitals, and

post-copulatory urination (Nunn 2003). Whether these behaviors are effective in preventing venereal disease, however, is another question, with few convincing correlations between these behaviors and measures of STD risk across primate species (Nunn 2003), and little evidence for their effectiveness in humans (Hooper et al. 1978). In wild primates, alternative motivations can better explain some behaviors, such as males inspecting female genitals to assess the probability or timing of ovulation (Dixson 1998).

Monogamy is another potential counter-measure to the problem of STDs. This strategy, discussed in previous chapters, is practiced (or, at least encouraged) in many human societies and should reduce the spread of STDs, although monogamy is far from a universal practice in humans (Marlowe 2000), and is not always practiced by so-called "monogamous" primates (Palombit 1994; Reichard 1995). In humans, monogamy as a favored mating strategy might also function as a means for males to control female reproduction, or as a strategy used by both sexes to maximize investment from each partner in offspring (e.g. Marlowe 2000). In modern humans, sexual acts are often motivated by non-reproductive benefits, and it is conceivable that this would result in more STDs in humans than in nonhuman primates. However, nonhuman primates also mate at times when conception is impossible, such as during pregnancy (van Schaik et al. 1999). Because many primate species are remarkably more promiscuous than humans, their mating systems should offer many opportunities for the establishment of STDs (Nunn and Altizer 2004).

In a provocatively titled paper, "Sexually transmitted disease and human evolution: survival of the ugliest?," Immerman (1986) proposed that STDs played a major role in the evolution of monogamy in human societies (see also Immerman and Mackey 1999). Specifically, the reproductive costs of STDs could have exerted substantial selective pressures on humans, particularly in terms of female sterility, resulting in behavioral and physical changes to reduce exposure to venereal disease. It remains unclear why STDs would have been more important in humans than in other primate lineages, other than the simple fact that humans appear to harbor an impressive array of STDs (Holmes et al. 1999; Immerman and Mackey 1999). The large number of STDs in humans in fact suggests that the behavioral strategies proposed by Immerman were *not* particularly effective, or that we simply know far less about STD infections in other species (Lockhart et al. 1996).

In modern-day human societies, some behaviors implemented to limit the risk of pregnancy and the spread of certain STDs could favor the sexual spread of other infections less commonly associated with venereal disease. As one example, herpes simplex virus-1 (HSV-1) typically causes oral herpes, whereas HSV-2 has been the most common cause of genital herpes. The highest rate of exposure to genital herpes infections occurs in young adults following the onset of sexual activity, and prevalence increases with age and the cumulative number of sexual partners (Stanberry and Rosenthal 1999). Changing sexual practices among adolescents and young adults, including more frequent oral–genital contact and increased condom use, has been linked to a growing number of cases of "first episode" genital herpes caused by HSV-1 relative to HSV-2, particularly among younger adults and women (reviewed

in Roberts 2005). This epidemiological change suggests that oral–genital sex might be an often-overlooked but important risk factor in the spread of STDs, and that studies aimed at quantifying different forms of sexual contact in relation to disease risk could provide insights into their consequences for the spread of pathogens transmitted sexually and by other forms of close contact.

To offer yet another possible behavioral defense against STDs, some people have a predilection for shaving their pubic hair, with this behavior potentially providing aesthetic or erotic benefits, and also reducing suitable habitat for pubic lice (*Phthirus pubis*, Donovan 2000a). Humans are also known for the sparseness of hair on most other parts of the body, raising the possibility that the evolutionary loss of hair more generally is a response to parasite risk, as proposed in a stimulating paper by Pagel and Bodmer (2003) titled "A naked ape would have fewer parasites." Mammalian hair offers an ideal habitat for a variety of ectoparasites, and some of these parasites can cause debilitating diseases such as plague (often transmitted by fleas from rodents) and scabies (Macfie 1996; Graczyk et al. 2001; Kalema-Zikusoka et al. 2002). Indeed, ectoparasites such as lice, mites, and ticks can lower the fitness of infected hosts, particularly among juveniles or hosts that are stressed for other reasons (Arnold and Lichtenstein 1993; Lehmann 1993). Pagel and Bodmer (2003) proposed that when humans began using clothing and fire, they depended less on their own layer of protective hair for maintaining body heat and reducing exposure to the sun and other elements. Like hair, clothing can harbor ectoparasites. But Pagel and Bodmer (2003) argued that parasites can be removed easily from clothing, and that heavily infested clothes can be exchanged for new ones. This interesting hypothesis deserves to be tested, for example by investigating levels of "hairiness" among human populations that vary in their exposure to ectoparasites (Pagel and Bodmer 2003). On the other hand, as noted by Pagel and Bodmer (2003), hirsuteness may also be important in sexual selection, for example in female choice for sexually mature males with more body hair as an indicator of age and endocrine condition (Dixson et al. 2003). Along similar lines, Kittler et al. (2003) used phylogenetic methods to date the divergence of human lice into a lineage that specializes on head hairs as a habitat, and another lineage that uses the rest of the body (and can also live in clothing). They estimated that this evolutionary split occurred 107,000 years ago (Kittler et al. 2004), thus providing an estimated date for the origins of clothing in human evolution.

8.3.1.2 Parasites and sexual selection in humans

Parasite mediated sexual selection provides an intriguing framework for considering the evolution of human behavior in the context of infectious disease. Parasites have been implicated as driving sexual selection in animals (Hamilton and Zuk 1982; Folstad and Karter 1992; Able 1996), with the benefits of choosing uninfected mates outlined in Chapter 5—but do similar processes operate in humans? One of the first studies to address this question used cross-cultural data covering 93 societies. With a database on seven types of acute or debilitating parasites, including *Leishmania,*

Plasmodium, Trypanosoma, Schistosoma, and *Wucheria*, Low (1987) found a positive association between a categorical measure of disease risk (reflecting the presence and prevalence of parasitic infections), and five measures of polygyny (out of six that she investigated, based on the percentage of women in polygynous relationships). Associations between pathogen pressure and human status signals were only marginally significant (see also Low 1990). These results indicated that parasites might drive increases in sexual selection and reproductive skew in human mating systems, possibly through a "good genes" mechanism.

A later study found a significant positive association between a similar measure of parasite pressure and the value placed on physical attractiveness in potential mates, using survey data from 29 human societies where both males and females rated the degree to which outward appearance was important in selecting a mate (Gangestad and Buss 1993). The association between mate choice and parasitism remained strong after the authors further controlled for other variables that likely influenced parasite risk (including latitude and average income). More recently Roberts et al. (2005) addressed possible mechanisms that underlie such associations by comparing measures of heterozygosity across three MHC loci in humans (HLA-*A*, HLA-*B*, and HLA-*DRB1*) against measures of human facial attractiveness. In this study, females assigned higher attractiveness scores to the faces of more heterozygous men as opposed to those who were homozygous at one or more loci. Heterozygosity was also positively associated with facial symmetry as determined by image analysis and "skin patch healthiness." Because the variety of molecules produced by MHC loci control the range of pathogens recognized by vertebrate immune systems (see Box 5.3), these results suggest that females might select mates resistant to a wider range of pathogens by using facial appearance as an indicator of underlying genetic variation at loci that influence susceptibility to disease. This study complements earlier work in humans suggesting that females can use olfactory cues to choose mates with dissimilar MHC genotypes (Wedekind et al. 1995). Future studies of the role of MHC polymorphism in relation to mate choice and disease resistance in wild primates should provide useful comparisons for evaluating the mechanisms that underlie these associations and their importance in primate evolution (see Section 5.2.1.5 and Box 5.3).

8.3.1.3 Sickness behaviors and medicinal plants

As in nonhuman primates, sickness behaviors are also an integral part of the recovery process in humans, especially in the case of resting during the day to facilitate recovery. Thus, "sick day" is a widely used term throughout industrialized societies, with schools and businesses allowing recovery time for those who have fallen ill. Just as chimpanzees build day nests and convalesce when they suffer from parasitic infections (Takasaki and Hunt 1987; Huffman and Seifu 1989; Krief et al. 2005), humans use their own sleeping quarters (or sleeping sites available elsewhere) when infected by virulent parasites.

Humans have long possessed a diverse pharmacopoeia, usually based on local plants thought to have medicinal properties (e.g. Etkin 1994; Schultes and Von Reis 1995; Sumner 2000). This knowledge has developed into a colossal economic interest based on plants used as herbal medicines, and plant derivatives as sources of medicinal drugs for the global pharmaceutical industry. In the United States, one quarter of all prescription drugs are derived from plant compounds (Farnsworth and Morris 1976). Yet despite the global importance of plant-derived drugs and record amounts of spending on research and development by pharmaceutical companies, Farnsworth (1988) noted that no firms in the United States engage in active research aimed at drug discovery from plants. Studies of natural compounds used in traditional medicine systems and variation in plant use by nonhuman primates could therefore represent an untapped resource for introducing new drugs or treatments for infectious disease into Western societies (Newton 1991; Glander 1994; Sumner 2000).

A comparative study that focused on the medicinal value of plant-derived products in relation to human–microbe interactions deserves mention here for its original approach. Billing and Sherman (1998) set out to answer a basic and fascinating question: why do humans include spices in food preparation? Using recipes for meat-based dishes from more than 30 countries, the authors quantified the use of 43 different spices, which also included onions and chili peppers. They showed quantitatively that (as expected) spices are more common in cuisines from countries characterized by a hotter climate (Fig. 8.3). Based on additional findings that spices inhibit the growth of a wide diversity of bacteria, Billing and Sherman (1998) concluded that the geographical distribution of spicy foods reflects a need to prevent food spoilage caused by bacteria in hotter climates. They were also able to rule out alternative explanations involving nutritional benefits of spices, use of spices to conceal the taste or smell of spoiled food, and use of spicy foods to promote perspiration for

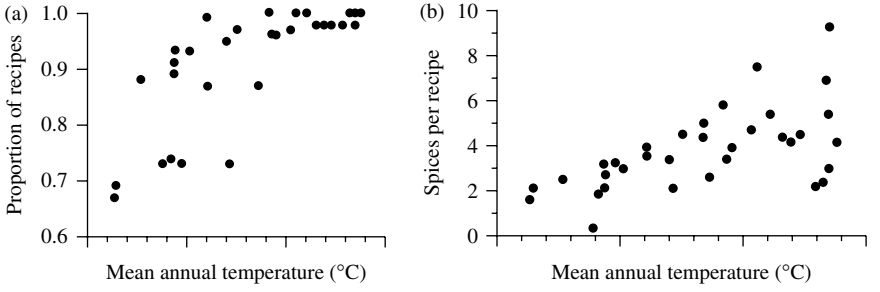


Fig. 8.3 Relationship between mean annual temperature and the spiciness of recipes among 36 cuisines. Significant positive associations were found between mean annual temperature and (a) proportion of meat-based recipes that require at least one spice and (b) average number of spices used per recipe. Both relationships are statistically significant. Reprinted from J. Billing, and P. W. Sherman. Antimicrobial functions of spices: Why some like it hot. *Quarterly Review of Biology*, 73, 3–49. Copyright (1998) by University of Chicago Press.

evaporative cooling. If this hypothesis is correct, enjoyment of a spicy curry or Mexican dish could owe as much to bacterial organisms as it does to human ingenuity and cultural evolution. It remains possible, however, that a greater diversity of plants near the equator could provide more opportunities for those societies living in equatorial regions to use spices.

Although human behaviors can improve hygiene and health, many cultural practices have the opposite effect and can actually enhance the spread of infectious diseases. One example popularized by Richard Rhodes's book "Deadly Feasts" (1997) is the role of cannibalistic post-mortem rituals in transmitting kuru, a prion disease of aboriginal humans inhabiting the New Guinea highlands. Similarly, increased contact with water, as occurs through irrigation of fields or via religious rituals, or dam building in developing or industrialized societies, can increase human exposure to schistosomiasis in areas where this disease is endemic (Inhorn and Brown 1990). Clearly, more studies are needed on cultural practices that influence disease transmission. To that end, increased collaboration between anthropologists, medical doctors, and primatologists interested in health issues will likely provide new insights to a wide range of basic research in biomedicine and health care. These insights might greatly reduce human exposure to and suffering from common health problems such as diarrheal diseases, vector-borne diseases and STDs.

8.3.2 Evolution of immune defenses and resistance traits

In free-living animal populations, parasite-mediated selection should increase the frequency of resistant phenotypes (briefly reviewed in Box 6.1). This same process applies to humans, with pathogens increasing the frequency of traits conferring resistance and generating divergence among populations exposed to different levels of infection. In some cases, selection driven by infectious diseases might follow rapid epidemics, as occurred when nearly one third of all Europeans died from the Black Death during the bubonic plague of 1348–1349 (Ziegler 1969), or during the 1918 influenza pandemic that killed 20–40 million people worldwide (Oldstone 1998). Other epidemic-prone human diseases include dengue and yellow fever, cholera, and leishmaniasis, some of which also infect nonhuman primates and have high case fatality rates in humans (between 10% and 50% in the absence of effective medical treatment, WHO 2000). Moderate disease-induced mortality or lost opportunities for reproduction might generate evolutionary responses over longer timescales, as could occur for STDs in women of child-bearing age.

Perhaps the best-known examples of parasite-mediated selection on humans are hemoglobin-related disorders that confer resistance to *Plasmodium*, including sickle-cell anemia (arising from the abnormal hemoglobin gene HbS) and glucose-6-phosphate dehydrogenase (G6PD) deficiency (Min-Oo and Gros 2005). These traits probably date back to the appearance of falciparum malaria (estimated as the earliest malaria parasite to infect humans) and can reach unusually high frequencies in some malaria-endemic regions. Balancing selection on both of these traits arises

from malaria resistance among heterozygotes on the one hand, and severe anemia in homozygous individuals (reviewed in Templeton 1982; Tishkoff and Verrelli 2003). Despite the incredible diversity (ca. 26 species) and often high prevalence of *Plasmodium* across a range of primate species (Box 8.1), data on genetic polymorphisms associated with blood disorders and malaria resistance are not widely available from natural primate populations (but see Migot-Nabias et al. 1999, Matsumoto et al. 2000). Population-level studies of malaria resistance traits in relation to *Plasmodium* prevalence in wild primates could reveal whether different malaria parasites have selected for similar resistance traits in other primate species, and how selection pressures have changed with the history and frequency of association with different parasite species.

Molecular genetic data can be combined with population genetic frameworks to uncover the effects of disease in human populations (Hill 2001). As one example, Galvani and Slatkin (2003) used population genetic approaches to infer past selection pressure on the gene deletion CCR5-Δ32, an allele that confers resistance to HIV infection. This gene occurs at elevated frequency in some northern European populations (around 10%) but is absent from native African populations (Liu et al. 1996). Although the CCR5 mutation is probably under intense selection in human populations with high HIV prevalence, the timing of its origin (now estimated at over 1000 years ago) and its geographic occurrence suggest that HIV did not cause the present distribution of CCR5-Δ32. Some authors instead attributed its distribution to episodic selection driven by plague in Europe between 1300 and 1600 (Stephens et al. 1998). However, other authors suggest that smallpox is a more plausible historical cause of the high frequency of CCR5-Δ32 in European populations (Galvani and Slatkin 2003).

Inferring past scenarios based on geographic variation in genes with major effects on disease susceptibility could be strengthened by population-genetic studies across species of wild primates that vary in their exposure to closely related pathogens. It is also important to note that whereas a few genes show strong effects on disease resistance in humans, many others have weaker associations (with example pathogens including viral hepatitis, tuberculosis, and leprosy)—suggesting that in the majority of studies, researchers will need to apply molecular and statistical tools that consider polygenic inheritance of disease susceptibility as opposed to inferences based on single-genes (Hill 2001). With the chimpanzee genome now completed and detailed comparisons with the human genome underway (Chimpanzee Sequencing and Analysis Consortium 2005), comparative genomics across primate species could point to new sites for disease resistance genes in humans.

In terms of MHC-complex genes, pathogen-mediated selection can generate diversity crucial for human immune defenses against infectious diseases. One might expect that humans should, on average, show a greater number of MHC alleles than many nonhuman primates, especially in comparison to primate species known to harbor relatively few parasites. Similarly, human populations historically exposed to fewer pathogenic diseases might show lower levels of MHC diversity than populations from parasite-rich regions. This latter hypothesis is supported in part by

observations of fewer MHC alleles among South American Indians relative to humans from other regions, which could be due to genetic bottlenecks during human colonization of the New World, but could also result from the lower historical exposure of Native Americans to infectious diseases (Van Blerkom 2003). As suggested by Frank (2002), finer-scale comparative studies of variation at particular MHC genes can point to evidence of past selection operating on genes that confer resistance to specific pathogens, as seen, for example, by lower variation across several MHC Class I loci in chimpanzees (de Groot et al. 2002).

More generally, research that examines human immune responses from ecological and evolutionary perspectives is badly needed to balance the large number of biomedical studies on immunity. This includes field studies that quantify immune function among human populations that differ in their ecological interactions with parasites (McDade 2003). For example, in light of the costly nature of some host defenses, tradeoff theory suggests that individuals that invest in "maintenance" functions like parasite resistance might have fewer resources to invest in growth and reproduction (Sheldon and Verhulst 1996; Norris and Evans 2000). Evidence supporting this idea has been reported from birds, mammals, and insects (Demas et al. 1997; Nordling et al. 1998; Moret and Schmid-Hempel 2000; Derting and Compton 2003; Lindstrom et al. 2004, see also Section 5.2.1.4). If applied to humans, this hypothesis predicts that both within and among populations, we should find a negative relationship between individual investment in immune defenses and measures of reproduction or growth, with high levels of immune defenses leading to lower rates of childhood development or lower than expected fertility (McDade 2003). Combined field and comparative studies across human cultures or populations could explore ecological variation in measures of immune defenses and their associations with parasite burdens and population demographic variables (McDade and Worthman 1999). It is important to note, however, that researchers will need to control for variation in resource levels, which should positively affect both growth and immune defenses, and for the infection status of individuals, which could elevate immunity and lower growth or other fitness measures.

Studies of immune defenses in nonhuman primates can stimulate and inform comparative studies of immune defenses conducted across human populations or cultures. For example, one recent analysis from nonhuman primates showed a positive relationship between investment in immune defenses and factors affecting disease risk (including mating promiscuity and body mass, see Box 5.1 and Fig. 1.2, Nunn et al. 2000; Nunn 2002a,b). Such work might also point to nutritional factors and other ecological variation important to the maintenance of immune defenses, and cross-cultural comparisons could identify immune defenses that appear to target specific types of disease-causing organisms (McDade 2003). Researchers could, for example, examine ethnographic variation in behaviors such as breast-feeding that are linked with infectious diseases, transmission of maternal antibodies, and infant health and survival. Thus, when the risk of infant mortality due to infectious diseases is high, women could spend more time breast-feeding to transfer antibodies that protect their infants from harmful diseases (McDade and Worthman 1999). This

prediction is complicated by socioeconomic factors, including use of infant formula in developing countries. More generally, the hypothesis could be tested easily in nonhuman primate populations in which variation is found among individuals, groups, or populations in rates of disease-related infant mortality.

Finally, it is worth noting that the loss of some parasites from Western societies could play a role in mechanisms that underlie seemingly maladaptive responses of the immune system, including allergic reactions, asthma, and even chronic bowel diseases. Correlative evidence indicates that children raised in more sterile urban environments or in smaller families (i.e. those with fewer siblings) are more likely to develop allergies such as hay fever or asthma, as compared with children raised in rural farm settings and those from larger families (Alm et al. 1999; Braun-Fahrlander et al. 1999; Upham and Holt 2005). In a different example, disorders such as ulcerative colitis, irritable bowel syndrome (IBS), and Crohn's disease (in which the gut lining becomes chronically inflamed) are more common among humans in Western societies where modern sanitation has dramatically reduced the frequency of infection with parasitic worms (reviewed in Weinstock et al. 2005). Experimental studies showed that mice that expressed IBS were less likely to develop disease when they were infected with parasitic nematodes (Elliott et al. 2004), and limited experimental trials in humans show that patients with Crohn's disease reported reduced symptoms following the ingestion of pig whipworm (*Trichuris suis*) eggs (Summers et al. 2005). Although the processes that cause human immune systems to overreact later in life remain uncertain, one hypothesis is that conditions like allergies and IBS are triggered by the relative development of humoral versus cell-mediated immunity in early childhood (Eisenbarth et al. 2004). While it remains too early to determine whether the loss of parasites that coevolved with humans over many millennia plays a significant role in triggering these disorders, these observations suggest that the elimination of infectious diseases might not always have positive consequences for human health and could point to novel strategies for treating such conditions in the future (Bufford and Gern 2005).

8.4 Global patterns of disease risk among contemporary human societies

Medical advances during the last two centuries, including progress in vaccine development and antimicrobial drugs, led many people to believe that human battles with infectious diseases were coming to an end. In 1967, the US Surgeon General, William H. Stewart, declared that "the war on infectious diseases has been won" (Fauci 2001). To counter this optimism, recent decades have witnessed the rapid evolution of drug resistance in microbes, the gradual disuse of DDT following the evolution of resistance in mosquitos and its negative effects on wildlife, and the appearance of new pathogens in human populations, including the discovery of AIDS in 1981 (Lederberg et al. 1992, 2000). In light of the fact that parasite burdens remain high in the twenty-first century (Morens et al. 2004), studies aimed at understanding

global patterns of parasitism in humans and wildlife provide a means to target at-risk populations before infections cause even greater problems.

Just as comparative studies of infectious disease provide insights to the links between parasites and primate socioecology, similar approaches can be taken to study infectious disease in humans, as illustrated by several examples earlier in this chapter. Recent "macro-epidemiological" studies examined whether life history variables and climatic factors correlated with disease risk across human populations (Low 1990; Gangestad and Buss 1993; Guégan et al. 2001; Guernier et al. 2004). Similarly, geographical approaches can provide insights to the areas where infectious disease is most likely to emerge as a threat to human populations. Thus, global maps of emerging infectious diseases (EIDs) in humans show that during the past-half century, most cases of disease emergence occurred in North America, Europe, and Japan (rather than in the tropics), a result that might reflect the chronic overuse of antibiotics and greater levels of international travel by individuals in Western societies (P. Daszak, personal communication and see Kaiser 2005). Studies such as these that capitalize on comprehensive bioinformatics databases of geo-referenced parasite occurrence can provide novel perspectives on global public health concerns.

A useful staring point for understanding contemporary patterns of infection is to investigate the demographic, ecological, and geographical factors that influence infectious disease risk in humans. In one comprehensive study spanning 150 different countries, Guégan et al. (2001) investigated whether the diversity of infectious diseases corresponded to human life history and socioeconomic variables, including population density and growth rates, mortality and fertility rates, and per capita gross national product (GNP). Parasite data reflected the presence or absence of up to 16 different infectious diseases or types of disease, including malaria, schistosomiasis, Dengue fever, and hepatitis A and B. Unlike cross-species patterns of parasite diversity observed in wild primates (Nunn et al. 2003a), population density was not a significant predictor in the analysis of human data, perhaps due to the tremendous heterogeneity in density captured by each country (suggesting that follow-up analyses at a finer spatial scale could be useful). Instead, results showed a consistently strong positive association between female fertility and the total diversity of infectious diseases (Fig. 8.4). In poorer countries, greater mortality rates (as might be caused by high parasite pressure) could lead to earlier female reproduction or higher total numbers of children—although the authors were unable to identify the causative mechanisms underlying this association (see also Guégan and Teriokhin 2000). In a related study, Thomas et al. (2004b) reported that human birth weights were higher than expected in countries with greater levels of parasite pressure, indicating that in developing countries, parasites might select for larger infants (as past studies showed that infants with low birth weights demonstrate poorer immune function and greater disease susceptibility, Chandra 1991; Moore 1998).

From an environmental perspective, several researchers have argued that the diversity and virulence of infectious diseases should be higher in the tropics than in more temperate areas (Møller 1998; Sattenspiel 2000). Such a pattern might arise from a higher diversity of host species—including vectors and intermediate hosts—so

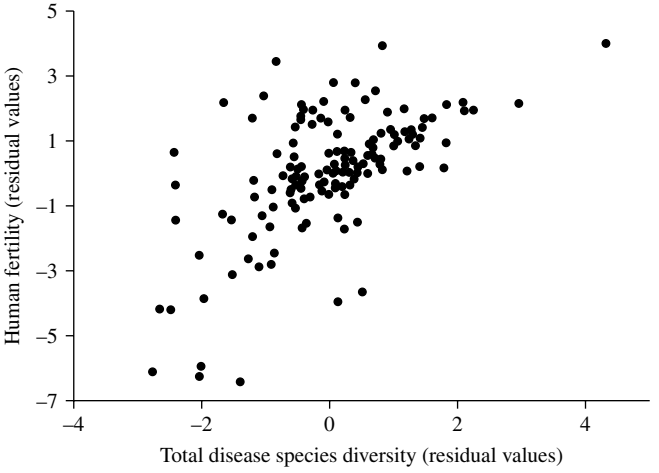


Fig. 8.4 Association between female fertility (measured on a per country basis) and the diversity of parasites and infectious diseases in humans (from a total of 16 possible pathogens). Data are shown as residual values from a multivariate analysis, controlling for key environmental, demographic, and socioeconomic factors. From "Disease diversity and human fertility" by J. F. Guégan, F. Thomas, M. E. Hochberg, T. de Meeus, and F. Renaud. *Evolution*, vol. 55, pp. 1308–1314. Copyright (2001), reproduced with permission of the Society for the Study of Evolution.

that global patterns of parasite diversity more generally mirror latitudinal biodiversity gradients (Rohde 1978; Gaston 2000; Willig et al. 2003). Warmer temperatures could also favor vector-borne diseases and other parasites with stages that persist outside of human hosts (for reasons addressed in Chapter 3). Among wild primate hosts, Nunn et al. (2005) showed that the diversity of protozoan parasites, including vector-borne protozoa, increased toward the equator (see Fig. 3.14). Across human societies, Guernier et al. (2004) also found that the diversity of parasites shows a latitudinal gradient, with more diverse pathogen communities closer to the equator (Fig. 8.5, see also Low 1990). This association held for both Northern and Southern Hemispheres and in most subgroups of parasites examined. The authors also investigated climatic variables, including mean annual temperature and precipitation, and found that the annual variation in precipitation corresponded most strongly (and positively) to the richness of several parasite groups, and that mean annual temperatures were positively related to the diversity of indirectly transmitted viruses and protozoa (Guernier et al. 2004).

Future studies could examine whether patterns of infection in humans and nonhuman primates show overlapping geographic distributions and respond to similar ecological drivers. Molecular analyses of geo-referenced samples of pathogens isolated from humans and wild primates—including vector-borne viruses that cause

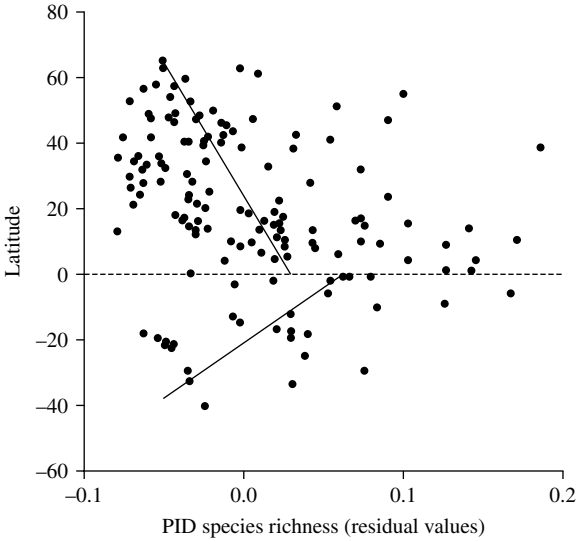


Fig. 8.5 Parasite diversity in relation to latitude in humans. Humans living in countries closer to the equator experience a higher diversity of parasitic and infectious diseases (PID). PID residuals controlled for total surface area, population size and density, gross national product, and multiple environmental and demographic variables. A similar pattern was found in a cross-species study of nonhuman primates (see Fig. 3.14 and Nunn et al. 2005). Figure redrawn from V. Guernier, M. E. Hochberg, and J. F. Guegan (2004). Ecology drives the worldwide distribution of human diseases. *PLoS Biology*, 2, 740–746.

Dengue and Mayaro fever, several *Plasmodium* and *Schistosoma* species, and bacteria associated with treponemal diseases (syphilis and yaws)—could further indicate whether these parasites have differentiated among host groups or are frequently exchanged between humans and nonhuman primates. Thus, data on the geographic heterogeneities and the host ranges of pathogens in wild primates could help generate "risk maps" for some human infectious diseases (see also next section).

Yellow fever is a prime example of a mosquito-borne virus that affects humans, is endemic in wild monkeys in tropical regions, and has a strong geographical component to its transmission. In humans, yellow fever causes a virulent hemorrhagic disease with symptoms including fever, chills, bodily hemorrhaging, and black vomit (Baldacchino and Bertagnoli 2002). African monkeys are the natural reservoirs for yellow fever virus, and the virus was probably transported to the Americas via the human slave trade in the 1600s. In South and Central America, yellow fever became established in New World monkeys (Haddow 1969; Oldstone 1998), which ultimately influenced patterns of infection among humans in this region. Perhaps indicative of its more recent arrival in the New World, yellow fever appears to cause greater pathology and mortality among Neotropical monkeys relative to Old World

primates (Sessa et al. 1999), although comprehensive mortality data in New and Old World primates are lacking. Of great relevance to humans, yellow fever undergoes both urban and sylvatic transmission cycles. In the sylvatic cycle, mosquitoes that feed on forest monkeys transmit the virus, leading to sporadic cases among humans exposed to forest mosquitoes; in the urban cycle, major epidemics can occur in areas of high human density that also support significant populations of the primary human vector, *Aedes aegypti*.

Once established in the Americas, yellow fever caused devastating outbreaks in humans, extending northward into the United States, including Philadelphia and Memphis (and causing up to 50% mortality rates). It is estimated that yellow fever delayed construction of the Panama Canal by 100 years because of the high mortality that it caused among workers (Oldstone 1998). In the early 1800s, the disease also reportedly helped US president Thomas Jefferson negotiate the Louisiana Purchase from the French, as Napoleon viewed the Americas as a hostile and unpleasant environment, due in part to yellow fever-induced deaths (Baldacchino and Bertagnoli 2002). Around 1900, US medical researcher Walter Reed uncovered the role of domestic mosquitoes in yellow fever transmission, and mosquito eradication efforts, together with an effective vaccine developed around 1950, largely eliminated yellow fever from human settlements (Oldstone 1998). However, eradication efforts for yellow fever slowed following a growing awareness of the sylvatic cycle in regions where this virus is endemic in wild primates. Under these circumstances, widespread vaccination of wild primates (and preventing human exposure to forest mosquitoes) would be needed to eliminate the risk of future human cases. Indeed, even though humans are no longer a dominant host for yellow fever, recurrent cases continue to arise when mosquitoes bite infected monkeys and pass the infection on to humans (Haddow 1969; Robertson et al. 1996). The high prevalence of yellow fever virus in some nonhuman primates (Felsenfeld 1972) and encroachment of humans into forested areas probably means that periodic outbreaks of yellow fever will continue in the Old and New World tropics for the foreseeable future.

8.5 Wild primates and emerging infections in humans

Recent decades have seen the appearance of many new infectious diseases in human populations, including HIV/AIDS, SARS, Ebola hemorrhagic fever, and hantavirus pulmonary syndrome (Garrett 1995; Schwartlander et al. 2000; Galvani 2004; Morens et al. 2004). Despite their importance, the factors that underlie emerging infectious diseases (EIDs) remain elusive. One finding is that most human EIDs are viral and can readily cross the boundaries between humans, wildlife, and domesticated animals. In one analysis, Taylor et al. (2001) found that 61% of human pathogens could be shared with animal hosts. Ashford (2000) suggested that this number may actually be higher, closer to 90%. In their study, Taylor et al. (2001) identified 175 parasites classified as EIDs and used this database to identify the characteristics that lead to the emergence of pathogens in humans. Not all of the EIDs were known to

be zoonotic, but most EIDs were viruses and protozoa that had previously been identified as zoonotic or vector-transmitted, or both.

As humans and wildlife continue to collide in developed areas, understanding factors that influence disease occurrence in wildlife will be increasingly important for predicting disease emergence at a global scale. Nonhuman primates likely represent a reservoir of parasites for humans due to our close phylogenetic relationships to primates (Tutin 2000), and with the exploitation of tropical forests, humans increasingly overlap with nonhuman primates, both spatially and ecologically. To that end, knowledge of the distribution of infectious diseases in wild primates, and routes of contact and transfer between primates and humans, might help predict future pathogen exchanges and risk factors for human disease emergence (Wolfe et al. 1998).

Human immunodeficiency virus (HIV), the causative agent of AIDS, represents a natural starting point for examining the role of wild primates as a source of human EIDs. A multitude of simian immunodeficiency virus (SIV) strains naturally infect African primates, with viruses or SIV-reactive antibodies found in 36 host species examined thus far. Each wild primate species appears to harbor its own genetically distinct strain of the virus (Peeters et al. 2002; Peeters 2004), although some cross-infections occur (Jin et al. 1994; Bibollet-Ruche et al. 1996), and infections appear to cause little or no pathology in their natural hosts. In humans, AIDS can be caused by any one of at least four strains of HIV that evolved from SIV strains following transfer into human populations (reviewed in Watanabe 2004). Tracing the origins of human infections showed that three forms of HIV-1 are closely related to SIVcpz from *Pan troglodytes troglodytes* (Korber et al. 2000), whereas HIV-2 was most similar to SIVsmm, a virus isolated from sooty mangabeys. This evidence suggests that multiple cross-species transmission events of SIV strains from wild primates to humans took place during the past century, with transmission of the most widespread human strain of HIV-1 estimated to have occurred around 1930 (Hahn et al. 2000; Korber et al. 2000).

Humans have been affected by several other primate retroviruses that spread following cross-species transmission, most notably the HTLVs (human T-lymphotropic viruses, HTLV-1 and 2). These viruses are currently widespread in human hosts (Slattery et al. 1999), and they are closely related to simian viruses (STLV-1 and STLV-2) that are present in a large number of primate species. Phylogenetic analysis of viral strains points to at least three distinct HTLV-1 subtypes that probably originated independently through cross-species transmission from wild primates in the past several thousand years (Liu et al. 1996; Dooren et al. 2001). Researchers have also discovered that humans from rural villages in Africa were infected with simian foamy virus (SFV), another spuma-retrovirus originating from contact with wild primates (Wolfe et al. 2004), and later documented two new retroviral infections previously unreported in humans (HTLV-3 and 4, Wolfe et al. 2005). Indeed, it appears that human populations in certain regions are infected with a wide range of primate-derived viruses, with a number of viruses actively crossing into humans from multiple primate species (Wolfe et al. 2004, 2005).

What routes of contact lead to cross-species transmission of viral agents between wild primates and humans? Among wild primate species, genetic analysis of SIV

strains shows that cross-species transmission is common (Jin et al. 1994; Bibollet-Ruche et al. 1996; Peeters 2004), and studies of captive primates indicate that transmission can occur via close contact, including biting or scratching, as might result from contact between hosts with overlapping ranges. Genetic analysis of the strain of SIV harbored by chimpanzees indicates that even this virus appears to have originated from recombination among SIV strains carried by monkeys that are preyed upon by chimpanzees (Bailes et al. 2003). In terms of human infections, hunting and consuming nonhuman primates as food represents the most obvious source of exposure (Hahn et al. 2000; Tutin 2000; Peeters 2004; Wolfe et al. 2004), although chimpanzees also attack humans (Wrangham et al. 2000). To become infected by retroviruses like SIV, STLV, and SFV, humans must contact infected primate blood, which probably occurs regularly during killing or butchering the animals or preparing the meat for sale or consumption (Hahn et al. 2000, Fig 8.6).

Cross-species transmission might also occur, although less frequently, among zoo or lab workers who regularly contact nonhuman primates, or when humans keep primates as pets. Exposure to primates during fieldwork or ecotourism can lead to infections in humans. For instance, researchers showed that workers and tourists at one site in Indonesia probably experience a high risk of infection by herpesvirus-B (*Cercopithecine herpesvirus 1*, endemic in macaques), due to high seroprevalence in the monkey population and frequent exposure via bites and scratches (Engel et al. 2002). In another example, an outbreak of Ebola in chimpanzees led to the infection of one member of the research team investigating primate deaths (Formenty et al. 1999b). Ebola virus outbreaks in humans were further linked with handling wild animal carcasses, including those of gorillas, chimpanzees, and duikers. Human cases between 2001 and 2003 immediately followed outbreaks in wildlife in neighboring locations (Fig. 8.7, Rouquet et al. 2005). Wild primates can also serve as reservoirs or sources of infection for pathogens that are acquired when humans encounter

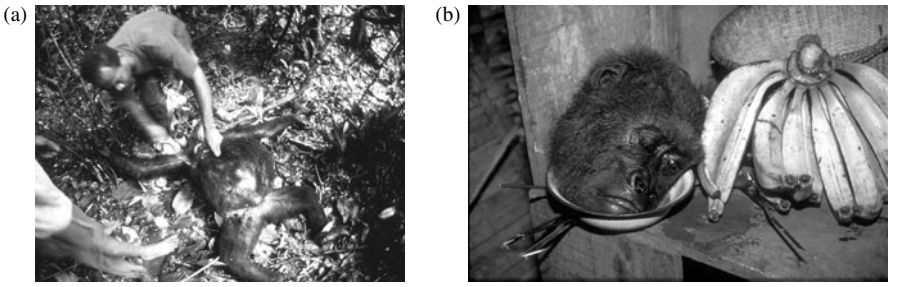


Fig. 8.6 Humans are exposed to primate blood through bushmeat hunting and preparation, particularly common in parts of Africa and Latin America. (a) Humans hunting and butchering a gorilla. (b) Head from a female gorilla killed for bushmeat near Mambele in Cameroon, placed on a pan near other food in the hunter's kitchen. Credits for both photos: K. Ammann, http://karlammann.com, reproduced with permission from the photographer.

infectious stages in the environment, and for pathogens spread by vectors like mosquitoes and flies that mainly feed on wild primates, but will also take blood meals from humans (as in the example of yellow fever described in Section 8.4). These transmission pathways are most likely to occur among tourists, field researchers, or forest workers, such as hunters or loggers that spend time in primate-inhabited areas.

It is important to recognize the somewhat blurry line between pathogens that have been transmitted from wild primates into humans—and are now maintained strictly as human diseases—versus zoonotic agents for which primates serve as reservoir hosts (and for which limited transmission among humans might occur). Rather than a strict dichotomy, these diseases probably fall along a continuum with one end represented by primate pathogens that became established in humans (and for which human-to-human is now common), and the other end anchored by parasites that primarily infect wild primates but occasionally cause human infections. In the case of Ebola, for example, outbreaks that occurred between 2000 and 2005 in Uganda, Gabon, Sudan, and the Republic of Congo typically lasted 3–6 months and tended to remain in localized areas (WHO 2005). The relatively short-lived duration of these outbreaks was largely due to the rapid mobilization of educational and health resources from agencies like WHO and was possibly also a function of the high virulence and relatively short incubation period of this virus (Sanchez et al. 1995; Formenty et al. 1999b).

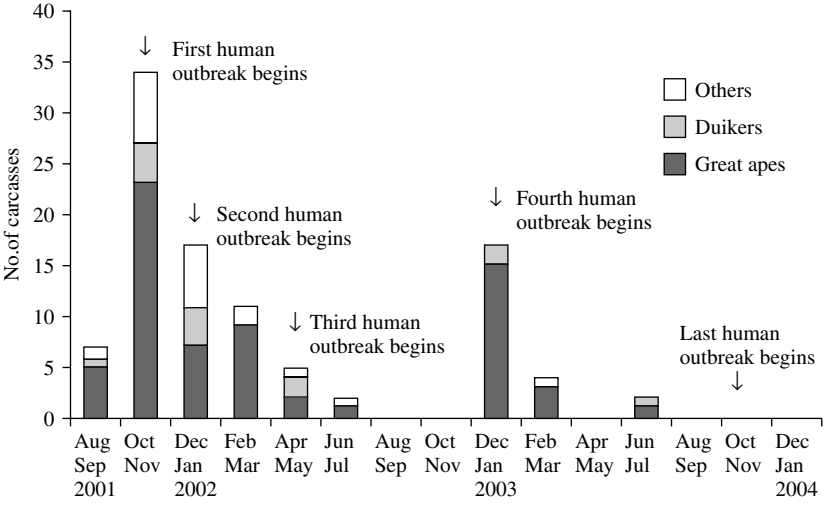


Fig. 8.7 Animal Mortality Monitoring Network in Gabon and Republic of Congo. Figure shows the temporal distribution of human Ebola outbreaks and number of carcasses found in wildlife. Fourteen of 21 carcasses from gorillas, chimpanzees, and duikers tested for Ebola returned a positive result. Reproduced from P. Rouquet, J. M. Froment, M. Bermejo, A. Kilbourn, W. Karesh, P. Reed, B. Kumulungui et al. (2005). Wild animal mortality monitoring and human Ebola outbreaks, Gabon and Republic of Congo, 2001–2003. *Emerging Infectious Diseases*, 11, 283–290.

Thus, even though human-to-human transmission occurs, repeated introductions via wild primates and other host species appear to be necessary to initiate outbreaks in humans (Rouquet et al. 2005). Epidemiologically, factors affecting the emergence of such pathogens are distinct from those spread solely within humans, in part because their transmission is decoupled from direct host-to-host contact, and because high densities of reservoir hosts (or vectors) can generate recurrent human cases of highly virulent diseases. Controlling outbreaks of these zoonotic infections hinges upon identifying and managing wild animal reservoirs and limiting human contacts with these species (Haydon et al. 2002a).

A more complete understanding of how parasites move between host species is important for understanding risks posed to humans from nonhuman primates, particularly as humans venture deeper into primate habitat (Tutin 2000). Hunting of wild primates is facilitated by the building of roads for logging, leading to easier access to bushmeat and potentially providing routes for the spread of infection (Walsh et al. 2003b). In fact, over 20% of sera from 788 monkeys discovered in bushmeat markets or as pets showed evidence of SIV infection, with infection found in 13 of 16 primate species tested (Peeters et al. 2002). Humans have a long evolutionary history of hunting primates (e.g. see Shipman et al. 1981 for description of a site at which gelada baboons were butchered by *Homo erectus* approximately 400,000 to 700,000 years ago). However, hunting and consumption of primates and other bushmeat is increasing at a shocking pace (Peterson and Ammann 2003; Brashares et al. 2004); trading of live animals, including primates, could also increase risk of disease transmission (Karesh et al. 2005). Of equal or greater importance are increases in human densities and changes in human behavior that can provide a means for infections to establish more readily in human populations. Thus, exchange of viruses between humans and wild primates probably occurred many times, but the majority of these events were more likely to be followed by local pathogen extinction rather than by subsequent human-to-human transmission. More recent developments allowed HIV and other pathogens to establish and spread in human populations, including the commercial sex trade and migrations of workers from rural areas to cities, reuse of dirty syringes for injecting drugs, and non-hygienic health care practices (Garrett 1995).

Human exposure to primate pathogens is not limited to viruses or other microparasites, and nonhuman primates are probably reservoirs for a variety of helminth infections in Africa, including multiple species of *Schistosoma* (Nelson et al. 1965) and *Strongyloides fulleborni* (Rothman and Bowman 2003). Our own research showed that over 25% of infectious diseases reported to infect wild primates also appear in human populations, and of these, 45% were classified as "emerging" in humans (Pedersen et al. 2005). These shared parasites included helminths representing genera such as *Brugia, Dirofilaria, Taenia*, and *Trichuris*, and protozoa such as *Entamoeba, Giardia, Leishmania* and *Trypanosoma*. Even several malaria species show evidence of cross-species transmission between humans and wild primates, with primate malarias documented to infect humans in Africa and Asia, and humans introducing malaria into New World monkeys (Box 8.1). Even so, over half of the

Table 8.3 Examples of viruses classified as emerging in humans that can also infect nonhuman primates. Data are described in Pedersen et al. (2005) and Nunn and Altizer (2005). Information on emergence in humans was obtained from Taylor et al. (2001). Note that primate immunodeficiency viruses (SIV/HIV) and primate T-lymphotrophic viruses (STLV/HTLV) were omitted because the human and simian forms have different virus names

Virus name	Family/Genus	Type[1]	Primates reported as hosts
Simbu virus	Bunyaviridae—*Orthobunyavirus*	ss RNA	New World monkeys; *Cebus, Alouatta, Ateles*
Ebola virus	Filoviridae	ss RNA	African apes; *Pan, Gorilla*
Dengue virus 1 and 2	Flaviviridae—Flavivirus	ss RNA	Asian monkeys; *Presbytis, Macaca*
Hepatitis G virus	Flaviviridae—Flavivirus	ss RNA	African apes; *Pan*
Japanese encephalitis virus	Flaviviridae—Flavivirus	ss RNA	Asian monkeys; *Macaca*
Kyasanur forest virus	Flaviviridae—Flavivirus	ss RNA	Asian monkeys; *Presbytis, Macaca*
St Louis Encephalitis virus	Flaviviridae—Flavivirus	ss RNA	New World monkeys; *Aotus, Ateles, Alouatta, Cebus, Saguinus*
Yellow fever virus	Flaviviridae—Flavivirus	ss RNA	Old World and New world primates; many species
Zika virus	Flaviviridae—Flavivirus	ss RNA	*Pan, Colobus*
Hepatitis B virus	Hepadnaviridae—Orthohepadnavirus	ss/ds DNA	Apes; *Pongo, Pan, Hylobates*
Influenza A virus	Orthomyxoviridae—Influenzavirus	ss RNA	*Papio*
Measles virus	Paramyxoviridae—Morbillivirus	ss RNA	Old World primates; *Macaca, Presbytis, Papio, Gorilla*
B19 virus	Parvoviridae—Erythrovirus	ss DNA	*Pan*
Poliovirus 1, 2, and 3	Picornaviridae—Enterovirus	ss RNA	Old World primates; *Macaca, Papio, Pan*
Heptatitis A virus	Picornaviridae—Hepatovirus	ss RNA	Old World and New World primates; many species
Monkeypox virus	Poxviridae—Orthopoxvirus	ds DNA	Old World primates; *Pan, Cercopithecus, Colobus*
Rotavirus A	Reoviridae—Rotavirus	ds RNA	Asian monkeys; *Presbytis, Macaca*
Chikungunya virus	Togaviridae—Alphavirus	ss RNA	African and Asian primates, many species
Mayaro fever virus	Togaviridae—Alphavirus	ss RNA	New World monkeys, many species
Sindbis virus	Togaviridae—Alphavirus	ss RNA	*Macaca*
Western and eastern equine encephalitis virus	Togaviridae—Alphavirus	ss RNA	New World and Old World monkeys; *Papio, Cebus, Ateles*

[1] ss: single-stranded, ds: double-stranded, see Chapter 2 (section 2.2.1) for further details on virus types.

"shared pathogens" listed as emerging in humans were viruses, with this list dominated by RNA viruses, including several vector-borne pathogens (Table 8.3).

The substantial and increasing risks posed by emerging and zoonotic diseases in human populations call for more comprehensive and coordinated surveillance efforts (Wolfe et al. 1998, 2004; Heymann 1999; Tutin 2000). Monitoring parasite occurrence not just in humans, but also tracking background infections in primates and other wildlife has the potential to serve as a warning system for possible human outbreaks. This benefit has been highlighted recently with the Animal Mortality Monitoring Network in Gabon and Republic of Congo (Rouquet et al. 2005). By keeping track of deaths in wildlife (Fig. 8.7), the network organizers aim to detect hotspots of Ebola emergence in humans and alert authorities of emerging threats. Similar efforts are needed for other infectious agents, including a range of RNA viruses, in wild primates living near humans. To uncover the extent to which humans might be exposed to novel SIVs and other retroviruses, non-invasive sampling could be used to characterize the diversity of viruses circulating in populations of wildlife and quantify their prevalence in different primate hosts (Watanabe 2004). Researchers are also monitoring potential viral crossover by collecting samples from bushmeat hunters in local villages that have frequent close contact with nonhuman primates (Wolfe et al. 2004, 2005). A non-trivial issue is which organizations or government entities will support surveillance activities, and as a related issue, how efforts will be coordinated among multiple public health agencies within these organizations and governments (Morens et al. 2004).

Basic and applied research combined with public health activities and educational efforts are needed to develop countermeasures to respond to human EIDs. At a very basic level, limiting human risk factors represents an essential step in lowering the probability of disease emergence, together with efforts to reduce human-to-human transmission. To that end, campaigns to raise global awareness of the bushmeat trade could increase pressure on governments, corporations, and conservation groups to step up efforts to discourage hunting of wild primates and also provide alternative means of subsistence for hunters (Wilkie and Carpenter 1999; Peeters et al. 2002; Peterson and Ammann 2003; Brashares et al. 2004; Wolfe et al. 2005). From a different angle, advances in understanding primate immune responses and mechanisms of pathogenesis are likely to lead to development of new vaccines and treatments. Comparing differential susceptibility of wild primates and humans to similar infectious agents might reveal why some agents, such as SIV, cause little pathology in their natural hosts, yet lead to devastating disease in many humans. Similarly, completion of genomics projects on parasites will enable scientists to identify selection on molecular pathways that are important for allowing emerging pathogens to infect humans, cause disease, and transmit between human hosts (Ito et al. 1998; Fraser et al. 2002).

8.6 Summary and synthesis

Understanding interactions between primates and their parasites helps us to understand the origins of many human infectious diseases and our responses to these

infectious organism. As agents of selection, infectious diseases have affected humans throughout ancient and recorded history, with human responses probably similar to many of those found in nonhuman primates, particularly with regard to avoiding arthropod vectors and the diseases they carry, consuming medicinal plants, swatting away flies, and sleeping in closed environments. This is not surprising, since the existence of some of these behaviors in humans informed the research on nonhuman primates (Nunn 2003). On the other hand, some striking differences exist between wild primates and humans, particularly with respect to the diversity and types of infectious diseases that are found in nonhuman primates and humans. A number of factors probably underlie these differences. Compared to nonhuman primates, for example, high human population densities and global connectedness provide a means to sustain diseases—such as many childhood infections and acute respiratory illnesses—that have fewer analogies in wild primate species. Similarly, long-term interactions between humans and domesticated animals probably dramatically expanded the repertoire of human infectious diseases, as compared to our closest relatives, by providing opportunities for parasites in carnivores and ungulates to infect humans. Finally, the global distribution of humans means that as a species, we are exposed to more parasites than other primate species, all of which have geographic ranges orders of magnitude smaller than humans.

At an applied level, it might be possible and practical to use knowledge of behavioral and immune defenses in wild primates to inform human health. A number of researchers have identified nonhuman primate defenses as a potential source for new strategies to combat human diseases (Newton 1991; Glander 1994; Lozano 1998; Sumner 2000). This approach is probably most readily appreciated in the case of pharmaceuticals, with medicinal plant use in nonhuman primates and ethnomedical practices among human cultures pointing toward sources of new drugs. Understanding behavioral defenses in primates could further reinforce low-cost prophylactic defenses already practiced by humans, such as sleeping in enclosed microhabitats to avoid disease-carrying vectors (Nunn and Heymann 2005). Furthermore, examining mechanisms that underlie differential susceptibility of humans and nonhuman primates to diseases like malaria, yellow fever and AIDS could help us understand why wild primates tolerate pathogens that make humans very sick.

The wealth of hypotheses that can be tested with comparative studies of human societies has barely been tapped. Returning to the example of behavioral defenses to STDs, for example, circumcision varies across human societies and might reduce the risk of acquiring STDs such as gonorrhea and HIV (Diseker et al. 2000; Gray et al. 2004; Reynolds et al. 2004). Phylogenetic and linguistic trees will prove increasingly useful in understanding patterns of disease spread across human societies, just as geographical information points to environmental conditions that influence patterns of infection (Guernier et al. 2004). In some cases, the phylogenetic trees will be of the parasites, rather than of human societies or primate species, with the resulting information placed into the context of human geography and behavior.

Finally, research on wild primates can provide insights to disease emergence. Human pathogens originating from wild primates include multiple strains of

HIV-AIDS (Hahn et al. 2000) and several other retroviruses (Wolfe et al. 2004). Wild primates are known to be important in maintaining sylvatic transmission cycles of arboviruses that cause acute diseases in humans and are also currently recognized as emerging (Taylor et al. 2001). Improved knowledge of the distribution of infectious diseases in wild primates, and routes of parasite transmission between primates and humans, should help predict the probability of future cross-species transmission events and evaluate risk factors for human disease emergence (Wolfe et al. 1998).

Given the general absence of knowledge on primate sickness behaviors, immune defenses, sleeping habits, and parental care activities aimed at reducing disease risk, the future is likely to hold many unexpected surprises (Heymann 1999; Phillips-Conroy and Jolly 1999). Certainly, it would be a wonderful outcome if future understanding of primate–parasite interactions resulted in practical benefits, such as those described above, in addition to basic knowledge of human evolution.

9

Concluding remarks and future directions

9.1 Introduction

Our goal in writing this book has been to draw attention to the fundamental role that parasites play in the lives of nonhuman primates, and to investigate how the daily activities of primates—including social and mating behaviors—mediate exposure to and defenses against infectious agents. To develop hypotheses and stimulate new ideas, we suggested how parasites might spread through primate populations, and we examined several real-world examples of behavioral and population-level responses to parasite infections. As mentioned throughout this book, we view infectious disease as a major frontier in our understanding of primate behavior and ecology—a situation that is all the more remarkable considering that many of the hypotheses involving links between infectious disease and primate socioecology have existed for three decades (Freeland 1976, 1977, 1979).

Given the explosive growth in research addressing the population biology of infectious diseases, and the development of new non-invasive techniques for collecting information on infection status, hormones, and genetics, scientists are now well positioned to address many exciting questions that were raised over the past 30 years. One direction for future research involves joining theory with behavioral and field data to examine relationships among social system parameters, contact patterns, and infection dynamics in the wild. Because even the tiniest viruses and bacteria cause declines in monkey and ape populations, as evidenced by recent deaths due to Ebola and anthrax in great apes, understanding how primate behavior influences patterns of parasitism is highly relevant to wildlife conservation, with implications for captive breeding programs, reserve design, ecotourism, and intervention strategies. Contact with wild primates also poses real threats to human health, in part due to growing evidence that retroviruses and other pathogens continue to move between wild primates and human populations.

With this intellectual motivation and applied importance in mind, we identify six key areas for future research, pointing to future challenges for testing the links between host and parasite traits in wild primate systems.

9.2 What is the diversity of parasites in wild primates?

Most living species on this planet are parasitic in nature (Price 1980; Windsor 1998), yet parasitologists have uncovered only a miniscule percentage of the diversity of

infectious organisms inhabiting wild animals. Studies of parasites in wild primates tend to focus on specific groups of parasitic organisms, such as viruses that also can infect humans (zoonotic pathogens), or on easily described host-specific parasites such as pinworms. Although informative, the motivations of these research programs (see Box 2.1) have generated biases in understanding the broad diversity of parasites that infect primates. As a case in point, analysis of a bioinformatics database spanning over 400 parasites reported from wild primates (Nunn and Altizer 2005) revealed what is almost certainly a deficiency in the numbers of fungal and bacterial parasites, with only 11 species of fungi and 37 bacteria collectively reported from over 110 wild primate species (see Fig. 2.3; Pedersen et al. 2005). This seems likely to be a gross underestimate, especially given that over 537 bacterial species and 311 fungi have been reported to infect humans as a single host species (Taylor et al. 2001), nearly ten times the number from all wild primates combined. Similarly, most primate parasites documented thus far are transmitted by vectors or through close contact (82% of 408 parasite species in Pedersen et al. 2005). The majority of primate parasites (68%) are also generalists capable of infecting more than one host species, possibly reflecting a greater interest in obtaining samples of zoonotic parasites from nonhuman primates.

These patterns could reflect deficiencies in understanding host-specific parasites and those spread through intermediate hosts. Ecologists have virtually no information on parasites from nearly half of all primate species, including many species of prosimians, threatened primates in small populations, and primates that live in inaccessible areas such as swamp forests or at high altitudes. More generally, there are no primate species for which biologists have come close to completely documenting the entire parasite community. This is indicated by a linear association between numbers of parasites recorded and measures of sampling effort, with no signs of exhausting the diversity at high levels of sampling effort (Fig 9.1).

In addition to covering a greater diversity of parasites and documenting parasites from a wider array of primates, we need to expand knowledge of traits that influence parasite population biology. Information on parasite transmission strategies and the duration of the incubation and infectious periods is crucial for explaining patterns of parasitism among primates, including the links between parasitism and social and mating systems. Similarly, information on the range of hosts infected is vitally important for making sense of perceived relationships between host and parasite diversity (Nunn et al. 2004). Finally, virulence and the duration of the infectious period are key variables that will influence the extent to which parasite establishment changes with host social organization, with less virulent parasites that infect hosts for a longer period of time better able to establish in socially structured populations (Cross et al. 2005). Alternatively, extremely virulent pathogens could spread rapidly through populations in some circumstances, particularly in cases where host death leads to greater dispersal or rates of contact (see Fig. 4.10, Box 7.1).

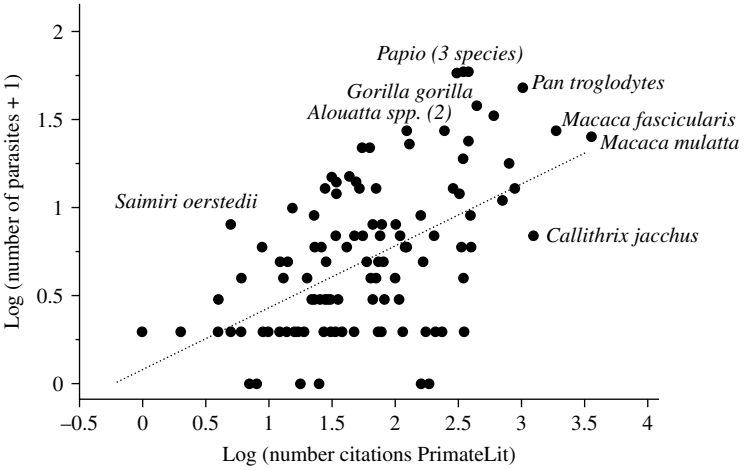


Fig. 9.1. Parasite diversity, measured as parasite species richness, among free-living primates relative to sampling effort, here measured as the number of citations for each host species in the online bibliographic resource PrimateLit (Wisconsin Primate Research Center and Washington National Primate Research Center). Each point represents counts for a single primate species ($N = 119$), and parasites included viruses, bacteria, fungi, protozoa, helminths, and arthropods. Primate species were included if there was evidence that they had been sampled for parasites. Data points for several primate species are identified. This plot shows that more parasites have been reported to infect those primates that have been better studied. Similar results were obtained with other measures of sampling effort, including counts of the cumulative number of animals sampled and citation counts from other bibliographic databases (see Nunn et al. 2003, 2004). The linear regression model explained 34% of the variance ($t_{118} = 7.81$, $P<0.0001$) and the relationship was linear, as indicated by a non-significant quadratic term in a nonlinear model (Nunn et al. 2004).

9.3 Population biology and impacts of parasites in wild primates

Although primates are among the best-studied and charismatic animals, at the present time researchers have little sense for the influence of parasites on primate populations relative to other factors that affect mortality, growth, and reproduction. This no doubt partly reflects that many primate species have slow reproductive rates, exist in small populations, and live mainly in the trees, all of which pose major challenges for approaches that rely on large samples sizes, invasive manipulations, and quantitative measures of lifetime reproductive success.

The literature provides many prominent examples of large die-offs of primates stemming from infectious disease (Carpenter 1964; Galindo and Srihongse 1967; Pope 1998; Walsh et al. 2003b; Leendertz et al. 2004). But these examples might actually be less important than the cumulative impacts of more cryptic infections,

with endemic parasites eroding individual reproductive success in fundamental, but not always immediately apparent, ways. Addressing this problem requires quantifying the effects of less virulent parasites on host fitness, including the effects of lost reproduction. Perhaps the most direct way to test for parasite impacts on primate populations is through field experiments (Tompkins and Begon 1999; Tompkins et al. 2002), specifically by treating a subset of animals with antimicrobial or anthelminthic drugs and subsequently evaluating their behavior and reproduction (reviewed in Tompkins et al. 2002). Populations in which this is appropriate would be primates that are monitored regularly and have relatively fast life histories, as the effects can be observed more quickly in these populations and compared to baseline parameters collected before treatment. Ideally, researchers will need to combine information on host population size, survival, and reproduction with data on infections from multiple parasite species. This requires intensive studies that span considerable timeframes and spatial scales, and would necessitate the screening of blood and fur, or the use of new non-invasive methods for assessing infection status.

It is also important to investigate how primate behaviors and spatial distributions influence infectious disease spread. Empirical studies in natural systems are badly needed to identify how prevalence and intensity of infection changes with host population parameters. Not surprisingly, advances gained by modeling approaches, including metapopulation models, mixing matrices, individual-based models, and social network theory (Hess 1996; Moore and Newman 2000; Thrall et al. 2000; McCallum and Dobson 2002; Dobson 2004) have rapidly outpaced field and experimental research. A major challenge for the future is to ground-truth these models with data from the field, including data on ranging patterns, contact among individuals, rates of dispersal between groups, and infection characteristics such as disease-related mortality and infectious periods. An enormous challenge in moving forward is the need to increase communication and collaboration between mathematical ecologists studying the dynamics of infectious disease and primatologists recording data and collecting samples from animals in their natural environments. Such communication should rapidly advance theoretical models for investigating the implications of different social systems for the spread of infections, including ways to quantify mating and social systems that are meaningful to host–parasite dynamics.

Capturing heterogeneities in contact among individuals within and between groups is crucial for tracking parasite spread in social species like primates, and this might be achieved by using "contact matrices" to account for how parasites spread among individuals of different age and sex classes, as well as across matrilines or between social groups. Grooming matrices are available for a wide variety of primates and could be used as an initial estimate of patterns of contact or associations among individual animals within groups; between-group contact patterns will be more challenging to quantify (see section 9.5). Studying how individual host traits covary with contact patterns and infection status can also point to classes of hosts that might serve as "super-spreaders" for infectious diseases (Perkins et al. 2003b; Ferrari et al. 2004b). Sudden outbreaks in protected or monitored wild primate populations, such as occurred when a bacterial infection caused severe genital lesions

among olive baboons in Tanzania in 2003 (e.g. *New Scientist*, "Horrific venereal disease strikes African baboons," May 2, 2003), should allow researchers to relate individual host characteristics (such as age, sex, rank, and contact patterns) to infection probabilities, with future potential for predicting patterns of infectious disease spread and identifying hosts for treatment and control efforts.

9.4 Immune and behavioral defenses: tradeoffs against different infectious agents

Behavioral and immune defenses are key players in the ongoing battle between primates and their infectious diseases. Although biomedical researchers regularly study how the immune systems of captive primates respond to infection by specific pathogens, virtually nothing is known about how primate immune systems function in the wild, aside from a handful of studies that have documented antibodies to infectious agents, mainly zoonotic viruses, in wild primates (Haddow 1951; Kalter 1972b; Kilbourn et al. 2003). Primates probably respond to parasites using a combination of innate defenses, adaptive immune responses, and complex behaviors to avoid infection and remove parasites from their bodies—but what are the relative costs of these defenses to animals faced with other demands on time and resources, and how effective are they against different types of parasites? As one example, biologists lack an understanding of the underlying mechanisms that drive differences in circulating leukocytes among different species of primates (see Box 5.1 and Read and Allen 2000; Anderson et al. 2004). Although among-species differences are striking and probably biologically meaningful (Nunn et al. 2000; Nunn 2002a,b; Semple et al. 2002; Anderson et al. 2004), it remains uncertain to what extent they reflect evolved differences in response to parasites or facultative responses, and the degree to which greater basal leukocyte counts actually translate into stronger measures of immunocompetence against different types of parasites.

In terms of behavioral defenses, much is known about some strategies such as fly swatting or applying "insect repellents" by primates such as howler monkeys and capuchins (Dudley and Milton 1990; Valderrama et al. 2000). Other primates use medicinal plants to reduce intestinal parasite burdens (Huffman 1997, 2006), although further research is needed on the efficacy of these putative defenses and the mechanisms underlying their effectiveness. Other behavioral defenses, such as postcopulatory grooming and sickness behaviors, are virtually unstudied, or conclusions from previous results remain ambiguous, as in the case of host movements to avoid fecal contamination of the environment (Hausfater and Meade 1982; Day and Elwood 1999; Di Bitetti et al. 2000). A major goal for the future should be to compile more information on behaviors that follow natural infection or experimental exposure to parasites. Also needed are data on behavioral responses by animals to infected conspecifics, including whether or not primates can ascertain and avoid contact with other infected hosts, the mechanisms by which this is achieved, and whether identification of infected conspecifics depends on the infectious agent involved.

An outstanding question related to balancing the costs of different defenses involves the relative roles of immune and behavioral responses in combating parasites. Behavioral avoidance strategies are probably more important for parasites in which immune defenses are incomplete or imperfect, and for parasites in which it is possible to avoid sources of infection. Immune defenses might play a larger role in defending against other types of parasites, such as sexually transmitted diseases (STDs), in which it may be impossible to identify infected mating partners (Knell 1999), and for situations in which the benefits of promiscuity outweigh the risks of infection (Nunn and Altizer 2004).

Finally, we know little about the selective pressures exerted by parasites on genetically based host defenses in wild primates, including major histocompatibility complex (MHC) evolution and other components of resistance (de Groot et al. 2002; Knapp 2005). As one avenue for further research, comparative studies using bioinformatics databases could address the role of MHC polymorphism in responding to pathogen-mediated selection in wild primates. With such an approach, it is possible to test the prediction that species that have been historically exposed to a broader spectrum of parasites harbor greater MHC variability (in terms of number of alleles and frequency of heterozygotes). Tiny amounts of tissue, including those extracted from hair follicles or animal feces collected in the field, could be used to amplify fragments of DNA for MHC typing in wild primates (Lukas et al. 2004). Indeed, studies of MHC in natural primate populations can provide answers to important questions in behavioral ecology, molecular evolution, and resistance to pathogens (Knapp 2005).

9.5 What are the links between primate sociality and parasitism?

We uncovered many fascinating associations between parasites and primate social systems, but we were also surprised by how few studies addressed fundamental questions related to parasites and primate sociality. For example, it is striking that almost no researchers have examined questions involving patterns of infection within primate groups, specifically in relation to age, sex, reproductive status, and dominance rank (e.g. Müller-Graf et al. 1996, 1997). This information is critical for understanding sources of infection within groups, and for developing theoretical models that take into account heterogeneities in contact among individuals. Similarly, when studies have been undertaken, there have been few attempts to replicate findings, as illustrated by Freeland's (1977) results showing that biting flies might drive primate polyspecific associations (see Fig. 1.3).

Although scientists lack information on parasite distributions within groups, this pales in comparison to the lack of understanding of the spread of parasites between groups. At a most basic level, do primates serve as "biological islands" for parasites, and is this true for all parasites? A major task for the future is to uncover more details about the structuring of infectious diseases among primate groups, especially relative

to parasite transmission mode. The effect of host sociality on the spread of contact-borne parasites depends on the duration of infectiousness, with parasites that cause more acute infections tending to "experience" greater spatial structure because hosts are more likely to recover or die before the infection can spread to new groups (Cross et al. 2005). Vector-borne diseases might spread more easily in socially structured populations regardless of the duration of infection in the primate host, provided that vectors are relatively unaffected by host social organization when searching for hosts.

Another point related to inter-group movements is the need to understand mechanisms that allow parasites to spread through primate populations, possibly using marker organisms to document the spread of infections. Of particular importance is the movement of parasites via the transfer of animals between groups (Freeland 1979; Barrett and Henzi 1998), as it appears that group size alone fails to account for significant variation in the risk of acquiring directly transmitted infections, especially in comparative tests (Nunn et al. 2000, 2003a; Nunn 2002a). To understand the links between infectious disease and primate social systems, it will be necessary to address questions such as: What is the rate of movement into groups, what percentage of dispersing individuals enter a new group, and how long does immigration require? Are socially transmitted diseases maintained in groups of "floater" individuals, such as all male groups of langurs? Do rates of movement into groups correlate positively with group size, as shown in one of the few systems (cliff swallows, Brown and Brown 2004) in which host dispersal has been studied in the context of disease? Home range overlap can also provide a major route for the spread of pathogens between primate groups, with fecally transmitted parasites potentially contacting multiple host groups in areas of range overlap. The possibility that ranging patterns influence parasitism is largely unexplored (Nunn and Dokey, in review), yet this possibility could be addressed through a combination of field, comparative, and theoretical research.

Although most attention has focused on the effects of host sociality on parasite fitness, parasites could generate changes in host social interactions (Freeland 1976; Loehle 1995). This remains one of the most challenging issues for future research, in part because it is difficult to assess whether responses by hosts are evolutionary or facultative. Another major challenge is that other ecological factors, including predation and resource competition, provide alternative explanations for variation in patterns of sociality. Even within the context of parasitism alone, numerous features of host biology will influence encounter probabilities and parasite transmission, and hence determine the number and types of parasites that exist in wild hosts (Møller et al. 1993; Thrall et al. 1993b; Gregory 1997; Morand 2000; Roberts et al. 2002; Altizer et al. 2003b). The effects of parasites on host social evolution have been modeled explicitly, for both socially (Bonds et al. 2005) and sexually transmitted parasites (Thrall et al. 2000; Kokko et al. 2002). But remarkably few, if any, empirical studies have tested whether parasites can modify patterns of sociality. As described in Chapter 6, comprehensive cross-species datasets, in combination with new phylogenetic comparative methods, provide a means to investigate whether parasites have influenced host social evolution.

9.6 Are parasites a significant threat to primate conservation efforts?

A key area for future research involves the conservation implications of parasites, along with action plans to limit the impacts of infectious disease outbreaks in wild primate populations. Research is needed on host and parasite characteristics that influence the risk of cross-species transmission to threatened primate species. Fundamental to these questions is the role of multi-host parasites that move easily among primates and other host species, and how their spread is affected by anthropogenic changes that alter host ranging patterns, resource use, and contact with domesticated animals (Daszak et al. 2000; Woolhouse et al. 2001; Chapman et al. 2005a). Understanding sources of infectious disease in domesticated animals and non-primate mammals will be important for conservation plans, especially in the case of parasites spread through contact with reservoir hosts. In the case of Ebola in African apes, for example, stopping the spread of disease by using breaks in the forest to prevent contact among gorilla populations will be less effective if bats or other highly mobile animals can spread the virus (Leroy et al. 2005). Thus, the development of effective conservation plans for Ebola will depend on identifying the reservoir that harbors this virus and mechanisms leading to transmission to apes (Karesh and Chapman 2005).

A more comprehensive view of the geographic distribution of disease risk is critical for conserving endangered species, many of which are clustered in biodiversity hotspots. Global analyses can be achieved using both GIS and comparative approaches. For example, Nunn et al. (2005) reported greater diversity of vector-borne protozoa from wild primates that live closer to the equator, indicating that tropical conditions might favor such parasites (Fig. 3.14). This result is important because vector-borne protozoan parasites cause some of the most virulent diseases known to humans (Ewald 1994a), including malaria and trypanosomiasis, and many of these parasites (and their close relatives) also infect nonhuman primates. Global climate change is widely believed to be a factor responsible for increases in the geographic ranges of arthropod species that spread these diseases, predicting future disease outbreaks as parasite ranges expand in response to climate warming (Harvell et al. 2002; Guernier et al. 2004).

Similarly, researchers can focus on the actual sampling of parasites to ask whether certain types of pathogens are found in particular areas, or whether areas of high primate endemicity and threat have been sufficiently sampled for parasites. Based on the IUCN Red List, for example, Southeast Asia harbors a relatively large number of threatened primates (Cowlishaw and Dunbar 2000). As shown in Fig. 9.2, however, geographic analysis of sampling for parasites in primates reveals a major gap in the knowledge of parasites from threatened primates in this geographical area. Similarly, researchers can examine whether particularly virulent pathogens, such as Ebola, anthrax, or vector-borne protozoa and RNA-viruses, are more common in biodiversity hotspots, or whether sampling for different classes of diseases varies among regions.

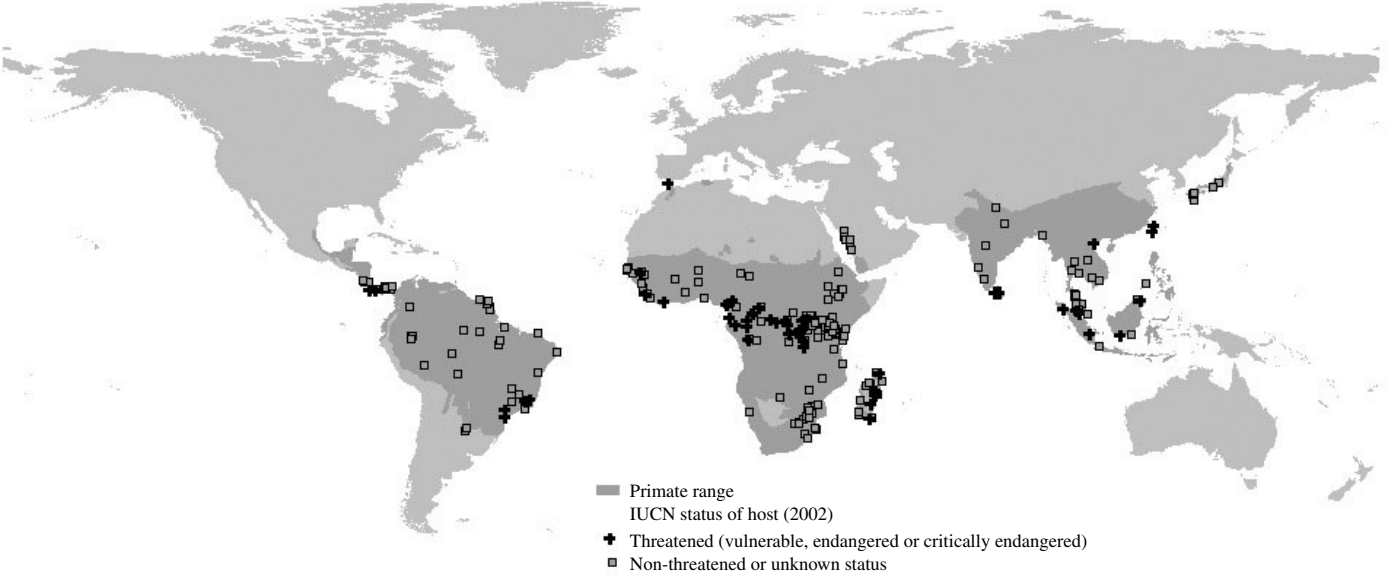


Fig. 9.2 Geographic sampling of primates for parasites in relation to primate geographic range and host threat level. This map shows the locations of studies where primates have been sampled for parasites in the wild, based on the *Global Mammal Parasite Database* (Nunn and Altizer 2005). Locations were only included if geographic coordinates could be identified in the publication or through on-line databases, and many localities represent multiple host-parasite records. Study sites for which at least one threatened host (vulnerable, endangered, or critically endangered) was sampled is indicated as crosses (+), while others are indicated by squares. Figure produced by N. Patel and M. Hopkins, using unpublished host-parasite locality data from C. Nunn and geographic ranges from W. Sechrest.

Primatologists should become increasingly aware of infectious disease when developing conservation plans, including captive breeding and release of animals in the wild. In the field, a particular concern is the possibility that parasites will be transmitted from human researchers and eco-tourists to nonhuman primates (Wallis and Lee 1999; Wallis 2000). Important questions remain about sources of infectious disease outbreaks in primate populations that have had contact with researchers, especially respiratory illnesses, and until these risks are better quantified, researchers should be strict about maintaining a safe distance from the primates they study. Similarly, human waste products and garbage can serve as sources of disease for wild primates (see Fig. 7.8), and efforts can be devoted to making latrines and trash pits inaccessible to wild primates and other animals. In terms of captive breeding and re-release of threatened primates, it is essential to ensure that new infections are not released along with animals into wild populations, and that tools are available for recapturing animals that show signs of infection following release (Britt et al. 2004).

Finally, the comparative approach, which is so fundamental to primate socioecology, has direct applications to animal conservation. In a recent review article, Fisher and Owens (2004) suggested that comparative methods provide insights to biodiversity conservation, but these studies are often conducted at a scale that limits the practical benefits that can emerge from this powerful approach. Their paper therefore serves as a "call to arms" to develop both the basic knowledge that comes from broad-scale comparisons, while also making predictions about future threats to biodiversity. Recent comparative studies have examined correlates of "extinction risk" in mammals relative to their intrinsic traits (like body size and life history) and the intensity of human pressures (such as hunting and habitat loss, Gittleman et al. 2001; Cardillo et al. 2004). This approach could be readily extended to include measures of infectious disease risk or anthropogenic factors that increase exposure to parasitic diseases, leading to predictive models for disease emergence.

9.7 From primates to understanding human-pathogen interaction

Knowledge of infectious disease in nonhuman primates can provide insights to human health at both basic and applied levels. At a basic level, understanding primate evolution in the context of infectious disease can inform studies of human evolution, and further highlights the striking differences between humans and wild animals. The high densities and the interconnectedness of human populations provide a means to sustain many infectious diseases that are absent in wild primate populations. Thus, childhood infections of humans appear to have fewer analogies in wild primates. Similarly, it is likely that through the domestication of wild animals, the repertoire of human infectious diseases is much larger than in our closest relatives.

Understanding the details of infectious disease in nonhuman primates could hold the key to many public health issues, including the origins of infectious diseases,

their emergence in human populations, and the maintenance of zoonotic pathogens in wildlife. In addition to their use as model systems for biomedical research on human diseases, behavioral responses to diseases in nonhuman primates might also point to novel strategies for countering infections, thus providing a means to identify low-cost interventions to improve public health at a global scale. These issues involve behavioral counterstrategies to infectious disease, ethnobotany to discover new medicinal plants that improve human health, and Darwinian medicine, in which human health and infectious disease are viewed in an evolutionary framework. This approach is already widely appreciated in the case of pharmaceuticals, with behavior in nonhuman primates and traditional (non-Western) societies pointing toward sources of new drugs in developed countries (Glander 1994; Sumner 2000).

Emerging infectious diseases currently represent one of the most important threats to human health at a global scale (Garrett 1995). Recent decades have witnessed the appearance of many new diseases that caused tremendous negative economic, social, and demographic impacts, including HIV/AIDS, severe acute respiratory syndrome (SARS), Ebola hemorrhagic fever, and hantavirus pulmonary syndrome (e.g. Schwartlander et al. 2000; Galvani 2004). Several authors pointed out that the majority of these diseases are viral in nature and zoonotic in origin, and can be shared between humans, domesticated animals, and wildlife (Hahn et al. 2000; Taylor et al. 2001; Woolhouse et al. 2001; Peeters et al. 2002; Wolfe et al. 2004). Despite their importance, however, many factors that underlie disease emergence remain elusive. To that end, improved knowledge of the geographic and phylogenetic distributions of infectious diseases in wild primates, and routes of pathogen transfer between primates and humans, can help predict risk factors for human disease emergence (Wolfe et al. 1998).

9.8 Concluding remarks

Writing this book has been an inspiration for our own research on infectious disease in primates and other mammals, and we hope to have shared our excitement about this burgeoning field with readers. We acknowledge that this book raises more questions than answers, and we will have succeeded if readers find the questions worth pursuing, or if this book leads to new insights that we missed. It has become abundantly clear that several fields of knowledge have matured to the point where it is now possible to assess the role of infectious disease in primate socioecology, specifically fields involving epidemiology, parasitology, and primate behavior and ecology. Methodologically, we are also well-positioned to make advances on the questions raised above and throughout this book, with comparative methods and phylogenetic information now available, as well as non-invasive field techniques, individual-based modeling approaches, and resources to pursue integrative research. We anticipate that the future will hold many surprises, including outcomes of great practical importance to human health, understanding human evolution, and conservation of biodiversity.

References

Abbott, D. P. and S. K. Majeed (1984). A survey of parasitic lesions in wild-caught, laboratory-maintained primates: (rhesus, cynomolgus, and baboon). *Veterinary Pathology*, **21**, 198–207.

Abbott, D. H., E. B. Keverne, F. B. Bercovitch, C. A. Shively, S. P. Medoza, W. Saltzman, C. T. Snowdon et al. (2003). Are subordinates always stressed? A comparative analysis of rank differences in cortisol levels among primates. *Hormones and Behavior*, **43**, 67–82.

Able, D. J. (1996). The contagion indicator hypothesis for parasite-mediated sexual selection. *Proceedings of the National Academy of Sciences USA*, **93**, 2229–2233.

Abouheif, E. (1999). A method for testing the assumption of phylogenetic independence in comparative data. *Evolutionary Ecology Research*, **1**, 895–909.

Acevedo-Whitehouse, K., F. Gulland, D. Greig, and W. Amos (2003). Disease susceptibility in California sea lions. *Nature*, **422**, 35.

Adamson, M. L. and J. N. Caira (1994). Evolutionary factors influencing the nature of parasite specificity. *Parasitology*, **109** (Supplement), S85–S95.

Agapow, P. M. and N. J. B. Isaac (2002). MacroCAIC: revealing correlates of species richness by comparative analysis. *Diversity and Distributions*, **8**, 41–43.

Aguirre, A. A., R. S. Ostfeld, G. M. Tabor, C. House, and M. C. Pearl (2002). *Conservation Medicine: Ecological Health in Practice*. Oxford University Press.

Aguilar, A., G. Roemer, S. Debenham, M. Binns, D. Garcelon, and R. K. Wayne (2004). High MHC diversity maintained by balancing selection in an otherwise genetically monomorphic mammal. *Proceedings of the National Academy of Sciences USA*, 101, 3490–3494.

Al- Doory, Y. (1969). The mycology of the free living baboon. *Mycopathologia et Mycologia Applicata*, **38**, 7–15.

Alberts, S. and J. Altmann (1995). Balancing costs and opportunities: dispersal in male baboons. *American Naturalist*, **145**, 279–306.

Alexander, R. D. (1974). The evolution of social behavior. *Annual Review of Ecology and Systematics*, **5**, 325–383.

Alexander, J. and W. H. Stimson (1988). Sex-hormones and the course of parasitic infection. *Parasitology Today*, **4**, 189–193.

Alexander, K. A., P. W. Kat, L. A. Munson, A. Kalake, and M. J. G. Appel (1996). Canine distemper-related mortality among wild dogs (*Lycaon pictus*) in Chobe national park, Botswana. *Journal of Zoo and Wildlife Medicine*, **27**, 426–427.

Alm, J., J. Swartz, G. Lilja, A. Scheynius, and G. Pershagen (1999). Atopy in children of families with anthroposophic lifestyle. *Lancet*, **353**, 1457–1458.

Alroy, J. (1999). Putting North America's end-Pleistocene megafaunal extinction in context: large-scale analyses of spatial patterns, extinction rates, and size distributions. In *Extinctions in Near Time: Causes, Contexts and Consequences* (ed. R. D. E. MacPhee). Kluwer/Plenum, New York.

Altizer, S. M. (2001). Migratory behaviour and host-parasite co-evolution in natural populations of monarch butterflies infected with a protozoan parasite. *Evolutionary Ecology Research*, **3**, 611–632.

Altizer, S. M. and D. J. Augustine (1997). Interactions between frequency-dependent and vertical transmission in host-parasite systems. *Proceedings of the Royal Society B: Biological Sciences*, **264**, 807–814.

Altizer, S., J. Foufopoulos, and A. Gager (2001). Conservation and disease. In *Encyclopedia of Biodiversity* (ed. S. Levin), pp. 109–126. Academic Press, San Diego, CA.

Altizer, S., D. Harvell, and E. Friedle (2003a). Rapid evolutionary dynamics and disease threats to biodiversity. *Trends in Ecology and Evolution*, **18**, 589–596.

Altizer, S., C. L. Nunn, P. H. Thrall, J. L. Gittleman, J. Antonovics, A. A. Cunningham, A. P. Dobson et al. (2003b). Social organization and parasite risk in mammals: integrating theory and empirical studies. *Annual Review of Ecology, Evolution and Systematics*, **34**, 517–547.

Altizer, S., W. M. Hochachka, and A. A. Dhondt (2004). Seasonal dynamics of mycoplasmal conjunctivitis in eastern North American House Finches. *Journal of Animal Ecology*, **73**, 309–322.

Altmann, J. (1980). *Baboon Mothers and Infants*. Harvard University Press, Cambridge.

Altmann, J. (1990). Primate males go where the females are. *Animal Behaviour*, **39**, 193–195.

Altmann, S. A. (1974). Baboons, space, time, and energy. *American Zoologist*, **14**, 221–248.

Altmann, S. A. and J. Altmann (1970). *Baboon Ecology*. University of Chicago Press, Chicago, IL.

Amaral, V. F., V. A. Ransatto, F. Conceicao-Silva, E. Molinaro, V. Ferreira, S. Coutinho, D. McMahon-Pratt et al. (1996). *Leishmania amazonensis*: the Asian rhesus macaques (*Macaca mulatta*) as an experimental model for study of cutaneous leishmaniasis. *Experimental Parasitology*, **82**, 34–44.

Ancel Meyers, L., M. E. Newman, M. Martin, and S. Schrag (2003). Applying network theory to epidemics: control measures for *Mycoplasma pneumoniae* outbreaks. *Emerging Infectious Diseases*, **9**, 204–210.

Ancrenaz, M., J. M. Setchell, and D. J. Curtis (2003). Handling, anaesthesia, health evaluation and biological sampling. In *Field and Laboratory Methods in Primatology: A Practical Guide* (eds. J. Setchell and D. J. Curtis), pp. 122–139. Cambridge University Press, Cambridge.

Andelman, S. J. (1986). Ecological and social determinants of cercopithecine mating patterns. In *Ecological Aspects of Social Evolution: Birds and Mammals* (eds. D. I. Rubenstein, and R. W. Wrangham), pp. 201–216. Princeton University Press, Princeton, N.J.

Anderson, C. M. (1986). Predation and primate evolution. *Primates*, **27**, 15–39.

Anderson, J. R. (1998). Sleep, sleeping sites, and sleep-related activities: awakening to their significance. *American Journal of Primatology*, **46**, 63–75.

Anderson, J. R. (2000). Sleep-related behavioural adaptations in free-ranging anthropoid primates. *Sleep Medicine Reviews*, **4**, 355–373.

Anderson, J. R. and W. C. McGrew (1984). Guinea baboons (*Papio papio*) at a sleeping site. *American Journal of Primatology*, **6**, 1–14.

Anderson, M. J., J. K. Hessel, and A. F. Dixson (2004). Primate mating systems and the evolution of immune response. *Journal of Reproductive Immunology*, **61**, 31–38.

Anderson, R. and R. May (1980). Infectious diseases and population cycles of forest insects. *Science*, **210**, 658–661.

Anderson, R. C. (1992). *Nematode Parasites of Vertebrates: Their Development and Transmission*. CAB International, Oxon, UK.

Anderson, R. M. (1978). The regulation of host population growth by parasitic species. *Parasitology*, **76**, 119–157.

Anderson, R. M. (1982a). *Population Dynamics of Infectious Diseases: Theory and Applications*. Chapman and Hall, New York.

Anderson, R. M. (1982b). Theoretical basis for the use of pathogens as biological control agents of pest species. *Parasitology*, **84**, 3–33.

Anderson, R. M. (1995). Evolutionary pressures in the spread and persistence of infectious agents in vertebrate populations. *Parasitology*, **111**, S15–S31.

Anderson, R. M. (1999). Sexually transmitted diseases. In *Sexually Transmitted Diseases* (eds. K. K. Holmes, P. F. Sparling, P.-A. Mardh, S. M. Lemon, W. E. Stamm, P. Piot, and J. N. Wasserheit), pp. 25–37. McGraw-Hill, New York.

Anderson, R. M. and D. M. Gordon (1982). Processes influencing the distribution of parasite numbers within host populations with special emphasis on parasite-induced host mortalities. *Parasitology*, **85**, 373–398.

Anderson, R. M. and R. M. May (1978). Regulation and stability of host-parasite population interactions. *Journal of Animal Ecology*, **47**, 219–247.

Anderson, R. M. and R. M. May (1979). Population biology of infectious diseases: Part 1. *Nature*, **280**, 361–367.

Anderson, R. M. and R. M. May (1982). Coevolution of hosts and parasites. *Parasitology*, **85**, 411–426.

Anderson, R. M. and R. M. May (1991). *Infectious Diseases of Humans: Dynamics and Control*. Oxford University Press.

Anderson, R. M., H. C. Jackson, R. M. May, and A. D. Smith (1981). Population dynamics of fox rabies in Europe. *Nature*, **289**, 765–771.

Anderson, R. M., R. M. May, and A. R. McLean (1988). Possible demographic consequences of AIDS in developing countries. *Nature*, **332**, 228–234.

Anderson, R. M., S. P. Blythe, S. Gupta, and E. Konings (1989). The transmission dynamics of the human immunodeficiency virus type 1 in the male homosexual community in the United Kingdom: the influence of changes in sexual behaviour. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **325**, 45–98.

Anderson, T. (2004). Mapping drug resistance genes in *Plasmodium falciparum* by genome-wide association. *Current Drug Targets-Infectious Disorders*, **4**, 65–78.

Andersson, M. (1994). *Sexual Selection*. Princeton University Press, Princeton, NJ.

Andrews, C. W. (1909). On the fauna of Christmas Island. *Proceedings of the Zoological Society of London*, Part 1, 101–103.

Antia, R., B. R. Levin, and R. M. May (1994). Within-host population dynamics and the evolution of maintenance of microparasite virulence. *American Naturalist*, **144**, 457–472.

Antia, R. and M. Lipsitch (1997). Mathematical models of parasite responses to host immune defences. *Parasitology*, **115** (Suppl), S155–S167.

Antia, R., R. R. Regoes, J. C. Koella, and C. T. Bergstrom (2003). The role of evolution in the emergence of infectious diseases. *Nature*, **426**, 658–661.

Antonovics, J. (1992). Towards community genetics. In *Plant Resistance to Herbivores and Pathogens: Ecology, Evolution and Genetic* (eds. R. S. Fritz, and E. L. Simms), pp. 426–449. University of Chicago Press, Chicago, IL.

Antonovics, J., Y. Iwasa, and M. P. Hassell (1995). A generalized model of parasitoid, venereal, and vector-based transmission processes. *American Naturalist*, **145**, 661–675.

Antonovics, J., M. Hood, and J. Partain (2002). The ecology and genetics of a host shift: *Microbotryum* as a model system. *American Naturalist*, **160**, S40–S53.

Antunes, S. G., N. G. de Groot, H. Brok, G. Doxiadis, A. A. L. Menezes, N. Otting, and R. E. Bontrop (1998). The common marmoset: a new world primate species with limited MHC class II variability. *Proceedings of the National Academy of Sciences USA*, **95**, 11745–11750.

Appleton, C. C. and S. Boinski (1991). A preliminary parasitological analysis of fecal samples from a wild population of Costa Rican squirrel-monkeys (*Saimiri oerstedi*). *Journal of Medical Primatology*, **20**, 402–403.

Arneberg, P. (2002). Host population density and body mass as determinants of species richness in parasite communities: comparative analyses of directly transmitted nematodes of mammals. *Ecography*, **25**, 88–94.

Arneberg, P., A. Skorping, B. Grenfell, and A. F. Read (1998). Host densities as determinants of abundance in parasite communities. *Proceedings of the Royal Society of London B: Biological Sciences*, **265**, 1283–1289.

Arnold, W. and A. V. Lichtenstein (1993). Ectoparasite loads decrease the fitness of alpine marmots *(Marmotamarmota*) but are not a cost of sociality. *Behavioral Ecology*, **4**, 36–39.

Ashford, R. W. (2000). Parasites as indicators of human biology and evolution. *Journal of Medical Microbiology*, **49**, 771–772.

Ashford, R. W. and W. Crewe (1998). *The Parasites of* Homo sapiens*: An Annotated Checklist of the Protozoa, Helminths and Arthropods for Which We Are Home*. Liverpool School of Tropical Medicine, Liverpool.

Ashford, R. W., G. D. F. Reid, and T. M. Butynski (1990). The intestinal faunas of man and mountain gorillas in a shared habitat. *Annals of Tropical Medicine and Parasitology*, **84**, 337–340.

Ashford, R. W., H. Lawson, T. M. Butynski, and G. D. F. Reid (1996). Patterns of intestinal parasitism in the mountain gorilla *Gorilla gorilla* in the Bwindi Impenetrable Forest, Uganda. *Journal of Zoology*, **239**, 507–514.

Aufderheide, A. C., W. Salo, M. Madden, J. Streitz, J. Buikstra, F. Guhl, B. Arriaza et al. (2004). A 9,000-year record of Chagas' disease. *Proceedings of the National Academy of Sciences USA*, **101**, 2034–2039.

Aufreiter, S., W. C. Mahaney, M. W. Milner, M. A. Huffman, R. G. V. Hancock, M. Wink, and M. Reich (2001). Mineralogical and chemical interactions of soils eaten by chimpanzees of the Mahale Mountains and Gombe Stream National Park, Tanzania. *Journal of Chemical Ecology*, **27**, 285–311.

Ayres, J. M. (1986). Uakaris and the Amazonian flooded forest. Ph.D. thesis, University of Cambridge, Cambidge.

Baer, G. M. (1991). *The Natural History of Rabies*. CRC Press, Boca Raton, FL.

Bagge, A. M., R. Poulin, and E. T. Valtonen (2004). Fish population size, and not density, as the determining factor of parasite infection: a case study. *Parasitology*, **128**, 305–313.

Bailes, E., F. Gao, F. Bibollet-Ruche, V. Courgnaud, M. Peeters, P. A. Marx, B. H. Hahn, and P. M. Sharp (2003). Hybrid origin of SIV in chimpanzees. *Science*, **300**, 1713.

Bakarr, M. I., A. A. Gbakima, and Z. Bah (1991). Intestinal helminth parasites in free-living monkeys from a West African rain forest. *African Journal of Ecology*, **29**, 170–172.

Baker, M. (1996). Fur rubbing: use of medicinal plants by capuchin monkeys (*Cebus capucinus*). *American Journal of Primatology*, **38**, 263–270.

Baldacchino, F. and S. Bertagnoli (2002). History of the yellow fever's epidemiology. *Revue De Medecine Veterinaire*, **153**, 779–784.

Ballou, J. D. (1993). Assessing the risks of infectious-diseases in captive breeding and reintroduction programs. *Journal of Zoo and Wildlife Medicine*, **24**, 327–335.

Barker, D., M. P. Fitzpatrick, and E. S. Dierenfeld (1998). Nutrient composition of selected whole invertebrates. *Zoo Biology*, **17**, 123–134.

Baron, S., I. Singh, A. Chopra, D. Coppenhaver, and J. Z. Pan (2000). Innate antiviral defenses in body fluids and tissues. *Antiviral Research*, **48**, 71–89.

Barr, R. G. (1999). Infant crying behavior and colic. In *Evolutionary Medicine* (eds. W. R. Trevathan, E. O. Smith, and J. J. McKenna), pp. 27–51. Oxford University Press, Oxford.

Barraclough, T., P. Harvey, and S. Nee (1995). Sexual selection and taxonomic diversity in passerine birds. *Proceedings of the Royal Society B: Biological Sciences*, **259**, 211–215.

Barratt, C. L. R., A. E. Bolton, and I. D. Cooke (1990). Functional significance of white blood cells in the male and female reproductive tract. *Human Reproduction*, **5**, 639–648.

Barrett, L. and S. P. Henzi (1998). Epidemic deaths in a chacma baboon population. *South African Journal of Medical Science*, **94**, 441.

Barrett, L., R. I. M. Dunbar, and J. E. Lycett (2002). *Human Evolutionary Psychology*. Princeton University Press, Princeton, NJ.

Barrett, R., C. W. Kuzawa, T. McDade, and G. J. Armelagos (1998). Emerging and re-emerging infectious diseases: the third epidemiologic transition. *Annual Review of Anthropology*, **27**, 247–271.

Bartlett, M. S. (1957). Measles periodicity and community size. *Journal of the Royal Statistical Society: Series A*, **120**, 48–70.

Bartlett, M. S. (1960). The critical community size for measles in the United States. *Journal of the Royal Statistical Society: Series A*, **123**, 37.

Barton, R. (1985). Grooming site preferences in primates and their functional implications. *International Journal of Primatology*, **6**, 519–532.

Barton, R. A. (1987). Allogrooming as mutualism in diurnal lemurs. *Primates*, **28**, 539–542.

Barton, R. A., R. W. Byrne, and A. Whiten (1996). Ecology, feeding competition and social structure in baboons. *Behavioral Ecology and Sociobiology*, **38**, 321–329.

Bascompte, J. and R. V. Solé (1996). Habitat fragmentation and extinction thresholds in spatially explicit models. *Journal of Animal Ecology*, **65**, 465–473.

Bauchop, T. and R. W. Martucci (1968). Ruminant-like digestion of the langur monkey. *Science*, **161**, 698–700.

Baylet, R., J. Thivolet, M. Sepetjian, and J. Bert (1971). Seroepidemiological studies on primate treponematosis in Senegal. *Bull Soc Pathol Exot Filiales*, **64**, 836–841.

Beck, B. (1995). Reintroduction, zoos, conservation, and animal welfare. In *Ethics of the Ark* (eds. B. G. Norton, M. Hutchins, E. F. Stevens, and T. L. Maple), pp. 155–163. Smithsonian Institution Press, Washington, DC.

Beck, B. B., M. I. Castro, T. S. Stoinski, and J. D. Ballou (2002). The effects of prerelease environments and postrelease management on survivorship in reintroduced golden lion tamarins. In *Lion Tamarins* (eds. D. G. Kleiman and A. B. Rylands), pp. 283–300. Smithsonian Institution Press, Washington, DC.

Begon, M., M. Bennett, R. G. Bowers, N. P. French, S. M. Hazel, and J. Turner (2002). A clarification of transmission terms in host-microparasite models: numbers, densities and areas. *Epidemiology and Infection*, **129**, 147–153.

Begon, M. and R. Bowers (1994). Host-host pathogen models and microbial pest control: the effect of host self-regulation. *Journal of Theoretical Biology*, **169**, 275–287.

Begon, M., S. M. Hazel, D. Baxby, K. Bown, R. Cavanagh, J. Chantrey, T. Jones et al. (1999). Transmission dynamics of a zoonotic pathogen within and between wildlife host species. *Proceedings of the Royal Society B: Biological Sciences*, **266**, 1939–1945.

Begon, M., M. Bennett, R. G. Bowers, N. P. French, S. M. Hazel, and J. Turner (2002). A clarification of transmission terms in host-microparasite models: numbers, densities and areas. *Epidemiology and Infection*, **129**, 147–153.

Behebani, A. M. (1983). The smallpox story: life and death of an old disease. *Microbiological Reviews*, **47**, 455–509.

Beisel, W. R. (2000). Interactions between nutrition and infection. In *Hunter's Tropical Medicine* (ed. G. Strickland), pp. 967–969. W. B. Saunders, Philadelphia, PA.

Beissinger, S. R. and D. R. McCullough (2002). *Population Viability Analysis*. Chicago University Press, Chicago, IL.

Bell, G. and A. Burt (1991). The comparative biology of parasite species-diversity—internal helminths of fresh-water fish. *Journal of Animal Ecology*, **60**, 1047–1063.

Bercovitch, F. B. and T. E. Ziegler (2002). Current topics in primate socioendocrinology. *Annual Review of Anthropology*, **31**, 45–67.

Berdoy, M., J. P. Webster, and D. W. Macdonald (2000). Fatal attraction in rats infected with *Toxoplasma gondii*. *Proceedings of the Royal Society B: Biological Sciences*, **267**, 1591–1594.

Berenbaum, M. R. (1996). Introduction to the symposium: on the evolution of specialization. *American Naturalist*, **148**, S78–S83.

Berger, L., R. Speare, P. Daszak, D. E. Green, A. A. Cunningham, C. L. Goggin, R. Slocombe et al. (1998). Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. *Proceedings of the National Academy of Sciences USA*, **95**, 9031–9036.

Berman, C. M. and J.-H. Li (2002). Impact of translocation, provisioning and range restriction on a group of *Macaca thibetana*. *International Journal for Primatology*, **23**, 383–397.

Bibollet-Ruche, F., A. Galat-Luong, G. Cuny, P. Sarni-Manchado, G. Galat, J. P. Durand, X. Pourrut et al. (1996). Simian immuno deficiency virus infection in a patas monkey (*Erythrocebus patas*): evidence for cross-species transmission from African green monkeys (*Cercopithecus aethiops sabaeus*) in the wild. *Journal of General Virology*, **77**, 773–781.

Bicca-Marques, J. C. and C. Calgero-Marques (1994). A case of geophagy in the black howling monkey *Aloutta caraya*. *Neotropical Primates*, **2**, 7–9.

Biek, R., A. Rodril, D. Hlley, A. Drummond, C. Anderson, H. Ross, and M. Poss (2003). Epidemiology, genetic diversity, and evolution of endemic feline immunodeficiency virus in a population of wild cougars. *Journal of Virology*, **77**, 9578–9589.

Billing, J. and P. W. Sherman (1998). Antimicrobial functions of spices: why some like it hot. *Quarterly Review of Biology*, **73**, 3–49.

Bitter, W. H. G., R. Kieft, and P. Borst (1998). The role of transferin-receptor variation in the host range of *Tyrpanosoma brucei. Nature*, **391**, 499–502.

Bjørnstad, O. N. and B. T. Grenfell (2001). Noisy clockwork: time series analysis of population fluctuations in animals. *Science*, **293**, 638–643.

Bjørnstad, O. N., B. Finkenstädt, and B. T. Grenfell (2002). Endemic and epidemic dynamics of measles. I. estimating epidemiological scaling with a time series SIR model. *Ecological Monographs*, **72**, 169–184.

Bleisch, W., C. Ao-Song, R. Xiao-Dong, and X. Jia-Hua (1993). Preliminary results from a field study of wild guizhou snub-nosed monkeys (*Rhinopithecus brelichi*). *Folia Primatologica*, **60**, 72–82.

Blewett, E. L., D. H. Black, N. W. Lerche, G. White, and R. Eberle (2000). Simian foamy virus infections in a baboon breeding colony. *Virology*, **278**, 183–193.

Blomberg, S. P. and T. Garland (2002). Tempo and mode in evolution: phylogenetic inertia, adaptation and comparative methods. *Journal of Evolutionary Biology*, **15**, 899–910.

Blomberg, S. P., T. Garland, and A. R. Ives (2003). Testing for phylogenetic signal in comparative data: behavioral traits are more labile. *Evolution*, **57**, 717–745.

Blower, S. M. and A. R. McLean (1991). Mixing ecology and epidemiology. *Proceedings of the Royal Society B: Biological Sciences*, **245**, 187–192.

Bock, G. and G. Cardew (1996). Olfaction in mosquito-host interactions, Ciba Foundation symposium. Wiley, Chichester, New York.

Boesch, C. and H. Boesch-Achermann (2000). *The Chimpanzees of the Taï Forest*. Oxford University Press, Oxford.

Boesch, C., G. Kohou, H. Néné, and L. Vigilant (2006). Male competition and paternity in wild chimpanzees of the Taï forest. *American Journal of Physical Anthropology*, in press.

Boily, M. C. and B. Masse (1997). Mathematical models of disease transmission: a precious tool for the study of sexually transmitted diseases. *Canadian Journal of Public Health*, **88**, 255–265.

Bolles, R. C. and M. S. Fanselow (1980). A perceptual-defensive-recuperative model of fear and pain. *Behavioral and Brain Sciences*, **3**, 291–301.

Bonds, M. H., D. C. Keenan, A. J. Leidner, and P. Rohani (2005). Infectious diseases can induce greater sociality: a game theoretic coevolutionary model. *Evolution*, **59**, 1859–1866.

Bonneaud, C., J. Mazuc, G. Gonzalez, C. Haussy, O. Chastel, B. Faivre, and G. Sorci (2003). Assessing the cost of mounting an immune response. *American Naturalist*, **161**, 367–379.

Boots, M. and A. Sasaki (1999). "Small worlds" and the evolution of virulence: infection occurs locally and at a distance. *Proceedings of the Royal Society B: Biological Sciences*, **266**, 1933–1938.

Boots, M. and R. J. Knell (2002). The evolution of risky behaviour in the presence of a sexually transmitted disease. *Proceedings of the Royal Society B: Biological Sciences*, **269**, 585–589.

Boots, M. and A. Sasaki (2002). Parasite-driven extinction in spatially explicit host-parasite systems. *American Naturalist*, **159**, 706–713.

Boots, M., P. J. Hudson, and A. Sasaki (2004). Large shifts in pathogen virulence relate to host population structure. *Science*, **303**, 842–844.

Borgia, G. (1986). Satin bowerbird parasites: a test of the bright male hypothesis. *Behavioral Ecology and Sociobiology*, **19**, 355–358.

Bostanci, A. (2005). A devil of a disease. *Science*, **307**, 1035.

Bouloux, C. and P. Cirera (1972). Nonhuman primates and treponematoses. In *Medical Primatology 1972* (eds. E. I. Goldsmith, and J. Moor- Jankowski), pp. 31–34. S. Karger, Basel.

Boyce, M. S. (1992). Population viability analysis. *Annual Review of Ecology and Systematics*, **23**, 481–506.

Boyse, E., G. Beauchamp, and K. Yamazaki (1987). The genetics of body scent. *Trends in Genetics*, **3**, 97–102.

Brack, M. (1987). *Agents Transmissible From Simians to Man*. Springer-Verlag, Berlin.

Brack, M. (1996). Gongylonematiasis in the common marmoset (*Callithrix jacchus*). *Laboratory Animal Science*, **46**, 266–270.

Brain, C. and R. Bohrmann (1992). Tick infestation of baboons (*Papio ursinus*) in the Namib Desert. *Journal of Wildlife Diseases*, **28**, 188–191.

Brashares, J. S., P. Arcese, M. K. Sam, P. B. Coppolillo, A. R. E. Sinclair, and A. Balmford (2004). Bushmeat hunting, wildlife declines, and fish supply in West Africa. *Science*, **306**, 1180–1183.

Braun-Fahrlander, C., M. Gassner, L. Grize, U. Neu, F. Sennhauser, H. Varonier, J. Vuille et al. (1999). Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. *Clinical and Experimental Allergy*, **29**, 28–34.

Braza, F., F. Alvarez, and T. Azcarate (1981). Behaviour of the red howler monkey (*Alouatta seniculus*) in the Llanos of Venezuela. *Primates*, **22**, 459–473.

Britt, A., C. Welch, and A. Katz (2003). Can small, isolated primate populations be effectively reinforced through the release of individuals from a captive population? *Biological Conservation*, **115**, 319–327.

Britt, A., C. Welch, A. Katz, B. Iambana, I. Porton, R. Junge, G. Crawford et al. (2004). The re-stocking of captive-bred ruffed lemurs (*Varecia variegata variegata*) into the Betampona Reserve, Madagascar: methodology and recommendations. *Biodiversity and Conservation*, **13**, 635–657.

Brooks, D. R. and D. R. Glen (1982). Pinworms and primates—a case-study in coevolution. *Proceedings of the Helminthological Society of Washington*, **49**, 76–85.

Brosch, R., A. Pym, S. Gordon, and S. Cole (2001). The evolution of mycobacterial pathogenicity: clues from comparative genomics. *Trends in Microbiology*, **9**, 452–458.

Brown, C. R. and M. B. Brown (1986). Ectoparasitism as a cost of coloniality in cliff swallows (*Hirundo pyrrhonota*). *Ecology*, **67**, 1206–1218.

Brown, C. R. and M. B. Brown (2004). Empirical measurement of parasite transmission between groups in a colonial bird. *Ecology*, **85**, 1619–1626.

Brown, D. W. G. (1997). Threat to humans from virus infections of non-human primates. *Reviews in Medical Virology*, **7**, 239–246.

Buckling, A. and P. B. Rainey (2002). The role of parasites in sympatric and allopatric host diversificaiton. *Nature*, **420**, 496–499.

Bufford, J. and J. Gern (2005). The hygiene hypothesis revisited. *Immunology and Allergy Clinics of North America*, **25**, 247–262.

Bull, J. J. (1994). Virulence. *Evolution*, **48**, 1423–1437.

Burdon, J. J. and P. H. Thrall (1999). Spatial and temporal patterns in coevolving plant and pathogen associations. *American Naturalist*, **153**, S15–S33.

Burr, P. and D. Snodgrass (2004). Demystifying diagnostic testing: serology. *In Practice*, **26**, 498–502.

Burrows, R., H. Hofer, and M. East (1994). Demography, extinction and intervention in a small population: the case of the Serengeti wild dogs. *Proceedings of the Royal Society B: Biological Sciences*, **256**, 281–292.

Burrows, R., H. Hofer, and M. L. East (1995). Population-dynamics, intervention and survival in African wild dogs (*Lycaon pictus*). *Proceedings of the Royal Society B: Biological Sciences*, **262**, 235–245.

Bush, A. O., J. C. Fernandez, G. W. Esch, and J. R. Seed (2001). *Parasitism: The Diversity and Ecology of Animal Parasites*. Cambridge University Press, Cambridge.

Bush, A. O., K. D. Lafferty, J. M. Lotz, and A. W. Shostak. (1997). Parasitology meets ecology on its own terms: Margolis et al. revisited. *Journal of Parasitology*, **83**, 575–583.

Butler, J. M. and T. J. Roper (1996). Ectoparasites and sett use in European badgers. *Animal Behaviour*, **52**, 621–629.

Butynski, T. M. and J. Kalina (1998). Gorilla tourism: a critical look. In *Conservation of Biological Resources* (eds. E. J. Millner-Gulland, and R. Mace), pp. 294–313. Blackwell Science, Oxford.

Bywater, J. E. C. and K. H. Mann (1960). Infestation of a monkey with the leech *Dinobdella ferox. The Veterinary Record*, **72**, 955.

Caley, P. and D. Ramsey (2001). Estimating disease transmission in wildlife, with emphasis on leptospirosis and bovine tuberculosis in possums, and effects of fertility control. *Journal of Applied Ecology*, **38**, 1362–1370.

Capitanio, J. P. and N. W. Lerche (1998). Social separation, housing relocation, and survival in simian AIDS: a retrospective analysis. *Psychosomatic Medicine*, **60**, 235–244.

Cardillo, M., A. Purvis, W. Sechrest, J. L. Gittleman, J. Bielby, and G. M. Mace (2004). Human population density and extinction risk in the world's carnivores. *PLoS Biology*, **2**, e197.

Carlsson-Graner, U. and P. H. Thrall (2002). The spatial distribution of plant populations, disease dynamics and evolution of resistance. *Oikos*, **97**, 97–110.

Caro, T. M. and M. K. Laurenson (1994). Ecological and genetic factors in conservation: a cautionary tale. *Science*, **263**, 485.

Carpenter, C. R. (1964). *Naturalistic Behavior of Nonhuman Primates*. Pennsylvania State University Press, University Park, PA.

Carrai, V., S. M. Borgognini-Tarli, M. A. Huffman, and M. Bardi (2003). Increase in tannin consumption by sifaka (*Propithecus verreauxi verreauxi*) females during the birth season: a case for self-medication in prosimians? *Primates*, **44**, 61–66.

Carrington, M. and R. E. Bontrop (2002). Effects of MHC class I on HIV/SIV disease in primates. *AIDS*, 16 (Suppl 4), S105–S114.

Carrington, M., G. W. Nelson, M. P. Martin, T. Kissner, D. Vlahov, J. J. Goedert, R. Kaslow et al. (1999). HLA and HIV-1: heterozygote advantage and B*35-Cw*04 disadvantage. *Science*, **283**, 1748–1752.

Carroll, L., D. Penn, and W. Potts (2002). Discrimination of MHC-derived odors by untrained mice is consistent with divergence in peptide binding region residues. *Proceedings of the National Academy of Sciences USA*, **99**, 2187–2192.

Carter, R. (2003). Speculations on the origins of *Plasmodium vivax* malaria. *Trends in Parasitology*, **19**, 214–219.

Cattadori, I. M., Boag, B., Bjørnstad, O. N., Cornell, S. J. & Hudson, P. J. (2005). Peak shift and epidemiology in a seasonal host–nematode system. *Proceedings of the Royal Society B: Biological Sciences*, **272**, 1163–1169.

CDC (2004a). 150th Anniversary of John Snow and the pump handle. *Morbidity and Mortality Weekly Report*, **53**, 783.

CDC (2004b). *Malaria Facts*, Centers for Disease Control and Prevention www.cdc.gov/malaria facts/htm.

Chandra, R. (1991). Interactions between early nutrition and the immune system. *Ciba Foundation Symposium*, **156**, 77–92.

Chapman, C. and C. Peres (2001). Primate conservation in the new millenium: the role of scientists. *Evolutionary Anthropology*, **10**, 16–33.

Chapman, C. A., T. R. Gillespie, and T. L. Goldberg (2005a). Primates and the ecology of their infectious diseases: how will anthropogenic change affect host-parasite interactions? *Evolutionary Anthroplogy*, **14**, 134–144.

Chapman, C. A., T. R. Gillespie, and M. L. Speirs (2005b). Parasite prevalence and richness in sympatric colobines: effects of host density. *American Journal of Primatology*, **67**, 259–266.

Chapman, C. A., M. L. Speirs, T. R. Gillespie, T. Holland, and K. M. Austad (2005c). Life on the edge: gastrointestinal parasites from forest edge and interior primate groups. *American Journal of Primatology*, **68**, 1–12.

Cheney, D. L. (1987). Interactions and relationships between groups. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Struhsaker), pp. 267–281. University of Chicago Press, Chicago, IL.

Cheney, D. L. (1992). Intragroup cohesion and intergroup hostility: the relation between grooming distributions and intergroup competition among female primates. *Behavioral Ecology*, **3**, 334–345.

Cheney, D. L. and R. W. Wrangham (1987). Predation. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Struhsaker), pp. 227–239. University of Chicago Press, Chicago, IL.

Cheney, D. L., R. M. Seyfarth, S. J. Andelman, and P. C. Lee (1988). Reproductive success in vervet monkeys. In *Reproductive Success* (ed. T. H. Clutton-Brock), pp. 384–402. Chicago University Press, Chicago, IL.

Chimpanzee Sequencing and Analysis Consortium (2005). Initial sequence of the chimpanzee genome and comparison with the human genome. *Nature*, **431**, 69–87.

Choisy, M., S. Brown, K. Lafferty, and F. Thomas (2003). Evolution of trophic transmission in parasites: why add intermediate hosts? *American Naturalist*, **162**, 172–181.

Chowell, G., N. W. Hengartnerb, C.Castillo-Chavez, P. W. Fenimorea, and J. M. Hyman (2004). The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. *Journal of Theoretical Biology*, **229**, 119–126.

Cichon, M., M. Chadzinska, A. Ksiazek, and M. Konarzewski (2002). Delayed effects of cold stress on immune response in laboratory mice. *Proceedings of the Royal Society B: Biological Sciences*, 1499, 1493–1497.

Clayton, D. H. (1991). The influence of parasites on host sexual selection. *Parasitology Today*, **7**, 329–334.

Clayton, D. H. and J. A. Moore. (1997). *Host-Parasite Evolution: General Principles and Avian Models*. Oxford University Press, Oxford.

Clayton, D. H., P. L. M. Lee, D. M. Tompkins, and E. D. Brodie (1999). Reciprocal natural selection on host-parasite phenotypes. *American Naturalist*, **154**, 261–270.

Clayton, D. H., S. E. Bush, B. M. Goates, and K. P. Johnson (2003). Host defense reinforces host-parasite cospeciation. *Proceedings of the National Academy of Science USA*, **100**, 15694–15699.

Cleaveland, S. and C. Dye (1995). Maintenance of a microparasite infecting several host species: rabies in the Serengeti. *Parasitology*, **111**, S33–S47.

Cleaveland, S., M. K. Laurenson, and L. H. Taylor (2001). Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **356**, 991–999.

Cleaveland, S., G. R. Hess, A. P. Dobson, M. K. Laurenson, and H. I. McCallum (2002). The role of pathogens in biological conservation. In *The Ecology of Wildlife Diseases* (eds. P. J. Hudson, A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. P. Dobson), pp. 139–150. Oxford University Press, New York.

Clifford, R. J., C. Callanan, and S. E. G. Smith (1972). The Barbary apes of Gibraltar. *The Blue Book for the Veterinary Profession*, **22**, 167–169.

Clifton-Hadley, R. S., C. M. Sauter-Louis, R. Jackson, P. A. Durr, and J. W. Wilesmith (2001). Mycobacterial diseases. In *Infectious Diseases of Wild Mammals* (eds. E. S. Williams, and I. K. Barker), pp. 340–361. Iowa State University Press, Ames, IA.

Clubb, R. and G. Mason (2003). Captivity effects on wide-ranging carnivores. *Nature*, **425**, 473–474.

Clutton-Brock, T. H. (1989). Mammalian mating systems. *Proceedings of the Royal Society B: Biological Sciences*, **236**, 339–372.

Clutton-Brock, T. H. and P. H. Harvey (1976). Evolutionary rules and primate societies. In *Growing Points in Ethology* (eds. P. P. G. Bateson, and R. A. Hinde), pp. 195–237. Cambridge University Press, Cambridge.

Clutton-Brock, T. H. and P. H. Harvey (1977). Primate ecology and social organization. *Journal of Zoology*, **183**, 1–39.

Clutton-Brock, T. H. and P. H. Harvey (1980). Primates, brains and ecology. *Journal of Zoology*, **190**, 309–323.

Clutton-Brock, T. H. and P. H. Harvey (1984). Comparative approaches to investigating adaptation. In *Behavioural Ecology* (eds. J. R. Krebs, and N. B. Davies), pp. 7–29. Blackwell, Oxford.

Clutton-Brock, T. H. and G. A. Parker (1995). Sexual coercion in animal societies. *Animal Behaviour*, **49**, 1345–1365.

Clutton-Brock, T. H., P. H. Harvey, and B. Rudder (1977). Sexual dimorphism, socionomic sex ratio and body weight in primates. *Nature*, **269**, 797–800.

Coatney, G. R., W. E. Collins, and W. McWilson (1971). *The Primate Malarias*. Bethesda, National Insitiute of Allergy and Infectious Diseases.

Cochran, G. M., P. W. Ewald, and K. D. Cochran (2000). Infectious causation of disease: an evolutionary perspective. *Perspectives in Biology and Medicine*, **43**, 406–448.

Coe, C. L. (1993). Psychosocial factors and immunity in nonhuman-primates—a review. *Psychosomatic Medicine*, **55**, 298–308.

Cohen, J. (1969). Natural primate troops and a stochastic population model. *American Naturalist*, **103**, 455–477.

Cohen, S. (1999). Social status and susceptibility to respiratory infections. *Annals of the New York Academy of Sciences*, 896.

Cohen, S., S. Line, S. B. Manuck, B. S. Rabin, E. R. Heise, and J. R. Kaplan (1997). Chronic social stress, social status, and susceptibility to upper respiratory infections in nonhuman primates. *Psychosomatic Medicine*, **59**, 213–221.

Cohen, S., D. Tyrrell, and A. Smith (1991). Psychological stress and susceptibility to the common cold. *New England Journal of Medicine*, **325**, 606–612.

Colley, F. C. and S. W. Mullin (1972). *Eimeria pachylepyron Sp. N.* (Protozoa: Eimeriidae) from the slow loris in Malaysia. *The Journal of Parasitology*, **58**, 110–111.

Coltman, D. W., K. Wilson, J. G. Pilkington, M. J. Stear, and J. M. Pemberton (2001). A microsatellite polymorphism in the gamma interferon gene is associated with resistance to gastrointestinal nematodes in a naturally parasitized population of Soay sheep. *Parasitology*, **122**, 571–582.

Colwell, D. D. (2001). Bot flies and warble flies (Order Diptera: Family Oestridae). In *Parasitic Diseases of Wild Mammals* (eds. W. M. Samuel, M. J. Pybus, and A. A. Kocan), pp. 46–71. Iowa State University Press, Ames, Iowa.

Colwell, R. R. (1996). Global climate and infectious disease: the cholera paradigm. *Science*, **274**, 2025–2031.

Combes, C. (2000). Parasites, hosts, questions. In *Evolutionary Biology of Host-Parasite Relationships* (eds. R. Poulin, S. Morand, and A. Skorping), pp. 1–8. Elsevier, Amsterdam.

Combes, C. (2001). *Parasitism: The Ecology and Evolution of Intimate Interactions*. University of Chicago Press, Chicago, IL.

Combes, C. and A. Theron (2000). Metazoan parasites and resource heterogeneity: constraints and benefits. *International Journal for Parasitology*, **30**, 299–304.

Conway, D. and S. Polley (2002). Measuring immune selection. *Parasitology*, **125**, S3–S16.

Conway, W. G. (1980). An overview of captive propagation. In *Conservation Biology: An Evolutionary-Ecological Perspective* (eds. M. E. Soule, and B. A. Wilcox), pp. 199–208. Sinauer Associates, Sunderland, Massachusetts.

Cooney, D. O. and T. T. Struhsaker (1997). Adsorptive capacity of charcoals eaten by Zanzibar red colobus monkeys: implications for reducing dietary toxins. *International Journal of Primatology*, **18**, 235–246.

Cooper, V. J. and G. R. Hosey (2003). Sexual dichromatism and female preference in *Eulemur fulvus* subspecies. *International Journal of Primatology*, **24**, 1177–1188.

Cords, M. and T. Rowell (1986). Group fission in blue monkeys of the Kakamega Forest, Kenya. *Folia Primatologica*, **46**, 70–82.

Côté, I. M. and R. Poulin (1995). Parasitism and group size in social animals: a meta-analysis. *Behavioral Ecology*, **6**, 159–165.

Cowlishaw, G. (1995). Behavioural patterns in baboon group encounters: the role of resource competition and male reproductive strategies. *Behaviour*, **132**, 75–86.

Cowlishaw, G. (1997). Trade-offs between foraging and predation risk determine habitat use in a desert baboon population. *Animal Behaviour*, **53**, 667–686.

Cowlishaw, G. and R. Dunbar (1991). Dominance rank and mating success in male primates. *Animal Behaviour*, **41**, 1045–1056.

Cowlishaw, G. and R. I. M. Dunbar (2000). *Primate Conservation Biology*. University of Chicago Press, Chicago, IL.

Cox, F. (2002). Systematics of the parasitic protozoa. *Trends in Parasitology*, **18**, 108.

Crandall, K. A., O. R. P. Bininda-Emonds, G. M. Mace, and R. K. Wayne (2000). Considering evolutionary processes in conservation biology. *Trends in Ecology & Evolution*, **15**, 290–295.

Crockett, C. M. (1984). Emigration by female red howler monkeys and the case for female competition. In *Female Primates: Studies by Women Primatologists* (ed. M. Small), pp. 159–173. Alan R. Liss, New York.

Crompton, D. W. T. (1984). Influence of parasitic infection on food intake. *Federation Proceedings*, **43**, 239–245.

Crompton, D. W. T. (1999). How much human helminthiasis is there in the world? *Journal of Parasitology*, **85**, 397–403.

Crook, J. H. (1970). The socio-ecology of primates. In *Social Behaviour in Birds and Mammals. Essays on the Social Ethology of Animals and Man* (ed. J. H. Crook), pp. 103–166. Academic Press, London.

Crook, J. H. and J. C. Gartlan (1966). Evolution of primate societies. *Nature*, **210**, 1200–1203.

Cross, P. C., J. O. Lloyd-Smith, J. A. Bowers, C. T. Hay, M. Hofmeyr, and W. M. Getz (2004). Integrating association data and disease dynamics in a social ungulate: Bovine tuberculosis in African buffalo in the Kruger National Park. *Annales Zoologici Fennici*, **41**, 879–892.

Cross, P. C., J. O. Lloyd-Smith, P. L. Johnson, and W. M. Getz (2005). Dueling time scales of host movement and disease recovery determine invasion of disease in structured populations. *Ecology Letters*, **8**, 587–595.

Cunningham, A. A. (1996). Disease risks of wildlife translocations. *Conservation Biology*, **10**, 349–353.

Damuth, J. (1981). Population density and body size in mammals. *Nature*, **290**, 699–700.

Daszak, P., L. Berger, A. A. Cunningham, A. D. Hyatt, D. E. Green, and R. Speare (1999). Emerging infectious diseases and amphibian population declines. *Emerging Infectious Diseases*, **5**, 735–748.

Daszak, P., A. A. Cunningham, and A. D. Hyatt (2000). Emerging infectious diseases of wildlife: threats to biodiversity and human health. *Science*, **287**, 443–449.

Daszak, P., A. A. Cunningham, and A. D. Hyatt (2003). Infectious disease and amphibian population declines. *Diversity and Distributions*, **9**, 141–150.

Davies, A. G. and I. C. Baillie (1988). Soil-eating by red leaf monkeys (*Presbytis rubicunda*) in Sabah, Northern Borneo. *Biotropica*, **20**, 252–258.

Davies, C. R., J. M. Ayres, C. Dye, and L. M. Deane (1991). Malaria infection rate of Amazonian primates increases with body weight and group size. *Functional Ecology*, **5**, 655–662.

Dawkins, R. (1982). *The Extended Phenotype*. W.H. Freeman and Company, Oxford.

Day, R. T. and R. W. Elwood (1999). Sleeping site selection by the golden-handed tamarin *Saguinus midas midas*: The role of predation risk, proximity to feeding sites, and territorial defence. *Ethology*, **105**, 1035–1051.

Day, T. (2001). Parasite transmission modes and the evolution of virulence. *Evolution*, **55**, 2389–2400.

de Castro, F. and B. Bolker (2005). Mechanisms of disease-induced extinction. *Ecology Letters*, **8**, 117–126.

de Groot, N., N. Otting, G. Doxiadis, S. Balla-Jhagjhoorsingh, J. Heeney, J. van Rood, P. Gagneux et al. (2002). Evidence for an ancient selective sweep in the MHC class I gene repertoire of chimpanzees. *Proceedings of the National Academy of Sciences USA*, **99**, 11748–11753.

de Gruijter, J. M., J. Ziem, J. J. Verweij, A. M. Polderman, and R. B. Gasser (2004). Genetic substructuring within *Oesophagostomum bifurcum* (Nematoda) from human and non-human primates from Ghana based on random amplified polymorphic DNA analysis. *American Journal of Tropical Medicine and Hygiene*, **71**, 227–233.

de Gruijter, J. M., R. B. Gasser, A. M. Polderman, V. Asigri, and L. Dijkshoorn (2005). High resolution DNA fingerprinting by AFLP to study the genetic variation among *Oesophagostomum bifurcum* (Nematoda) from human and non-human primates from Ghana. *Parasitology*, **130**, 229–237.

De Leo, G. A. and A. P. Dobson (1996). Allometry and simple epidemic models for microparasites. *Nature*, **379**, 720–722.

de Roode, J. C., R. Pansini, S. J. Cheesman, M. E. H. Helinski, S. Huijben, A. R. Wargo, A. S. Bell et al. (2005). Virulence and competitive ability in genetically diverse malaria infections. *Proceedings of the National Academy of Sciences USA*, **102**, 7624–7628.

de Waal, F. (1986). The brutal elimination of a rival among captive male chimpanzees. *Ethology and Sociobiology*, **7**, 237–251.

Deane, L. M. (1992). Simian malaria in Brazil. *Memorias Do Instituto Oswaldo Cruz*, **87**, 1–20.

Deane, L. M., J. A. Ferreira Neto, M. Okumura, and M. O. Ferreira (1969). Malaria parasites of Brazilian monkeys. *Revista do Instituto de Medicina Tropical de Sao Paulo*, **11**, 71–86.

Deaner, R. O. and C. L. Nunn (1999). How quickly do brains catch up with bodies? A comparative method for detecting evolutionary lag. *Proceedings of the Royal Society B: Biological Sciences*, **266**, 687–694.

Demas, G. E., V. Chefer, M. I. Talan, and R. J. Nelson (1997). Metabolic costs of mounting an antigen-stimulated immune response in adult and aged C57BL/6J mice. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, **42**, R1631–R1637.

Derting, T. and S. Compton (2003). Immune response, not immune maintenance, is energetically costly in wild white-footed mice (*Peromyscus leucopus*). *Physiological and Biochemical Zoology*, **76**, 744–752.

Desdevises, Y., S. Morand, and P. Legendre (2002). Evolution and determinants of host specificity in the genus *Lamellodiscus* (Monogenea). *Biological Journal of the Linnean Society*, **77**, 431–443.

Devilliers, M. S., D. G. A. Meltzer, J. Vanheerden, M. G. L. Mills, P. R. K. Richardson, and A. S. Vanjaarsveld (1995). Handling-induced stress and mortalities in African wild dogs (*Lycaon pictus*). *Proceedings of the Royal Society B: Biological Sciences*, **262**, 215–220.

Dewsbury, D. A. and J. D. Pierce (1989). Copulatory patterns of primates as viewed in broad mammalian perspective. *American Journal of Primatology*, **17**, 51–72.

Dhondt, A. A., S. Altizer, E. G. Cooch, A. K. Davis, A. Dobson, M. J. L. Driscoll, B. K. Hartup et al. (2005). Dynamics of a novel pathogen in an avian host: *Mycoplasmal conjunctivitis* in house finches. *Acta Tropica*, **94**, 77–93.

Di Bitetti, M. S., E. M. L. Vidal, M. C. Baldovino, and V. Benesovsky (2000). Sleeping site preferences in tufted capuchin monkeys (*Cebus apella nigritus*). *American Journal of Primatology*, **50**, 257–274.

Di Fiore, A. (2003). Ranging behavior and foraging ecology of lowland woolly monkeys (*Lagothrix lagotricha poeppigii*) in Yasuni National Park, Ecuador. *American Journal of Primatology*, **59**, 47–66.

Diamond, J. (1997). *Guns, Germs, and Steel*. W.W. Norton & Co., New York.

Diamond, J. M. (1975). The island dilemma: lessons of modern biogeographic studies for the design of natural reserves. *Biological Conservation*, **7**, 129–146.

Dias, L. G. and K. B. Strier (2003). Effects of group size on ranging patterns in *Brachyteles arachnoides hypoxanthus*. *International Journal of Primatology*, **24**, 209–221.

Diekmann, O., J. A. P. Heesterbeek, and J. A. J. Metz (1990). On the definition and the computation of the basic reproductive ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*, **28**, 365–382.

Dietz, K. (1993). The estimation of the basic reproduction number for infectious diseases. *Statistical Methods in Medical Research*, **2**, 23–41.

Diseker, R. A., T. A. Peterman, M. L. Kamb, C. Kent, J. M. Zenilman, J. M. Douglas, F. Rhodes et al. (2000). Circumcision and STD in the United States: cross sectional and cohort analyses. *Sexually Transmitted Infections*, **76**, 474–479.

Dixson, A. F. (1998). *Primate Sexuality*. Oxford University Press, Oxford.

Dixson, A. F. and M. J. Anderson (2004). Sexual behavior, reproductive physiology and sperm competition in male mammals. *Physiology and Behavior*, **83**, 361–371.

Dixson, A. F., G. Halliwell, R. East, P. Wignarajah, and M. J. Anderson (2003). Masculine somatotype and hirsuteness as determinants of sexual attractiveness to women. *Archives of Sexual Behavior*, **32**, 29–39.

Dobson, A. (1995). The ecology and epidemiology of rinderpest virus in Serengeti and Ngorongoro conservation area. In *Serengeti II: Dynamics, management, and conservation of an ecosystem* (eds. A. R. E. Sinclair, and P. Arcese), pp. 485–505. University of Chicago Press, Chicago, IL.

Dobson, A. and R. Carper (1992). Global warming and potential changes in host-parasite and disease-vector relationships. In *Global Warming and Biodiversity* (eds. R. L. Peters, and T. E. Lovejoy), pp. 201–207. Yale University Press, New Haven, CT.

Dobson, A. and J. Foufopoulos (2001). Emerging infectious pathogens of wildlife. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **356**, 1001–1012.

Dobson, A. and P. J. Hudson (1992). Regulation and stability of a free-living host-parasite system: *Trichostrongylus tenuis* in red grouse. II. Population models. *Journal of Animal Ecology*, **61**, 487–498.

Dobson, A. P. (1988). The population biology of parasite-induced changes in host behavior. *Quarterly Review of Biology*, **63**, 139–165.

Dobson, A. P. (1999). Introduction: genetics and conservation biology. In *Genetics and the Extinction of Species* (eds. L. F. Landweber, and A. P. Dobson), pp. xiii–xviii. Princeton University Press, Princeton, NJ.

Dobson, A. P. (2004). Population dynamics of pathogens with multiple host species. *American Naturalist*, **164**, S64–S78.

Dobson, A. P. and E. R. Carper (1996). Infectious diseases and human population history. *BioScience*, **46**, 115–126.

Dobson, A. P. and M. Crawley (1994). Pathogens and the structure of plant communities. *Trends in Ecology and Evolution*, **9**, 393–398.

Dobson, A. P. and P. J. Hudson (1986). Parasites, disease and the structure of ecological communities. *Trends in Ecology and Evolution*, **1**, 11–15.

Dobson, A. P. and A. Lyles (2000). Black-footed ferret recovery. *Science*, **5468**, 985–988.

Dobson, A. P. and M. Meagher (1996). The population dynamics of brucellosis in the Yellowstone National Park. *Ecology*, **77**, 1026–1036.

Doebeli, M. and U. Dieckmann (2000). Evolutionary branching and sympatric speciation caused by different types of ecological interactions. *American Naturalist*, **156**, S77–S101.

Doherty, P. C. and R. M. Zinkernagel (1975). A biological role for the major histocompatibility antigens. *Lancet*, **1**, 1406–1409.

Domingo, E. and J. J. Holland (1997). RNA virus mutations and fitness for survival. *Annual Review of Microbiology*, **51**, 151–178.

Donovan, B. (2000a). The repertoire of human efforts to avoid sexually transmissible diseases: past and present—Part 1: strategies used before or instead of sex. *Sexually Transmitted Infections*, **76**, 7–12.

Donovan, B. (2000b). The repertoire of human efforts to avoid sexually transmissible diseases: past and present. Part 2: strategies used during or after sex. *Sexually Transmitted Infections*, **76**, 88–93.

Dooren, S. V., M. Salemi, and A.-M. Vandamme (2001). Dating the origin of the African Human T-Cell Lymphotropic Virus Type-I (HTLV-I) subtypes. *Molecular Biology and Evolution*, **18**, 661–671.

Dowell, S. F. (2001). Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerging Infectious Diseases*, **7**, 369–373.

Dragon, D. C. and R. P. Rennie (1995). The ecology of anthrax spores: tough but not invincible. *Canadian Veterinary Journal*, **36**, 295–301.

Drake, J. W. (1991). A constant rate of spontaneous mutation in DNA-based microbes. *Proceedings of the National Academy of Sciences USA*, **88**, 7160–7164.

Dritschilo, W., H. Cornell, D. Nafus, and B. O'Connor (1975). Of mice and mites. *Science*, **190**, 467–469.

Duckworth, R. A., M. T. Mendonca, and G. E. Hill (2001). A condition dependent link between testosterone and disease resistance in the house finch. *Proceedings of the Royal Society B*: *Biological Sciences*, **268**, 2467–2472.

Dudley, R. (2000). Evolutionary origins of human alcoholism in primate frugivory. *Quarterly Review of Biology*, **75**, 3–15.

Dudley, R. (2002). Fermenting fruit and the historical ecology of ethanol ingestion: is alcoholism in modern humans an evolutionary hangover? *Addiction*, **97**, 381–388.

Dudley, R. (2004). Ethanol, fruit ripening, and the historical origins of human alcoholism in primate frugivory. *Integrative and Comparative Biology*, **44**, 315–323.

Dudley, R. and K. Milton (1990). Parasite deterrence and the energetic costs of slapping in howler monkeys, *Alouatta palliata*. *Journal of Mammalogy*, **71**, 463–465.

Dunbar, R. I. M. (1980). Demographic and life history variables of a population of gelada baboons (*Theropithecus gelada*). *Journal of Animal Ecology*, **49**, 485–506.

Dunbar, R. I. M. (1988). *Primate Social Systems*. Cornell University Press, Ithaca, NY.

Dunbar, R. I. M. (1991). Functional significance of social grooming in primates. *Folia Primatologica*, **57**, 121–131.

Duncan, P. and P. Cowtan (1980). An unusual choice of habitat helps Camargue horses to avoid blood-sucking horse-flies. *Biology of Behaviour*, **5**, 55–60.

Dunn, F. L. (1968). The parasites of *Saimiri*: in the context of platyrrhine parasitism. In *The Squirrel Monkey* (eds. L. A. Rosenblum, and R. W. Cooper), pp. 31–68. Academic Press, New York.

Dupain, J., L. Van Elsacker, C. Nell, P. Garcia, F. Ponce, and M. A. Huffman (2002). New evidence for leaf swallowing and *Oesophagostomum infection* in bonobos (*Pan paniscus*). *International Journal of Primatology*, **23**, 1053–1062.

Durden, L. A. and J. E. Keirans (1996). Host-parasite coextinction and the plight of tick conservation. *American Entomologist*, **42**, 87–91.

Durden, L. A., D. L. Sly, and A. T. Buck (1985). Parasitic arthropods of bushbabies (*Galago senegalensis* and *G. crassicaudatus*) recently imported to the U.S.A. *Laboratory Primate Newsletter*, **24**, 5–6.

Durette-Desse, M. and M. Corvione (1998). A new *Moleineus* species (Nematoda, Trichostrongylina, Molineoidea), parasite of a South American primate. *Zoosystema*, **20**, 445–450.

Dwyer, G., S. A. Levin, and L. Buttel (1990). A simulation model of the population dynamics and evolution of myxomatosis. *Ecological Mongraphs*, **60**, 423–447.

Dybdahl, M. F. and C. M. Lively (1998). Host parasite coevolution: evidence for rare advantage and time-lagged selection in a natural population. *Evolution*, **52**, 1057–1066.

Earn, D., P. Rohani, B. M. Bolker, and B. T. Grenfell (2000). A simple model for complex dynamical transitions in epidemics. *Science*, **287**, 667–670.

Eberhard, W. G. (1985). *Sexual Selection and Animal Genitalia*. Harvard University Press, Cambridge, MA.

Eberle, R. (1992). Evidence for an alpha-herpesvirus indigenous to mountain gorillas. *Journal of Medical Primatology*, **21**, 246–251.

Ebert, D. (1994). Virulence and local adaptation of a horizontally transmitted parasite. *Science*, **265**, 1084–1086.

Ebert, D. (1999). The evolution and expression of parasite virulence. In *Evolution in Health and Disease* (ed. S. C. Stearns), pp. 161–172. Oxford University Press.

Ebert, D. and W. D. Hamilton (1996). Sex against virulence: the coevolution of parasitic diseases. *Trends in Ecology and Evolution*, **11**, 79–82.

Edman, J. D. (1988). Disease control through manipulation of vector-host interaction: some historical and evolutionary perspectives. In *Proceedings of a Symposium: The Role of Vector-Host Interactions in Disease Transmission* (eds. T. W. a. Scott, and J. Grumstrup-Scott), pp. 43–50. Entomological Society of America, Lanham, MD.

Edman, J. D. and H. W. Kale (1971). Host behavior: its influence on the feeding success of mosquitoes. *Annals of the Entomological Society of America*, **64**, 513–516.

Edwards, J. C., and C. J. Barnard (1987). The effects of *Trichinella* infection on intersexual interactions between mice. *Animal Behaviour*, **35**, 533–540.

Edwards, R. (2000). *Immunodiagnostics: A Practical Approach*. Oxford University Press, Oxford, UK.

Ehman, K. D. and M. E. Scott (2002). Female mice mate preferentially with non-parasitized males. *Parasitology*, **125**, 461–466.

Eilenberger, U. (1997). Endoparasites in gorillas and humans in the same habitat. *Gorilla Journal*, **15**, 11–14.

Eisenbarth, S., S. Cassel, and K. Bottomly (2004). Understanding asthma pathogenesis: linking innate and adaptive immunity. *Current Opinions in Pediatrics*, **16**, 659–666.

Eley, R. M., S. C. Strum, G. Muchemi, and G. D. F. Reid (1989). Nutrition, body condition, activity patterns, and parasitism of free-ranging troops of olive baboons (*Papio anubis*) in Kenya. *American Journal of Primatology*, **18**, 209–219.

Elliott, D., T. Setiawan, A. Metwali, A. Blum, J. J. Urban, and J. Weinstock (2004). *Heligmosomoides polygyrus* inhibits established colitis in IL-10-deficient mice. *European Journal of Immunology*, **34**, 2690–2698.

Elliot, S., S. Blanford, and M. Thomas (2002). Host-pathogen interactions in a varying enviornment: temperature, behavioural fever, and fitness. *Proceedings of the Royal Society B: Biological Sciences*, **269**, 1599–1607.

Else, J. G., M. Satzger, and R. F. Sturrock (1982). Natural infections of *Schistosoma mansoni* and *Schistosoma haematobium* in *Cercopithecus* monkeys in Kenya. *Annals of Tropical Medicine and Parasitology*, **76**, 111–112.

Emlen, S. T. and L. W. Oring (1977). Ecology, sexual selection, and the evolution of mating systems. *Science*, **197**, 215–223.

Endler, J. A. (1986). *Natural Selection in the Wild*. Princeton University Press, Princeton, NJ.

Engel, G. A., L. Jones-Engel, M. A. Schillaci, K. G. Suaryana, A. Putra, A. Fuentes, and R. Henkel (2002). Human exposure to herpesvirus B-seropositive macaques, Bali, Indonesia. *Emerging Infectious Diseases*, **8**, 789–795.

Escalante, A. and F. Ayala (1994). Phylogeny of the malarial genus *Plasmodium* derived from rRNA gene sequences. *Proceedings of the National Academy of Sciences USA*, **91**, 11373–11377.

Escalante, A. A., D. E. Freeland, W. E. Collins, and A. A. Lal (1998). The evolution of primate malaria parasites based on the gene encoding cytochrome b from the linear mitochondrial genome. *Proceedings of the National Academy of Sciences USA*, **95**, 8124–8129.

Escalante, A. A., O. E. Cornejo, D. E. Freeland, A. C. Poe, E. Durrego, W. E. Collins, and A. A. Lal (2005). A monkey's tale: The origin of *Plasmodium vivax* as a human malaria parasite. *Proceedings of the National Academy of Sciences USA*, **102**, 1980–1985.

Etkin, N. L. (1994). *Eating on the Wild Side*: *The Pharmacologic, Ecologic, and Social Implications of Using Noncultigens*, Tucson, University of Arizona Press.

Eubank, S., H. Guclu, V. S. Kumar, M. V. Marathe, A. Srinivasan, Z. Toroczkai, and N. Wang (2004). Modelling disease outbreaks in realistic urban social networks. *Nature*, **429**, 180–184.

Ewald, P. W. (1980). Evolutionary biology and the treatment of signs and symptoms of infectious-disease. *Journal of Theoretical Biology*, **86**, 169–176.

Ewald, P. W. (1983). Host-parasite relations, vectors, and the evolution of disease severity. *Annual Review of Ecology and Systematics*, **14**, 465–485.

Ewald, P. W. (1993). The evolution of virulence. *Scientific American*, **268**, 186–93.

Ewald, P. W. (1994a). *Evolution of Infectious Disease*. Oxford University Press, Oxford.

Ewald, P. W. (1994b). Evolution of mutation-rate and virulence among human retroviruses. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **346**, 333–341.

Ewald, P. W. (2000). *Plague Time: How Stealth Infections Cause Cancers, Heart Disease, And Other Deadly Ailments*. Free Press, New York.

Ezenwa, V. O. (2003). Habitat overlap and gastrointestinal parasitism in sympatric African bovids. *Parasitology*, **126**, 379–388.

Ezenwa, V. O. (2004). Host social behavior and parasitic infection: a multifactorial approach. *Behavioral Ecology*, **15**, 446–454.

Fa, J., J. Juste, J. del Val, and J. Castroviejo (1995). Impact of market hunting on mammal species in equatorial Guinea. *Conservation Biology*, **9**, 1105–1115.

Fa, J. E. (1992). Visitor-directed aggression among the Gibraltar macaques. *Zoo Biology*, **11**, 43–52.

Fa, J. E. and C. H. Southwick (1988). *Ecology and Behavior of Food-Enhanced Primate Groups*. Alan R. Liss, Inc., New York.

Fa, J. E. and R. Lind (1996). Population management and viability of the Gibraltar Barbary macaques. In *Evolution and Ecology of Macque Societies* (eds. J. E. Fa, and D. G. Lindburg), pp. 235–262. Cambridge University Press, Cambridge.

Farnsworth, N. R. (1988). Screening plants for new medicines. In *Biodiversity* (ed. E. Wilson). National Academy Press, Washington, DC.

Farnsworth, N. R. and R. W. Morris (1976). Higher plants—the sleeping giant of drug development. *American Journal of Pharmaceutical Education*, **148**, 46–52.

Farrell, B. (1998). Inordinate fondness explained: why are there so many beetles? *Science*, **281**, 555–559.

Fauci, A. S. (2001). Infectious diseases: considerations for the 21st century. *Clinical Infectious Diseases*, **32**, 675–685.

Fauquet, C. and M. Mayo (2001). The 7th ICTV report. *Archives of Virology*, **146**, 189–194.

Faustino, C., C. S. Jennelle, V. Connolly, A. K. Davis, E. C. Swarthout, A. Dhondt, and E. G. Cooch (2004). *Mycoplasma gallisepticum* infection dynamics in a house finch population: analysis of seasonal variation in survival and transmission rate. *Journal of Animal Ecology*, **73**, 651–669.

Fedigan, L. M. and S. Zohar, (1997). Sex differences in mortality of Japanese macaques: twenty-one years of data from the Arashiyama West population. *American Journal of Physical Anthropology*, **102**, 161–175.

Felsenfeld, A. D. (1972). The arboviruses. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 523–536. S. Karger, London.

Felsenfeld, A. D. and R. H. Wolf (1971). Serological reactions with treponemal antigens in nonhuman primates and natural history of treponematosis in man. *Folia Primatologica*, **16**, 294–305.

Felsenstein, J. (1985). Phylogenies and the comparative method. *American Naturalist*, **125**, 1–15.

Fenner, F. and B. Fantini (1999). *Biological Control of Vertebrate Pests: The History of Myxomatosis—An Experiment in Evolution*. CABI Publishing, Wallingford, Oxon, UK.

Fenner, F., D. A. Henderson, I. Arita, Z. Jezek, and I. D. Ladnyi (1988). *Smallpox and Its Eradication*. World Health Organization, Geneva.

Fenton, A. and A. P. Pedersen (2005). Community epidemiology framework for classifying disease threats. *Emerging Infectious Diseases*, **11**, 1815–1821.

Fenton, A., J. P. Fairbairn, R. Norman, and P. J. Hudson (2002). Parasite transmission: reconciling theory and reality. *Journal of Animal Ecology*, **71**, 893–905.

Ferguson, N. M., C. A. Donnelly, M. E. Wollhouse, and R. M. Anderson (1999). Estimation of the basic reproduction number of BSE: The intensity of transmission in British cattle. *Proceedings of the Royal Society B*: *Biological Sciences*, **266**, 23–32.

Ferguson, N. M., C. A. Donnelly, and R. M. Anderson (2001). The foot-and-mouth epidemic in Great Britain: pattern of spread and impact of interventions. *Science*, **292**, 1155–1160.

Ferrari, N., I. M. Cattadori, J. Nespereira, A. Rizzoli, and P. J. Hudson (2004). The role of host sex in parasite dynamics: field experiments on the yellow-necked mouse *Apodemus flavicollis. Ecology Letters*, **7**, 88–94.

Festa-Bianchet, M. (1989). Individual-differences, parasites, and the costs of reproduction for bighorn ewes (*Ovis canadensis*). *Journal of Animal Ecology*, **58**, 785–795.

Fiennes, R. (1967). Zoonoses of primates. In *Manuals in Biology* (eds. R. Carrington, and L. H. Matthews), pp. 30–37. Weidefeld and Nicholson, London.

Fiennes, R. (1972a). *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases*. Karger, S., London.

Fiennes, R. N. T. W. (1972b). Ectoparasites and vectors. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 158–176. Karger, S., London.

Finlay, B. B. and S. Falcow (1997). Common themes in microbial pathogenicity revisited. *Microbiology and Molecular Biology Reviews*, **61**, 136–169.

Fisher, D. O. and I. P. F. Owens (2004). The comparative method in conservation biology. *Trends in Ecology and Evolution*, **19**, 391–398.

Flaxman, S. M. and P. W. Sherman (2000). Morning sickness: a mechanism for protecting mother and embryo. *Quarterly Review of Biology*, **75**, 1–36.

Flegr, J., J. Havlicek, P. Kodym, M. Maly, and Z. Smahel (2002). Increased risk of traffic accidents in subjects with latent toxoplasmosis: a retrospective case-control study. *BMC Infectious Diseases*, 2, published online at http://www.biomedcentral.com/1471-2334/2/11.

Flegr, J., M. Preiss, J. Klose, J. Havlicek, M. Vitakova, and P. Kodym (2003). Decreased level of psychobiological factor novelty seeking and lower intelligence in men latently infected with the protozoan parasite *Toxoplasma gondii* Dopamine, a missing link between schizophrenia and toxoplasmosis? *Biological Psychology*, **63**, 253–268.

Flegr, J., S. Zitkova, P. Kodym, and D. Frynta (1996). Induction of changes in human behaviour by the parasitic protozoan *Toxoplasma gondii*. *Parasitology*, **113**, 49–54.

Foerg, R. (1982). Reproductive behavior in *Varecia variegata*. *Folia Primatologica*, **38**, 108–121.

Folstad, I. and A. J. Karter (1992). Parasites, bright males, and the immunocompetence handicap. *American Naturalist*, **139**, 603–622.

Folstad, I., A. C. Nilssen, O. Halvorsen, and J. Andersen (1991). Parasite avoidance—the cause of post-calving migrations in rangifer? *Canadian Journal of Zoology*, **69**, 2423–2429.

Folstad, I., P. Arneberg, and A. J. Karter (1996). Antlers and parasites. *Oecologia*, 105, 556–558.

Formenty, P., C. Boesch, M. Wyers, C. Steiner, F. Donati, F. Dind, F. Walker et al. (1999a). Ebola virus outbreak among wild chimpanzees living in a rain forest of Cote d'Ivoire. *Journal of Infectious Diseases*, **179**, S120–S126.

Formenty, P., C. Hatz, B. Le Guenno, A. Stoll, P. Rogenmoser, and A. Widmer (1999b). Human infection due to Ebola virus, subtype Cote d'Ivoire: clinical and biologic presentation. *Journal of Infectious Diseases*, **179**, S48–S53.

Fossey, D. (1983). *Gorillas in the Mist*. Houghton Mifflin, Boston, MA.

Foufopoulos, J., S. Altizer, and A. Dobson (2002). Interactions between wildlife and domestic livestock in the tropics. In *Tropical Agroecosystems* (ed. J. Vandermeer). CRC Press, Boca Raton, FL.

Fowler, M. E. (1976). *Zoological Medicine: A Teaching Outline for Nondomestic Mammalian, Reptilian and Amphibian Animal Medicine*. University of California, School of Veterinary Medicine, Davis, CA.

Fox, J. G. and R. D. Ediger (1970). Nasal leech infestation in the rhesus monkey. *Laboratory Animal Care*, **20**, 1137–1138.

Frank, S. A. (1993). Specificity versus dectable polymorphism in host-parasite genetics. *Proceedings of the Royal Society B*: *Biological Sciences,* **254**, 191–197.

Frank, S. A. (1996). Models of parasite virulence. *The Quarterly Review of Biology*, **71**, 37–78.

Frank, S. A. (2002). *Immunology and Evolution of Infectious Disease*. Princeton University Press, Princeton, NJ.

Frankel, O. H. and M. E. Soule (1981). *Conservation and Evolution*. Cambridge University Press, Cambridge.

Fraser, C., J. Eisen, K. Nelson, P. IT, and S. Salzberg (2002). The value of complete microbial genome sequencing: you get what you pay for. *Journal of Bacteriology*, **184**, 6403–6405.

Freckleton, R. P., P. H. Harvey, and M. Pagel (2002). Phylogenetic analysis and comparative data: a test and review of evidence. *American Naturalist*, **160**, 712–726.

Freeland, W. J. (1976). Pathogens and the evolution of primate sociality. *Biotropica*, **8**, 12–24.

Freeland, W. J. (1977). Blood-sucking flies and primate polyspecific associations. *Nature*, **269**, 801–802.

Freeland, W. J. (1979). Primate social groups as biological islands. *Ecology*, **60**, 719–728.

Freeland, W. J. (1980). Mangabey (*Cercocebus albigena*) movement patterns in relation to food availability and fecal contamination. *Ecology*, **61**, 1297–1303.

Freeland, W. J. (1981a). Functional aspects of primate grooming. *Ohio Journal of Science*, **81**, 173–177.

Freeland, W. J. (1981b). Parasitism and behavioral dominance among male-mice. *Science*, **213**, 461–462.

Freeland, W. J. and W. J. Boulton (1992). Coevolution of food webs—parasites, predators and plant secondary compounds. *Biotropica*, **24**, 309–327.

Freeland, W. J. and D. H. Janzen (1974). Strategies in herbivory by mammals: the role of plant secondary compounds. *American Naturalist*, **108**, 269–289.

Fribourg-Blanc, A. (1972). *Treponema*. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 255–262. Karger, S., London.

Fribourg-Blanc, A. and H. H. Mollareet (1969). Natural treponematosis of the African Primate. *Primates in Medicine*, **3**, 113–121.

Fribourg-Blanc, A., H. Mollaret, and G. Niel (1966). Serologic and microscopic confirmation of treponematosis in Guinea baboons. *Bulletin de la Societe de pathologie exotique et de ses filiales*, **59**, 54–59.

Friedman, E. M. and D. A. Lawrence (2002). Environmental stress mediates changes in neuroimmunological interactions. *Toxicological Sciences*, **67**, 4–10.

Friedman, M. and G. W. Friedland (1998). *Medicine's Ten Greatest Discoveries*. Yale University Press, New Haven, CT.

Froeschke, G. and S. Sommer (2005). MHC class II DRB variability and parasite load in the striped mouse (*Rhabdomys pumilio*) in the southern Kalahari. *Molecular Biology and Evolution*, **22**, 1254–1259.

Fruth, B. and G. Hohmann (1994). Comparative analyses of nest-building behavior in bonobos and chimpanzees. In *Chimpanzee Cultures* (eds. R. W. Wrangham, W. C. McGrew, F. B. M. de Waal, and P. G. Heltne), pp. 109–128. Harvard University Press, Cambridge, MA.

Fujita, M., T. Furuta, S. Kojima, T. Kurata, and Y. Yoshikawa (1996). Survey for *Pneumocystis carinii* infection of wild-born and laboratory-bred monkeys by indirect immunofluorescence and cyst-staining methods. *Japanese Journal of Medical Science and Biology*, **49**, 113–120.

Fultz, P. N., T. P. Gordon, D. C. Anderson, and H. M. Mcclure (1990). Prevalence of natural infection with simian immunodeficiency virus and simian T-cell leukemia-virus type-I in a breeding colony of sooty mangabey monkeys. *AIDS*, **4**, 619–625.

Funk, S. M., C. V. Fiorello, S. Cleaveland, K. Laurenson, and M. E. Gompper (2001). The importance of disease in carnivore conservation. In *Carnivore Conservation* (eds. J. L. Gittleman, S. Funk, D. W. Macdonald, and R. K. Wayne), pp. 11–34. Cambridge University Press, Cambridge.

Gagneux, P., M. K. Gonder, T. L. Goldberg, and P. A. Morin (2001). Gene flow in wild chimpanzee populations: what genetic data tell us about chimpanzee movement over space and time. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **356**, 889–897.

Galat-Luong, A. and G. Galat (2005). Conservation and survival adaptations of Temminck's red colobus (*Procolobus badius temmincki*), in Senegal. *International Journal of Primatology*, **26**, 585—603.

Galat Luong, A. F. Bibollet-Ruche, X. Pourrut, J. P. Durand, P. Sarni, G. Pichon, and G. Galat (1994). Social-organization and SIV seroepidemiology of a patas monkey population in Senegal. *Folia Primatologica*, **63**, 226–228.

Galindo, P. and S. Srihongse (1967). Evidence of recent jungle yellow-fever activity in eastern Panama. *Bulletin of the World Health Organization*, **36**, 151–161.

Galvani, A. P. (2004). Emerging infections: what have we learned from SARS? *Emerging Infectious Diseases*, **10**, 1351–1352.

Galvani, A. P. and M. Slatkin (2003). Evaluating plague and smallpox as historical selective pressures for the CCR5-Delta 32 HIV-resistance allele. *Proceedings of the National Academy of Sciences USA*, **100**, 15276–15279.

Gandon, S. (2002). Local adaptation and the geometry of host-parasite coevolution. *Ecology Letters*, **5**, 246–256.

Gandon, S. (2004). Evolution of multihost parasites. *Evolution*, **58**, 455–469.

Gangestad, S. W. and D. M. Buss (1993). Pathogen prevalence and human mate preferences. *Ethology and Sociobiology*, **14**, 89–96.

Gani, R. and S. Leach (2001). Transmission potential of smallpox in contemporary populations. *Nature*, **414**, 748–751.

Gao, F., E. Bailes, D. L. Robertson, Y. L. Chen, C. M. Rodenburg, S. F. Michael, L. B. Cummins et al. (1999). Origin of HIV-1 in the chimpanzee *Pan troglodytes troglodytes*. *Nature*, **397**, 436–441.

Garland, T., Jr. and S. C. Adolph (1994). Why not to do two-species comparative studies: limitations on inferring adaptation. *Physiological Zoology*, **67**, 797–828.

Garland, T. J. P. H. Harvey, and A. R. Ives (1992). Procedures for the analysis of comparative data using phylogenetically independent contrasts. *Systematic Biology*, **4**, 18–32.

Garnett, G. P., S. O. Aral, D. V. Hoyle, W. Cates, and R. M. Anderson (1997). The natural history of syphilis: implications for the transmission dynamics and control of infection. *Sexually Transmitted Diseases*, **24**, 185–200.

Garnham, P. C. C. (1966). *Malaria Parasites and Other Haemosporidia*. Blackwell Scientific, Oxford, 1114.

Garrett, L. (1995). *The Coming Plague: Newly Emerging Diseases in a World Out of Balance*. Penguin Books.

Garrigan, D. and P. W. Hedrick (2001). Class I MHC polymorphism and evolution in endangered California chinook and other Pacific salmon. *Immunogenetics*, **53**, 483–489.

Gascoyne, S. C., M. K. Laurenson, S. Lelo, and M. Borner (1993). Rabies in African wild dogs (*Lycaon pictus*) in the Serengeti region, Tanzania. *Journal of Wildlife Diseases*, **29**, 396–402.

Gaston, K. J. (2000). Global patterns in biodiversity. *Nature*, **405**, 220–227.

Gavrilets, S. (2000). Rapid evolution of reproductive barriers driven by sexual conflict. *Nature*, **403**, 886–889.

Geisbert, T. W., L. E. Hensley, P. B. Jahrling, T. Larsen, J. B. Geisbert, J. Paragas, H. A. Young et al. (2003). Treatment of Ebola virus infection with a recombinant inhibitor of factor Vila/tissue factor: a study in rhesus monkeys. *Lancet*, **362**, 1953–1958.

Gerber, L. and G. VanBlaricom (2001). Implications of three viability models for the conservation status of the western population of Steller sea lions (*Eumetopias jubatus*). *Biological Conservation*, **102**, 261–269.

Getz, W. M. and J. Pickering (1983). Epidemic models—thresholds and population regulation. *American Naturalist*, **121**, 892–898.

Ghandour, A. M., N. Z. Zahid, A. A. Banaja, K. B. Kamal, and A. I. Bouq (1995). Zoonotic intestinal parasites of hamadryas baboons *Papio hamadryas* in the western and northern regions of Saudi Arabia. *Journal of Tropical Medicine and Hygiene*, **98**, 431–439.

Gilbert, K. A. (1997). Red howling monkey use of specific defacation sites as a parasite avoidance strategy. *Animal Behaviour*, **54**, 451–455.

Gilbert, L., R. Norman, K. Laurenson, H. Reid, and P. J. Hudson (2001). Disease persistence and apparent competition in a three-host community: an empirical and analytical study of large-scale, wild populations. *Journal of Animal Ecology*, **70**, 1053–1061.

Gillespie, T. R., C. A. Chapman, and E. C. Greiner (2005). Effects of logging on gastrointestinal parasite infections and infection risk in African primates. *Journal of Applied Ecology*, **42**, 699–707.

Gimblett, H. R. 2002. *Integrating Geographic Information Systems and Agent-based Modeling Techniques*. Oxford, Oxford University Press.

Ginsberg, J. R., G. M. Mace, and S. Albon (1995). Local extinction in a small and declining population—wild dogs in the Serengeti. *Proceedings of the Royal Society B*: *Biological Sciences,* **262**, 221–228.

Gittleman, J. L., M. E. Gompper, and K. E. Jones (2001). Extinction: complexity of assessing risk. *Science*, **292**, 217–218.

Glander, K. E. (1992). Dispersal patterns in Costa Rican mantled howling monkeys. *International Journal of Primatology*, **13**, 415–436.

Glander, K. E. (1994). Nonhuman primate self-medication with wild plant foods. In *Eating on the Wild Side: The Pharmacologic, Ecologic, and Social Implications of Using Noncultigens* (ed. E. Etkin), pp. 227–239. University of Arizona Press, Tuscon, Arizona.

Glander, K. E., L. M. Fedigan, L. Fedigan, and C. Chapman (1991). Field methods for capture and measurement of three monkey species in Costa Rica. *Folia Primatologica*, **57**, 70–82.

Gog, J., R. Woodroffe, and J. Swinton (2002). Disease in endangered metapopulations: the importance of alternative hosts. *Proceedings of the Royal Society B*: *Biological Sciences,* **269**, 671–676.

Goldsby, R., T. Kindt, J. Kuby, and B. Osborne (2002). *Immunology*. W. H. Freeman & Co. New York.

Gompper, M. E. and A. M. Hoylman (1993). Grooming with *Trattinnickia* resin: possible pharmaceutical plant use by coatis in Panama. *Journal of Tropical Ecology*, **9**, 533–540.

Gompper, M. E. and E. S. Williams (1998). Parasite conservation and the black-footed ferret recovery program. *Conservation Biology*, **12**, 730–732.

Good, R. C. (1984). Diseases in nonhuman primates. In *The Mycobacteria: A Sourcebook* (eds. G. P. Kubica, and L. G. Wayne), pp. 903–924. Marcel Dekker, New York.

Goodall, J. (1965). Chimpanzees of the Gombe Stream Reserve. In *Primate Behavior* (ed. I. DeVore), pp. 425–473. Holt, Rinehart and Winston.

Goodall, J. (1986). *The Chimpanzees of Gombe: Patterns of Behavior*. Harvard University Press, Cambridge, MA.

Gordon, H. M. (1948). The epidemiology of parasitic diseases, with special reference to studies with nematode parasites of sheep. *Australian Veterinary Journal*, **24**, 17.

Gordon, R. M., T. H. Davey, and H. Peaston (1934). The transmission of human bilharziasis in Sierra Leone, with an account of the life cycle of the schistosomes concerned, *S. mansoni* and *S. haematobium. Annals of Tropical Medicine and Parasitology*, **28**, 323.

Graczyk, T. K., A. B. Mudakikwa, M. R. Cranfield, and U. Eilenberger (2001). Hyperkeratotic mange caused by *Sarcoptes scabiei* (Acariformes: Sarcoptidae) in juvenile human-habituated mountain gorillas (*Gorilla gorilla beringei*). *Parasitology Research*, **87**, 1024–1028.

Graham, A. (2002). When T-helper cells don't help: immunopathology during concomitant infections. *Quarterly Review of Biology*, **77**, 409–434.

Grant, B. F., D. A. Dawson, F. S. Stinson, S. P. Chou, M. C. Dufour, and R. P. Pickering (2004). The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991–1992 and 2001–2002. *Drug And Alcohol Dependence*, **74**, 223–234.

Grassly, N. C., C. Fraser, and G. P. Garnett (2005). Host immunity and synchronized epidemics of syphilis across the United States. *Nature*, **433**, 417–421.

Gratz, N. G. (1999). Emerging and resurging vector-borne diseases. *Annual Review of Entomology*, **44**, 51–75.

Graves, B. M. and D. Duvall (1995). Effects of sexually-transmitted diseases on heritable variation in sexually selected systems. *Animal Behaviour*, **50**, 1129–1131.

Gray, R., J. Azire, D. Serwadda, N. Kiwanuka, G. Kigozi, M. Kiddugavu, F. Nalugoda et al. (2004). Male circumcision and the risk of sexually transmitted infections and HIV in Rakai, Uganda. *AIDS*, **18**, 2428–2430.

Greenman, J. and P. Hudson (2000). Parasite-mediated and direct competition in a two-host shared macroparasite system. *Theoretical Population Biology*, **57**, 13–34.

Greenman, J. V. and P. J. Hudson (1999). Host exclusion and coexistence in apparent and direct competition: an application of bifurcation theory. *Theoretical Population Biology*, **56**, 48–64.

Gregory, R. D. (1990). Parasites and host geographic range as illustrated by waterfowl. *Functional Ecology*, **4**, 645–654.

Gregory, R. D. (1997). Comparative studies of host-parasite communities. In *Host-Parasite Evolution. General Principles and Avian Models* (eds. D. H. Clayton, and J. Moore), pp. 198–211. Oxford University Press, Oxford.

Gregory, R. D., A. E. Keymer, and P. H. Harvey (1996). Helminth parasite richness among vertebrates. *Biodiversity and Conservation*, **5**, 985–997.

Grenfell, B. T. and O. N. Bjørnstad (2005). Epidemic cycling and immunity. *Nature*, **433**, 366–367.

Grenfell, B. T., Bjørnstad, O.N., and Finkenstädt, B. (2002). Endemic and epidemic dynamics of measles. II. Scaling noise, determinism and predictability with the time series SIR model. *Ecological Monographs*, **72**, 185–202.

Grenfell, B. T. and A. P. Dobson, (1995). *Ecology of Infectious Diseases in Natural Populations*. Cambridge, Cambridge University Press.

Grenfell, B. T. and J. Harwood (1997). (Meta)population dynamics of infectious diseases. *Trends in Ecology and Evolution*, **12**, 395–399.

Grimm, V. and S. F. Railsback (2005). *Individual-based Modeling and Ecology*. Princeton University Press, Princeton, NJ.

Grüter, C. C. and D. Zinner (2004). Nested societies, convergent adaptations of baboons and snub-nosed monkeys. *Primate Report*, **70**, 1–98.

Guégan, J. F. and A. T. Teriokhin (2000). Human life history traits on a parasitic landscape. In *Evolutionary Biology of Host-Parasite Relationships: Theory Meets Reality* (eds. R. Poulin, S. Morand, and A. Skorping), pp. 143–161. Elsevier Science, Amsterdam.

Guégan, J. F., F. Thomas, M. E. Hochberg, T. de Meeus, and F. Renaud (2001). Disease diversity and human fertility. *Evolution*, **55**, 1308–1314.

Guernier, V., M. E. Hochberg, and J. F. Guégan (2004). Ecology drives the worldwide distribution of human diseases. *PLoS Biology*, **2**, 740–746.

Guerra, M. A., E. D. Walker, and U. Kitron (2001). Canine surveillance system for Lyme borreliosis in Wisconsin and northern Illinois: geographic distribution and risk factor analysis. *American Journal of Tropical Medicine and Hygeine*, **65**, 546–552.

Guerrant, R., M. Kosek, S. Moore, B. Lorntz, R. Brantley, and A. Lima (2002). Magnitude and impact of diarrheal diseases. *Archival Medical Research*, **33**, 351–355.

Guiler, E. R. (1961). The former distribution and decline of the thylacine. *Australian Journal of Science*, **23**, 207–210.

Gulland, F. M. D. (1992). The role of nematode parasites in soay sheep (*Ovis aries* L) mortality during a population crash. *Parasitology*, **105**, 493–503.

Gulland, F. M. D. (1995). The impact of infectious diseases on wild animal populations — a review. In *Ecology of Infectious Disease in Natural Populations* (eds. B. Grenfell, and A. Dobson), pp. 20–51. Cambridge University Press, Cambridge.

Gulland, F. M. D., S. D. Albon, J. M. Pemberton, P. R. Moorcroft, and T. H. Clutton-Brock (1993). Parasite-associated polymorphism in a cyclic ungulate population. *Proceedings of the Royal Society B*: *Biological Sciences,* **254**, 7–13.

Gupta, S., N. Ferguson, and R. Anderson (1998). Chaos, persistence, and evolution of strain structure in antigenically diverse infectious agents. *Science*, **280**, 912–915.

Gutierrez-Espeleta, G., P. W. Hedrick, S. Kalinowski, D. Garrigan, and W. Boyce (2001). Is the decline of desert bighorn sheep from infectious disease the result of low MHC variation? *Heredity*, **86**, 439–450.

Haddow, A. J. (1951). Field and laboratory studies on an African monkey, *Cercopithecus ascanius schmidti* Matschie. *Proceedings of the Zoological Society of London*, **122**, 297–394.

Haddow, A. J. (1969). The natural history of yellow fever in Africa. *Proceedings of the Royal Society of Edinburgh*, **70B**, 191–227.

Hafner, M. S. and R. D. M. Page (1995). Molecular phylogenies and host-parasite cospeciation—gophers and lice as a model system. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **349**, 77–83.

Hafner, M. S., J. W. Demastes, D. J. Hafner, T. A. Spradling, P. D. Sudman, and S. A. Nadler (1998). Age and movement of a hybrid zone: implications for dispersal distance in pocket gophers and their chewing lice. *Evolution*, **52**, 278–282.

Hagenaars, T. J., C. A. Donnelly, and N. M. Ferguson (2004). Spatial heterogeneity and the persistence of infectious diseases. *Journal of Theoretical Biology*, **229**, 349–359.

Hager, R. (2003). Models of reproductive skew applied to primates. In *Sexual Selection and Reproductive Competition in Primates: New Perspectives and Directions,* pp. 65–101. American Society of Primatologists, Norman, OK.

Hahn, B. H., G. M. Shaw, K. M. De Cock, and P. M. Sharp (2000). AIDS as a zoonosis: scientific and public health implications. *Science*, **287**, 607–614.

Hahn, N. E., D. Proulx, P. M. Muruthi, S. Alberts, and J. Altmann (2003). Gastrointestinal parasites in free-ranging Kenyan baboons (*Papio cynocephalus* and *P. anubis*). *International Journal of Primatology*, **24**, 271–279.

Hakkarainen, H., P. Ilmonen, V. Koivunen, and E. Korpimaki (1998). Blood parasites and nest defense behaviour of Tengmalm's owls. *Oecologia*, **114**, 574–577.

Hall, K. R. L. (1965). Behavior and ecology of the wild patas monkey, *Erythrocebus patas*, in Uganda. *Journal of Zoology*, **148**, 15–87.

Hallem, E. A., A. N. Fox, L. J. Zwiebel, and J. R. Carlson (2004). Mosquito receptor for human-sweat odorant. *Nature*, **427**, 212–213.

Halloran, M., I. J. Longini, A. Nizam, and Y. Yang (2002). Containing bioterrorist smallpox. *Science*, **298**, 1428–1432.

Halvorsen, O. (1986). On the relationship between social status of host and risk of parasitic infection. *Oikos*, **47**, 71–74.

Hamilton, W. D. (1963). The evolution of altruistic behavior. *American Naturalist*, **97**, 354–356.

Hamilton, W. D. (1964). The genetical evolution of social behavior, I. *Journal of Theoretical Biology*, **7**, 1–16.

Hamilton, W. D. (1971). Geometry for the selfish herd. *Journal of Theoretical Biology*, **31**, 295–311.

Hamilton, W. D. (1980). Sex versus non-sex versus parasite. *Oikos*, **35**, 282–290.

Hamilton, W. D. (1982). Pathogens as causes of genetic diversity in their host populations. In *Population Biology of Infectious Diseases* (eds. R. M. Anderson and R. M. May), pp. 269–296. Springer-Verlag, Berlin.

Hamilton, W. D. (1987). Kinship, recognition, disease and intelligence: constraints of social evolution. In *Animal Societies: Theories and Facts* (eds. Y. Ito, J. L. Brown, and J. Kikkawa), pp. 81–102. Japan Sci. Soc. Press, Tokyo.

Hamilton, W. D. (1990). Mate choice near or far. *American Zoologist*, **30**, 341–352.

Hamilton, W. D. and M. Zuk (1982). Heritable true fitness and bright birds: a role for parasites? *Science*, **218**, 384–387.

Hamilton, W. J., III, R. E. Buskirk, and W. H. Buskirk (1976). Defense of space and resources by chacma (*Papio ursinus*) baboon troops in an African desert and swamp. *Ecology*, **57**, 1264–1272.

Hamilton, W. J., R. E. Buskirk, and W. H. Buskirk (1978). Omnivory and utilization of food resources by chacma baboons, *Papio ursinus*. *American Naturalist*, **112**, 911–924.

Hanski, I. and D. Simberloff (1997). The metapopulation approach, its history, conceptual domain, and application to conservation. In *Metapopulation Biology*, pp. 5–26. Academic Press, Inc, San Diego.

Haraguchi, Y. and A. Sasaki (2000). The evolution of parasite virulence and transmission rate in a spatially structured population. *Journal of Theoretical Biology*, **203**, 85–96.

Harcourt, A. H. (2001). Gorilla socioecology: conflict and compromise between the sexes. In *Model Systems in Behavioral Ecology* (ed. L. A. Dugatkin), pp. 491–511. Princeton University Press, Princeton, N.J.

Harcourt, A. H. and K. G. Stewart (1978). Coprophagy by wild mountain gorillas. *East African Wildlife Journal*, **16**, 223–225.

Harcourt, A. H., P. H. Harvey, S. G. Larson, and R. V. Short (1981). Testis weight, body weight and breeding system in primates. *Nature*, **293**, 55–57.

Harcourt, A. H., A. Purvis, and L. Liles (1995). Sperm competition: mating system, not breeding season, affects testes size of primates. *Functional Ecology*, **9**, 468–476.

Hardin, G. (1968). The tragedy of the commons. *Science*, **162**, 1243–1248.

Harding, K. C., T. Harkonen, and H. Caswell (2002). The 2002 European seal plague: epidemiology and population consequences. *Ecology Letters*, 5, 727–732.

Harris, J., J. E. Hillerton, and S. V. Morant (1987). Effect on milk production of controlling muscid flies, and reducing fly-avoidance behaviour, by the use of Fenvalerate ear tages during the dry period. *Journal of Dairy Research*, **54**, 165–171.

Hart, B. J., E. Korinek, and P. Brennan (1987). Postcopulatory genital grooming in male rats: prevention of sexually transmitted infections. *Physiology and Behavior*, **41**, 321–325.

Hart, B. L. (1990). Behavioral adaptations to pathogens and parasites: five strategies. *Neuroscience and Biobehavioral Reviews*, **14**, 273–294.

Hart, B. L. (1994). Behavioral defense against parasites—interaction with parasite invasiveness. *Parasitology*, **109**, S139–S151.

Hart, B. L. (1997). Behavioural defence. In *Host-Parasite Evolution: General Principles and Avian Models* (eds. D. H. Clayton, and J. Moore), pp. 59–77. Oxford University Press, Oxford.

Hart, B. L. and L. A. Hart (1994). Fly switching by asian elephants—tool use to control parasites. *Animal Behaviour*, **48**, 35–45.

Harvell, C. D. (1990). The ecology and evolution of inducible defenses. *Quarterly Review of Biology*, **65**, 323–340.

Harvell, C. D., K. Kim, J. M. Burkholder, R. R. Colwell, P. R. Epstein, D. J. Grimes, E. E. Hofmann et al. (1999). Emerging marine diseases: climate links and anthropogenic factors. *Science*, **285**, 1505–1510.

Harvell, C. D., C. E. Mitchell, J. R. Ward, S. Altizer, A. Dobson, R. S. Ostfeld, and M. D. Samuels (2002). Climate warming and disease risks for terrestrial and marine biota. *Science*, **296**, 2158–2162.

Harvey, J. W. (2001). *Hematology: Blood and Bone Marrow of Domestic Animals*. W.B. Saunders Company, Philadelphia, PA.

Harvey, P. H. and T. H. Clutton-Brock (1985). Life history variation in primates. *Evolution*, **39**, 559–581.

Harvey, P. H. and A. E. Keymer (1991). Comparing life histories using phylogenies. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **332**, 31–39.

Harvey, P. H. and M. D. Pagel (1991). *The Comparative Method in Evolutionary Biology*. Oxford University Press, Oxford.

Harvey, P. H., A. F. Read, J. L. John, R. D. Gregory, and A. E. Keymer (1991). An evolutionary perspective: using the comparative method. In *Parasite-Host Associations* (eds. C. A. Toft, A. Aeschlimann, and L. Bolis). Oxford University Press, Oxford.

Harwood, H. 2000. Updating estimates of the economic costs of alcohol abuse in the United States: estimates, update methods, and data. Rockville, MD, National Institute on Alcohol Abuse and Alcoholism.

Hassell, M. P., H. N. Comins, and R. M. May (1991). Spatial structure and chaos in insect population dynamics. *Nature*, **353**, 255–258.

Hastings, B. E. (1991). The veterinary management of a laryngeal air sac infection in a free-ranging mountain gorilla. *Journal of Medical Primatology*, **20**, 361–364.

Hatalski, C. G. and W. I. Lipkin (1997). Behavioral abnormalities and disease caused by viral infections of the central nervous system. In *Parasites and Pathogens: Effects on Host Hormones and Behaviour* (eds. N. E. Beckage, S. N. Thompson, and B. A. Federici), pp. 201–209. Academic Press, San Diego, CA.

Hausfater, G. and S. B. Hrdy (1984). *Infanticide. Comparative and Evolutionary Perspectives*, Aldine de Gruyter, New York.

Hausfater, G. and B. J. Meade (1982). Alternation of sleeping groves by yellow baboons (*Papio cynocephalus*) as a strategy for parasite avoidance. *Primates*, **23**, 287–297.

Hausfater, G. and R. Sutherland (1984). Little things that tick off baboons. *Natural History*, **93**, 54–61.

Hausfater, G. and D. F. Watson (1976). Social and reproductive correlates of parasite ova emissions by baboons. *Nature*, **262**, 688–689.

Havlicek, J., Z. Gasova, A. P. Smith, K. Zvara, and J. Flegr (2001). Decrease of psychomotor performance in subjects with latent "asymptomatic" toxoplasmosis. *Parasitology*, **122**, 515–520.

Hay, S., C. Tucker, D. Rogers, and M. Packer (1996). Remotely sensed surrogates of meteorological data for the study of the distribution and abundance of arthropod vectors of disease. *Annals of Tropical Medicine and Parasitology*, **90**, 1–19.

Hay, S. I., J. Cox, D. J. Rogers, S. E. Randolph, D. I. Stern, G. D. Shanks, M. F. Myers et al. (2002). Climate change and the resurgence of malaria in the East African highlands. *Nature*, **415**, 905–909.

Haydon, D. T., S. Cleaveland, L. H. Taylor, and M. K. Laurenson (2002a). Identifying reservoirs of infection: a conceptual and practical challenge. *Emerging Infectious Diseases*, **8**, 1468–1473.

Haydon, D. T., M. K. Laurenson, and C. Sillero-Zubiri (2002b). Integrating epidemiology into population viability analysis: managing the risk posed by rabies and canine distemper to the Ethiopian wolf. *Conservation Biology*, **16**, 1372–1385.

Hedrick, P. W. and T. J. Kim (2000). Genetics of complex polymorphisms: parasites and maintenance of the major histocompatibility complex variation. In *Evolutionary Genetics: From Molecules to Morphology* (eds. R. S. Singh, and C. B. Krimbas), pp. 204–234. Cambridge University Press, Cambridge.

Hedrick, P. W., K. M. Parker, E. Miller, and P. Miller (1999). Major histocompatibility complex variation in the endangered Przewalski's horse. *Genetics*, **152**, 1701–1710.

Hedrick, P. W., K. M. Parker, G. Gutierrez-Espeleta, A. Rattink, and K. Lievers (2000). Major histocompatibility complex variation in the Arabian oryx. *Evolution*, **54**, 2145–2151.

Hedrick, P. W., T. J. Kim, and K. M. Parker (2001). Parasite resistance and genetic variation in the endangered Gila topminnow. *Animal Conservation*, **4**, 103–109.

Hedrick, P. W., R. N. Lee, and D. Garrigan (2002). Major histocompatibility complex variation in red wolves: evidence for common ancestry with coyotes and balancing selection. *Molecular Ecology*, **11**, 1905–1913.

Heeney, J. L., J. F. Evermann, A. J. McKeirnan, L. Markerkraus, M. E. Roelke, M. Bush, D. E. Wildt et al. (1990). Prevalence and implications of feline coronavirus infections of captive and free-ranging cheetahs (*Acinonyx jubatus*). *Journal of Virology*, **64**, 1964–1972.

Heesterbeek, J. A. P. (2002). A brief history of R_0 and a recipe for its calculation. *Acta Biotheoretica*, **50**, 189–204.

Heesterbeek, J. A. P. and J. A. J. Metz (1993). The saturating contact rate in marriage- and epidemic models. *Journal of Mathematical Biology*, **31**, 529–539.

Heide-Jorgensen, M. P., T. Harkonen, and P. Aberg (1992). Long-term effects of epizootic in harbor seals in the Kattegat-Skagerrak and adjacent areas. *Ambio*, **21**, 511–516.

Hemelrijk, C. and A. Ek (1991). Reciprocity and interchange of grooming and "support" in captive chimpanzees. *Animal Behaviour*, **41**, 923–336.

Hemelrijk, C. K. and M. Lutejin (1998). Philopatry, male presence and grooming reciprocation among female primates: a comparative perspective. *Behavioral Ecology and Sociobiology*, **42**, 207–215.

Henderson, D. A. (1998). Bioterrorism as a public health threat. *Emerging Infectious Diseases*, **4**, 488–492.

Henry, R. E. and L. Winkler (2001). Foraging feeding and defecation site selection as a parasite avoidance strategy of *Alouatta palliata* in a dry tropical forest. *American Journal of Physical Anthropology* (supp.), **32**, 79.

Herre, E. A. (1993). Population structure and the evolution of virulence in nematode parasites of fig wasps. *Science*, **259**, 1442–1445.

Herre, E. A. (1995). Factors affecting the evolution of virulence: nematode parasites of fig wasps as a case study. *Parasitology*, 111, S179–S191.

Hess, G. (1996). Disease in metapopulation models: implications for conservation. *Ecology*, **77**, 1617–1632.

Hess, G. R., S. E. Randolph, P. Arneberg, C. Chemini, C. Furlanello, J. Harwood, M. G. Roberts et al. (2002). Spatial aspects of disease dynamics. In *The Ecology of Wildlife Diseases* (eds. P. J. Hudson, A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. Dobson), pp. 102–118. Oxford University Press, Oxford.

Hethcote, H. W. and J. A. Yorke (1984). Gonorrhea transmission dynamics and control. *Lecture Notes in Biomathematics*, **56**. Springer-Verlag, Berlin.

Heymann, E. W. (1995). Sleeping habits of tamarins, *Saguinus mystax* and *Saguinus fuscicollis* (Mammalia: Primates; Callitrichidae), in north-eastern Peru. *Journal of Zoology,* **237**, 211–226.

Heymann, E. W. (1999). Primate behavioural ecology and diseases: Some perspectives for a future primatology. *Primate Report*, **55**, 53–65.

Heymann, E. W. (2001). Malaria infection rate of Amazonian primates: the role of sleeping habits. *Folia Primatologia*, **72**, 153.

Hill, A. B., A. Mullbacher, C. Parrish, G. Coia, E. G. Westaway, and R. V. Blanden (1992). Broad cross-reactivity with marked fine specificity in the cytotoxic T cell response to flaviviruses. *Journal of General Virology*, **73**, 1115–1123.

Hill, A. V. S. (2001). The genomics and genetics of human infectious disease susceptibility. *Annual Review of Genomics and Human Genetics*, **2**, 373–400.

Hill, R. A. and R. A. Barton (2005). Psychology: red enhances human performance in contests. *Nature*, **435**, 293.

Hill, R. A. and R. I. M. Dunbar (1998). An evaluation of the roles of predation rate and predation risk as selective pressures on primate grouping behaviour. *Behaviour*, **135**, 411–430.

Hill, R. A. and P. C. Lee (1998). Predation risk as an influence on group size in cercopithecoid primates: implications for social structure. *Journal of Zoology,* **245**, 447–456.

Hillgarth, N. and J. C. Wingfield (1997). Parasite-mediated sexual selection: endocrine aspects. In *Host-Parasite Evolution. General Principles and Avian Models.* (eds. D. H. Clayton and J. Moore), pp. 78–104. Oxford University Press, Oxford.

Hilton-Taylor, C. (2002). *IUCN Red List of Threatened Species*. Morges, IUCN.

Hinde, R. A. (1976). Interactions, relationships and social structure. *Man*, **11**, 1–17.

Hirsch, V., Santra, S, S. Goldstein, R. Plishka, A. Buckler-White, A. Seth, I. Ourmanov et al. (2004). Immune failure in the absence of profound CD4+ T-lymphocyte depletion in simian immunodeficiency virus-infected rapid progressor macaques. *Journal of Virology*, **78**, 275.

Hochachka, W. M. and A. A. Dhondt (2000). Density-dependent decline of host abundance resulting from a new infectious disease. *Proceedings of the National Academy of Sciences USA*, **97**, 5303–5306.

Hochachka, W. M., K. McGowan, L. Kramer, and A. A. Dhondt (2004). Impact of West Nile Virus on American crows in the Northeastern United States, and its relevance to existing monitoring programs. *EcoHealth*, **1**, 60–69.

Hodges, J. K. and M. Heistermann (2003). Field endocrinology: monitoring hormonal changes in free-ranging primates. In *Field and Laboratory Methods in Primatology: A Practical Guide* (eds. J. Setchell, and D. J. Curtis), pp. 282–294. Cambridge University Press, Cambridge.

Hoekstra, H., J. Hoekstra, D. Berrigan, S. Vignieri, A. Hoang, C. Hill, P. Beerli et al. (2001). Strength and tempo of directional selection in the wild. *Proceedings of the National Academy of Sciences USA*, **98**, 9157–9160.

Hogan, J. (2003). Horrific venereal disease strikes African baboons, pp. 7, *New Scientist,* May 2, 2003.

Hogg, K. L. (2002). Effects of habitat disturbance on parasite load and diversity in two species of lemur (*Eulemur rubriventer, Propithecus diadema edswardsi*) at Ranomafana National Park, Madagascar. Masters thesis, SUNY Stony Brook, Stony Brook.

Holmes, E. C. (2003). Error thresholds and the constraints to RNA virus evolution. *Trends in Microbiology*, **11**, 543–546.

Holmes, E. C. (2004). The phylogeography of human viruses. *Molecular Ecology*, **13**, 745–756.

Holmes, J. C. (1996). Parasites as threats to biodiversity in shrinking ecosystems. *Biodiversity and Conservation*, **5**, 975–983.

Holmes, J. C. and S. Zohar (1994). Pathology and host behaviour. In *Parasitism and Host Behaviour* (eds. C. J. Barnard and J. M. Behnke), pp. 34–63. Taylor and Francis, London.

Holmes, K. K., P. F. Sparling, P.-A. Mardh, S. M. Lemon, W. E. Stamm, P. Piot, and J. N. Wasserheit (1999). *Sexually Transmitted Diseases*. New York, McGraw Hill.

Holt, R., A. Dobson, M. Begon, R. Bowers, and E. Schauber (2003). Parasite establishment in host communities. *Ecology Letters*, **6**, 837–842.

Holt, R. D. (2003). On the evolutionary ecology of species' ranges. *Evolutionary Ecology Research*, **5**, 159–178.

Holt, R. D. and J. H. Lawton (1994). The ecological consequence of shared natural enemies. *Annual Review of Ecology and Systematics*, **25**, 495–520.

Holt, R. D. and J. Pickering (1985). Infectious disease and species coexistence: a model in Lotka-Volterra form. *American Naturalist*, **126**, 196–211.

Homsy, J. (1999). Ape tourism and human diseases: how close should we get? A critical review of the rules and regulations governing park management and tourism for the wild mountain gorilla, *Gorilla gorilla beringei. Report of a Consultancy for the International Gorilla Conservation Programme*.

Hoogland, J. L. (1979). Aggression, ectoparasitism, and other possible costs of prairie dog (Sciuridae, *Cynomys* spp) coloniality. *Behaviour*, **69**, 1–35.

Hoogland, J. L. (1995). *The Black-Tailed Prairie Dog*. University of Chicago Press, Chicago, IL.

Hooper, R. R., G. H. Reynolds, O. G. Jones, A. Zaidi, P. J. Wiesner, K. P. Latimer, A. Lester et al. (1978). Cohort study of venereal disease. I: The risk of gonorrhea transmission from infected women to men. *American Journal of Epidemiology*, **108**, 136–144.

Hotchkiss, E., A.K. Davis, J. J. Cherry, and S. Altizer (2004). *Mycoplasmal conjunctivitis* and the behavior of wild house finches (*Carpodacus mexicanus*) at bird feeders. *Bird Behavior*, **17**, 1–8.

Howard, R. D. and D. J. Minchella (1990). Parasitism and mate competition. *Oikos*, **58**, 120–122.

Hrdy, S. B. (1974). Male-male competition and infanticide among the langurs (*Presbytis entellus*) of Abu, Rajasthan. *Folia Primatologica*, **22**, 19–58.

Hrdy, S. B. (1977). *The langurs of Abu*. Harvard University Press, Cambridge, MA.

Hrdy, S. B. (1979). Infanticide among animals: a review, classification, and examination of the implications for the reproductive strategies of females. *Ethology and Sociobiology*, **1**, 13–40.

Hrdy, S. B. and P. L. Whitten (1987). Patterning of sexual activity. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Stuhsaker), pp. 370–384. The University of Chicago Press, Chicago, IL.

Hudson, P. J., A. Dobson, and D. Newborn (1985). Cyclic and non-cyclic populations of red grouse: a role for parasitism? In *Ecology and Genetics of Host-Parasite Interactions* (eds. D. Rollinson, and R. M. Anderson), pp. 79–89. Academic Press, London.

Hudson, P. J., A. Dobson, and D. Newborn (1998a). Prevention of population cycles by parasite removal. *Science*, **282**, 2256–2258.

Hudson, P. J., A. P. Dobson, and D. Newborn (1992). Do parasites make prey vulnerable to predation? Red grouse and parasites. *Journal of Animal Ecology*, **61**, 681–692.

Hudson, P. J., A. P. Dobson, and D. Newborn (1998b). Prevention of population cycles by parasite removal. *Science*, **282**, 2256–2258.

Hudson, P. J., A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. P. Dobson (2002). *The Ecology of Wildlife Diseases*. Oxford University Press, Oxford.

Huffman, M. A. (1997). Current evidence for self-medication in primates: a multidisciplinary perspective. *Yearbook of Physical Anthropology*, **40**, 171–200.

Huffman, M. A. (2001). Self-medicative behavior in the African great apes: an evolutionary perspective into the origins of human traditional medicine. *Bioscience*, **51**, 651–661.

Huffman, M. A. (2006). Primate self-medication. In *Primates in Perspective* (eds. C. J. Campbell, A. Fuentes, K. C. MacKinnon, M. Panger, and S. K. Bearder). Oxford University Press, Oxford.

Huffman, M. A. and J. M. Caton (2001). Self-induced increase of gut motility and the control of parasitic infections in wild chimpanzees. *International Journal of Primatology*, **22**, 329–346.

Huffman, M. A. and S. Hirata (2003). The biology of traditions: models and evidence. In *Biological and Ecological Foundations of Primate Behavioral Tradition* (eds. D. M. Fragaszy and S. Perry), pp. 267–296. Cambridge University Press, NY.

Huffman, M. A. and S. Hirata (2004). An experimental study of leaf swallowing in captive chimpanzees: insights into the origin of a self-medicative behavior and the role of social learning. *Primates*, **45**, 113–118.

Huffman, M. A. and M. Seifu (1989). Observations on the illness and consumption of a possibly medicinal plant *Vernonia amygdalina* (DEL.), by a wild chimpanzee in the Mahale Mountains National Park, Tanzania. *Primates*, **30**, 51–63.

Huffman, M. A. and R. W. Wrangham (1994). Diversity of medicinal plant use by chimpanzees in the wild. In *Chimpanzee Cultures* (eds. R. W. Wrangham, W. C. McGrew, F. B. M. de Waal, and P. G. Heltne), pp. 129–148. Harvard University Press, Cambridge, MA.

Huffman, M. A., S. Gotooh, D. Izutsu, K. Koshimizu, and M. S. Kalund (1993). Further observations on the use of the medicinal plant, *Vernonia amygdalina* (Del), by a wild chimpanzee, its possible effect on parasite load, and its phytochemistry. *African Study Monographs*, **14**, 227–240.

Huffman, M. A., J. E. Page, M. V. K. Sukhdeo, S. Gotoh, M. S. Kalunde, T. Chandrasiri, and G. H. N. Towers (1996). Leaf-swallowing by chimpanzees: a behavioral adaptation for the control of strongyle nematode infections. *International Journal of Primatology*, **17**, 475–503.

Huffman, M. A., S. Gotoh, L. A. Turner, M. Hamai, and K. Yoshida (1997). Seasonal trends in intestinal nematode infection and medicinal plant use among chimpanzees in the Mahale Mountains, Tanzania. *Primates*, **38**, 111–125.

Hughes, A. L. (1991). MHC polymorphism and the design of captive breeding programs. *Conservation Biology*, **5**, 249–251.

Hughes, A. L. and M. Nei (1988). Pattern of nucleotide substitution at major histocompatibility complex class I loci reveals overdominant selection. *Nature*, **335**, 167–170.

Hugot, J. P. (1993). Rediscription of *Enterobius anthropopitheci* (Gedoelst, 1916) (Nematoda, Oxyurida), a parasite of chimpanzees. *Systematic Parasitiology*, **26**, 201–207.

Hugot, J. P. (1998). Phylogeny of Neotropical monkeys—the interplay of morphological, molecular, and parasitological data. *Molecular Phylogenetics and Evolution*, **9**, 408–413.

Hugot, J. P. (1999). Primates and their pinworm parasites: the Cameron hypothesis revisited. *Systematic Biology*, **48**, 523–546.

Hunter, D. L. (1996). Tuberculosis in free-ranging, semi-free-ranging and captive cervids. *Revue Scientifique Et Technique De L Office International Des Epizooties*, **15**, 171–181.

Hutchings, M. R., S. Athanasiadou, I. Kyriazakis, and I. J. Gordon (2003). Can animals use foraging behaviour to combat parasites? *Proceedings of the Nutrition Society*, **62**, 361–370.

Hutchins, M. and D. P. Barash (1976). Grooming in primates: implications for its utilitarian function. *Primates*, **17**, 145–150.

Hutchins, M., T. Foose, and U. S. Seal (1991). The role of veterinary medicine in endangered species conservation. *Journal of Zoo and Wildlife Medicine*, **22**, 277–281.

Imhoof, B. and P. Schmid-Hempel (1998). Single-clone and mixed-clone infections versus host environment in *Chritidia bombi* infecting bumblebees. *Parasitology*, **117**, 331–336.

Immerman, R. S. (1986). Sexually transmitted disease and human evolution: survival of the ugliest? *Human Ethology Newsletter*, **4**, 6–7.

Immerman, R. S. and W. C. Mackey (1999). A model of hominid evolution as a partial function of sexually transmitted diseases. *Mankind Quarterly*, **40**, 3–39.

Inhorn, M. and P. Brown (1990). The anthropology of infectius disease. *Annual Review of Anthropology*, **19**, 89–117.

Innes, J. R., M. W. Colton, P. P. Yevich, and C. L. Smith (1954). Lung mites: pulmonary acariasis as an enzootic disease caused by *Pneumonyssus simicola* in imported monkeys. *American Journal of Pathology*, **30**, 813–827.

International Union for Conservation (1987). *The IUCN Position Statement on Translocation of Living Organisms: Introductions, Re-introductions and Re-stocking*, Gland, Switzerland, International Union for Conservation.

International Species Information System (1999). *PhysioIological Reference Values CD-ROM*, International Species Information System, Minnesota Zoological Garden, Apple Valley, MN, USA.

Isaac, N. J. B., P.-M. Agapow, P. H. Harvey, and A. Purvis (2003). Phylogenetically nested comparisons for testing correlates of species richness: a simulation study of continuous variables. *Evolution*, **57**, 18–26.

Isbell, L. A. (1991). Contest and scramble competition: patterns of female aggression and ranging behavior among primates. *Behavioral Ecology*, **2**, 143–155.

Isbell, L. A. and J. D. Pruetz (1998). Differences between vervets (*Cercopithecus aethiops*) and patas monkeys (*Erythrocebus patas*) in agonistic interactions between adult females. *International Journal of Primatology*, **19**, 837–855.

Isbell, L. A. and D. VanVuren (1996). Differential costs of locational and social dispersal and their consequences for female group-living primates. *Behaviour*, **133**, 1–36.

Isbell, L. A. and T. P. Young (2002). Ecological models of female social relationships in primates: similarities, disparities, and some directions for future clarity. *Behaviour*, **139**, 177–202.

Ito, T., J. N. S. S. Couceiro, S. Kelm, L. G. Baum, S. Krauss, M. R. Castrucci, I. Donatelli et al. (1998). Molecular basis for the generation in pigs of influenza A viruses with pandemic potential. *Journal of Virology*, **72**, 7367–7373.

Jacquez, J. A., C. P. Simon, J. Koopman, L. Sattenspiel, and T. Perry (1988). Modeling and analyzing HIV transmission: the effect of contact patterns. *Mathematics Biosciences*, **92**, 119–199.

James, R. A., P. L. Leberg, J. M. Quattro, and R. C. Vrijenhoek (1997). Genetic diversity in black howler monkeys (*Alouatta pigra*) from Belize. *American Journal of Physical Anthropology*, **102**, 329–336.

Janson, C. H. (1988b). Intra-specific food competition and primate social structure: a synthesis. *Behaviour*, **105**, 1–17.

Janson, C. H. (1992). Evolutionary ecology of primate social structure. In *Evolutionary Ecology and Human Behavior* (eds. E. A. Smith, and B. Winterhalder), pp. 95–130. Aldine de Gruyter, New York.

Janson, C. H. (1998). Testing the predation hypothesis for vertebrate sociality: prospects and pitfalls. *Behaviour*, **135**, 389–410.

Janson, C. H. (2000). Primate socio-ecology: the end of a golden age. *Evolutionary Anthropology*, **9**, 73–86.

Janson, C. H. and M. L. Goldsmith (1995). Predicting group-size in primates—foraging costs and predation risks. *Behavioral Ecology*, **6**, 326–336.

Janson, C. H. and C. P. v. Schaik (1993). Ecological risk aversion in juvenile primates: slow and steady wins the race. In *Juvenile Primates. Life History, Development, and Behavior*. (ed. M. E. P. a. L. A. Fairbanks), pp. 57–74. Oxford University Press, New York.

Janzen, D. (1980). When is it coevolution? *Evolution*, **34**, 611–612.

Janzen, D. H. (1978). Complications in interpreting the chemical defenses of trees against tropical arboreal vertebrates. In *The Ecology of Arboreal Folivores* (ed. G. G. Montgomery), pp. 73–84. Smithsonian Institution Press, Washington, DC.

Jennelle, C. S., E. G. Cooch, M. J. Conroy, and J. C. Senar (in preparation). Provisionally accepted. State-specific detection probabilities and disease prevalence: an index by any other name. *Ecological Applications*.

Jenni, L., D. H. Molyneux, J. L. Livesey, and R. Galun (1980). Feeding-behavior of tsetse flies infected with salivarian trypanosomes. *Nature*, **283**, 383–385.

Jensen, T., M. v. d. Bildt, H. H. Dietz, T. H. Andersen, A. S. Hammer, T. Kuiken, and A. Osterhaus (2002). Another phocine distemper outbreak in Europe. *Science*, **297**, 209.

Jensen-Seamann, M. and K. Kidd (2001). Mitochondrial DNA variation and biogeography of eastern gorillas. *Molecular Ecology*, **10**, 2241–2247.

Jin, M. J., J. Rogers, J. E. Phillips-Conroy, J. S. Allan, R. C. Desrosiers, G. M. Shaw, P. M. Sharp et al. (1994). Infection of a yellow baboon with simian immunodeficiency virus from African-green monkeys—evidence for cross-species transmission in the wild. *Journal of Virology*, **68**, 8454–8460.

Johnson, K., B. Williams, D. Drown, R. Adams, and D. Clayton (2002). The population genetics of host specificity: genetic differentiation in dove lice (Insecta: Phthiraptera). *Molecular Ecology*, **11**, 25–38.

Johnson, R. W. (2002). The concept of sickness behavior: a brief chronological account of four key discoveries. *Veterinary Immunology and Immunopathology*, **87**, 443–450.

Jolly, A. (1966). *Lemur behavior*. University of Chicago Press, Chicago, IL.

Jolly, C. J., J. E. Phillips-Conroy, T. R. Turner, S. Broussard, and J. S. Allan (1996). SIV_{agm} incidence over two decades in a natural population of Ethiopian grivet monkeys (*Cercopithecus aethiops aethiops*). *Journal of Medical Primatology*, **25**, 78–83.

Jones, C. B. (2003). Sexual selection and reproductive competition in primates: new perspectives and directions. Norman, OK, Special Topics in Primatology.

Jones, D. M. (1982). Conservation in relation to animal disease in Africa and Asia. *Symposia of the Zoological Society, London*, **50**, 271–285.

Jones, J. H. and M. S. Handcock (2003). An assessment of preferential attachment as a mechanism for human sexual network formation. *Proceedings of the Royal Society B*: *Biological Sciences,* **270**, 1123–1128.

Jones, K. C. (1983). Inter-troop transfer of *Lemur catta* males at Berenty, Madagascar. *Folia Primatologica **40***, 145–160.

Jones-Engel, L., G. A. Engel, M. A. Schillaci, K. Kyes, J. Froehlich, U. Paputungan, and R. C. Kyes (2004). Prevalence of enteric parasites in pet macaques in Sulawesi, Indonesia. *American Journal of Primatology*, **62**, 71–82.

Joy, D. A., X. Feng, J. Mu, T. Furuya, K. Chotivanich, A. U. Krettli, M. Ho et al. (2003). Early origin and recent expansion of *Plasmodium falciparum*. *Science*, **300**, 318–321.

Kaiser, J. (2005). More infectious diseases emerge in North. *Science*, **307**, 1190.

Kalema-Zikusoka, G., R. A. Kock, and E. J. Macfie (2002). Scabies in free-ranging mountain gorillas (*Gorilla beringei beringei*) in Bwindi Impenetrable National Park, Uganda. *Veterinary Record*, **150**, 12–15.

Kalter, S. S. (1972a). Identification and study of viruses. In *Pathology of Simian Primates, Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 382–468. S. Karger, Basel.

Kalter, S. S. (1972b). Serologic surveys. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 469–496. S. Karger, London.

Kalter, S. S. (1983). National and international services for primate animal research. *Journal of Medical Primatology*, **12**, 146–154.

Kalter, S. S. and R. L. Heberling (1990). Primate viral diseases in perspective. *Journal of Medical Primatology*, **19**, 519–535.

Kalter, S. S., R. E. Kuntz, Y. Al- Doory, and A. A. Katzberg (1966). Collection of biomedical study materials from baboons in East Africa: preliminary report. *Laboratory Animal Care*, **16**, 161–177.

Kappeler, P. M. (1993). Variation in social-structure—the effects of sex and kinship on social interactions in three lemur species. *Ethology*, **93**, 125–145.

Kappeler, P. M. (1998a). Nests, tree holes and the evolution of primate life histories. *American Journal of Primatology*, **46**, 7–33.

Kappeler, P. M. (1998b). To whom it may concern: the transmission and function of chemical signals in *Lemur catta*. *Behavioral Ecology and Sociobiology*, **42**, 411–421.

Kappeler, P. M. and M. E. Pereira (2003). *Primate Life Histories and Socioecology*. Chicago University Press. Chicago, IL.

Kappeler, P. M. and C. P. van Schaik (2002). Evolution of primate social systems. *International Journal of Primatology*, **23**, 707–740.

Karesh, W. and C. A. Chapman (2005). Ebola: a crisis and wake-up call for better understanding of reservoir and transmission routes. *Evolutionary Anthroplogy*, **14**, 140.

Karesh, W. B., R. B. Wallace, R. L. E. Painter, D. Rumiz, W. E. Braselton, E. S. Dierenfeld, and H. Puche (1998). Immobilization and health assessment of free-ranging black spider monkeys (*Ateles paniscus chamek*). *American Journal of Primatology*, **44**, 107–123.

Karesh, W. B., R. A. Cook, E. L. Bennett, and J. Newcomb (2005). Wildlife trade and global disease emergence. *Emerging Infectious Diseases*, **11**, 1000–1002.

Kaschula, V. R., A. F. Vandellen, and V. Devos (1978). Some infectious-diseases of wild vervet monkeys (*Cercopithecus aethiops pygerythrus*) in South-Africa. *Journal of the South African Veterinary Association*, **49**, 223–227.

Kavaliers, M. and D. D. Colwell (1995a). Discrimination by female mice between the odors of parasitized and non-parasitized males. *Proceedings of the Royal Society B*: *Biological Sciences,* **261**, 31–35.

Kavaliers, M., and D. D. Colwell (1995b). Reduced spatial-learning in mice infected with the nematode, *Heligmosomoides polygyrus*. *Parasitology*, **110**, 591–597.

Kavaliers, M., D. D. Colwell, and E. Choleris (1999). Parasites and behavior: an ethopharmacological analysis and biomedical implications. *Neuroscience and Biobehavioral Reviews*, **23**, 1037–1045.

Kavaliers, M., D. D. Colwell, K. P. Ossenkopp, and T. S. Perrot-Sinal (1997). Altered responses to female odors in parasitized male mice: neuromodulatory mechanisms and relations to female choice. *Behavioral Ecology and Sociobiology*, **40**, 373–384.

Kawabata, M. and T. Nishida (1991). A preliminary note on the intestinal parasites of wild chimpanzees in the Mahale Mountains, Tanzania. *Primates*, **32**, 275–278.

Keddy-Hector, A. C. (1992). Mate choice in nonhuman-primates. *American Zoologist*, **32**, 62–70.

Keeling, M. and B. T. Grenfell (1997a). Disease extinction and community size: modeling the persistence of measles. *Science*, **275**, 65–67.

Keeling, M. J. (1999a). The effects of local spatial structure on epidemiological invasions. *Proceedings of the Royal Society B*: *Biological Sciences,* **266**, 859–867.

Keeling, M. J. (1999b). The effects of local spatial structure on epidemiological invasions. *Proceedings of the Royal Society B*: *Biological Sciences,* **266**, 859–867.

Keeling, M. J. and C. A. Gilligan (2000). Metapopulation dynamics of bubonic plague. *Nature*, **407**, 903–906.

Keeling, M. J. and B. T. Grenfell (1997b). Disease extinction and community size: modeling the persistence of measles. *Science*, **275**, 65–67.

Keeling, M. J., P. Rohani, and B. Grenfell (2001). Seasonally forced disease dynamics explored as switching between attractors. *Physica D*, **148**, 317–335.

Keeling, M. J., M. E. J. Woolhouse, R. M. May, G. Davies, and B. T. Grenfell (2003). Modelling vaccination strategies against foot-and-mouth disease. *Nature*, **421**, 136–142.

Keet, D. F., N. P. J. Kriek, M. L. Penrith, A. Michel, and H. Huchzermeyer (1996). Tuberculosis in buffaloes (*Syncerus caffer*) in the Kruger National Park: spread of the disease to other species. *Onderstepoort Journal of Veterinary Research*, **63**, 239–244.

Keet, D. F., N. P. J. Kriek, R. G. Bengis, D. G. Grobler, and A. Michel (2000). The rise and fall of tuberculosis in a free-ranging chacma baboon troop in the Kruger National Park. *Onderstepoort Journal of Veterinary Research*, **67**, 115–122.

Kennedy, C. R. and A. O. Bush (1994). The relationship between pattern and scale in parasite communities—a stranger in a strange land. *Parasitology*, **109**, 187–196.

Kermack, W. O. and A. G. McKendrick (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society A: Mathematical*, *Physical and Engineering Sciences*, **115**, 700–721.

Ketch, L. A., D. Malloch, W. C. Mahaney, and M. A. Huffman (2001). Comparative microbial analysis and clay mineralogy of soils eaten by chimpanzees (*Pan troglodytes schweinfurthii*) in Tanzania. *Soil Biology and Biochemistry*, **33**, 199–203.

Khan, A. S., R. F. Khabbaz, L. R. Armstrong, R. C. Holman, S. P. Bauer, J. Graber, T. Strine et al. (1996). Hantavirus pulmonary syndrome: the first 100 U.S. cases. *J. Infectious Diseases*, **173**, 1297–1303.

Kiesecker, J. M., D. K. Skelly, K. H. Beard, and E. Preisser (1999). Behavioral reduction of infection risk. *Proceedings of the National Academy of Sciences USA*, **96**, 9165–9168.

Kilbourn, A. M., W. B. Karesh, E. J. Bosi, R. A. Cook, M. Andau, and N. D. Wolfe (1998). Disease evaluation of free-ranging orangutans (*Pongo pygmaeus pygmaeus) in Sabah, Malaysia.* In *Proceedings of the American Association of Zoo Veterinarians and American Association of Wildlife Veterinarians, Joint Conference* (ed. C. K. Baer), pp. 417–421. American Association of Zoo Veterinarians, Media, Philadelphia, PA.

Kilbourn, A. M., W. B. Karesh, N. D. Wolfe, E. J. Bosi, R. A. Cook, and M. Andau (2003). Health evaluation of free-ranging and semi-captive orangutans (*Pongo pygmaeus pygmaeus*) in Sabah, Malaysia. *Journal of Wildlife Diseases*, **39**, 73–83.

Kim, J. C. S. and S. S. Kalter (1975). Pathology of pulmonary acariasis in baboons (*Papio sp*). *Journal of Medical Primatology*, **4**, 70–82.

Kim, K. C. and K. C. Emerson (1973). *Anoplura* of tropical West Africa with descriptions of new species and nymphal stages. *Revue de Zoologie et de Botanique Africaines*, **87**, 425–455.

King, N., B. Shrestha, and A. Kesson (2003). Immune modulation by flaviviruses. *Advances in Virus Research*, **60**, 121–155.

Kingsolver, J. G., H. E. Hoekstra, J. M. Hoekstra, D. Berrigan, S. N. Vignieri, C. E. Hill, A. Hoang et al. (2001). The strength of phenotypic selection in natural populations. *American Naturalist*, **157**, 245–261.

Kirkpatrick, R. C., Y. C. Long, T. Zhong, and L. Xiao (1998). Social organization and range use in the Yunnan snub-nosed monkey *Rhinopithecus bieti*. *International Journal of Primatology*, **19**, 13–51.

Kitala, P. M., J. J. McDermott, P. G. Coleman, and C. Dye (2002). Comparison of vaccination strategies for the control of dog rabies in Machakos district, Kenya. *Epidemiological Infections*, **129**, 215–222.

Kittler, R., M. Kayser, and M. Stoneking (2003). Molecular evolution of *Pediculus humanus* and the origin of clothing. *Current Biology*, **13**, 1414–1417.

Kittler, R., M. Kayser, and M. Stoneking (2004). Erratum. Molecular evolution of *Pediculus humanus* and the origin of clothing (vol 13, pg 1414, 2003). *Current Biology*, **14**, 2309–2309.

Kleiman, D. G., B. B. Beck, J. M. Dietz, L. A. Dietz, J. D. Ballou, and A. F. Coimbra-Filho (1986). Conservation program for the golden lion tamarin: captive research and management, ecological studies, educational studies, and reintroduction. In *Primates: The Road to Self-Sustaining Populations* (ed. K. Benirschke), pp. 959–980. Springer-Verlag, New York.

Klein, L. L. and D. B. Klein (1977). Feeding behaviour of the Colombian spider monkey. In *Primate Ecology* (ed. T. H. Clutton-Brock), pp. 153–180. Academic Press, London.

Klein, S. L. and R. J. Nelson (1999). Influence of social factors on immune function and reproduction. *Reviews of Reproduction*, **4**, 168–178.

Klein, S. L., H. R. Gamble, and R. J. Nelson (1999). *Trichinella spiralis* infection in voles alters female odor preference but not partner preference. *Behavioral Ecology and Sociobiology*, **45**, 323–329.

Kluger, M. J. (1979). *Fever*. Princeton University Press, Princeton, NJ.

Kluger, M. (1991). Fever: role of pyrogens and cryogens. *Physiological Review*, **71**, 93–127.

Kluger, M. J., D. H. Ringler, and M. R. Anver (1975). Fever and survival. *Science*, **188**, 166–168.

Knapp, L. A. (2005). The ABCs of MHC. *Evolutionary Anthropology*, **14**, 28–37.

Knapp, L. A., J. C. Ha, and G. P. Sackett (1996). Parental MHC antigen sharing and pregnancy wastage in captive pigtailed macaques. *Journal of Reproductive Immunology*, **32**, 73–88.

Knell, R. J. (1999). Sexually transmitted disease and parasite-mediated sexual selection. *Evolution*, **53**, 957–961.

Knell, R. J. (2004). Syphilis in Renaissance Europe: rapid evolution of an introduced sexually transmitted disease? *Proceedings of the Royal Society B*: *Biological Sciences,* **271**, S174–S176.

Knell, R. J., M. Begon, and D. J. Thompson (1996). Transmission dynamics of *Bacillus thuringiensis* infecting *Plodia interpunctella*: a test of the mass action assumption with an insect pathogen. *Proceedings of the Royal Society B*: *Biological Sciences,* **263**, 75–81.

Knell, R. J., M. Begon, and D. J. Thompson (1998). Transmission of *Plodia interpunctella* granulosis virus does not conform to the mass action model. *Journal of Animal Ecology*, **67**, 592–599.

Knezevich, M. (1998). Geophagy as a therapeutic mediator of endoparasitism in a free-ranging group of rhesus macaques (*Macaca mulatta*). *American Journal of Primatology*, **44**, 71–82.

Kock, R. A., J. M. Wambua, J. Mwanzia, H. Wamwayi, E. K. Ndungu, T. Barrett, N. D. Kock et al. (1999). Rinderpest epidemic in wild ruminants in Kenya 1993–97. *Veterinary Record*, **145**, 275–283.

Kodama, T., D. P. Silva, M. D. Daniel, J. E. Phillipsconroy, C. J. Jolly, J. Rogers, and R. C. Desrosiers (1989). Prevalence of antibodies to SIV in baboons in their native habitat. *AIDS Research and Human Retroviruses*, **5**, 337–343.

Koella, J., F. Sørensen, and R. Anderson (1998). The malaria parasite *Plasmodium falciparum* increases the frequency of multiple feeding of its mosquito vector *Anopheles gambiae. Proceedings of the Royal Society B*: *Biological Sciences,* **265**, 763–768.

Koenig, A., J. Beise, M. K. Chalise, and J. U. Ganzhorn (1998). When females should contest for food—testing hypotheses about resource density, distribution, size, and quality with Hanuman langurs (*Presbytis entellus*). *Behavioral Ecology and Sociobiology*, **42**, 225–237.

Koh, L. P., R. R. Dunn, N. S. Sodhi, R. K. Colwell, H. C. Proctor, and V. S. Smith (2004). Species coextinctions and the biodiversity crisis. *Science*, **305**, 1632–1634.

Kokko, H., E. Ranta, G. Ruxton, and P. Lundberg (2002). Sexually transmitted disease and the evolution of mating systems. *Evolution*, **56**, 1091–1100.

Kollias, G., K. Sydenstricker, H. Kollias, D. Ley, P. Hosseini, V. Connolly, and A. Dhondt (2004). Experimental infection of house finches with *Mycoplasma gallisepticum. Journal of Wildlife Diseases*, **40**, 79–86.

Koopman, J. S., S. E. Chick, C. P. Simon, C. S. Riolo, and G. Jacquez (2002). Stochastic effects on endemic infection levels of disseminating versus local contacts. *Mathematical Biosciences*, **180**, 49–71.

Korber, B., M. Muldoon, J. Theiler, F. Gao, R. Gupta, A. Lapedes, B. H. Hahn et al. (2000). Timing the ancestor of the HIV-1 pandemic strains. *Science*, **288**, 1789–1796.

Korey, K. A. (1978). A critical appraisal of methods for measuring admixture. *Human Biology*, **50**, 343–360.

Kosek, M., C. Bern, and R. Guerrant (2003). The global burden of diarrhoel disease, as estimated from studies published between 1992 and 2000. *Bulletin of the World Health Organization*, **81**, 197–204.

Koski, K. and M. Scott (2001). Gastrointestinal nematodes, nutrition and immunity: breaking the negative spiral. *Annual Review of Nutrition*, **21**, 297–321.

Koski, K., Z. Su, and M. Scott (1999). Energy deficits suppress both systemic and gut immunity during infection. *Biochemical and Biophysical Research Communications*, **264**, 796–801.

Kourany, M. and J. A. J. Porter (1969). A survey for enteropathogenic bacteria in Panamanian primates. *Laboratory Animal Care*, **19**, 336–341.

Kovats, R. S., D. H. Campbell-Lendrum, A. J. McMichael, A. Woodward, and J. S. Cox (2001). Early effects of climate change: do they include changes in vector-borne disease? *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **356**, 1057–1068.

Krause, J. and G. D. Ruxton (2002). *Living in Groups*. Oxford University Press, Oxford.

Kreis, H. A. (1932). A new pathogenic nematode of the family Oxyuroidea, *Oxyuronema atelophora* n. g. n. sp. in the red spider monkey, *Ateles geoffroyi. Journal of Parasitology*, **18**, 295–302.

Kreulen, D. A. (1985). Lick use by large herbivores—a review of benefits and banes of soil consumption. *Mammal Review*, **15**, 107–123.

Krief, S., A. Jamart, and C.-M. Hladik (2004). On the possible adaptive value of coprophagy in free-ranging chimpanzees. *Primates*, **45**, 141–145.

Krief, S., M. A. Huffman, T. Sevenet, J. Guillot, C. Bories, C. M. Hladik, and R. W. Wrangham (2005). Noninvasive monitoring of the health of *Pan troglodytes schweinfurthii* in the Kibale National Park, Uganda. *International Journal of Primatology*, **26**, 467–490.

Krishnamani, R. and W. C. Mahaney (2000). Geophagy among primates: adaptive significance and ecological consequences. *Animal Behaviour*, **59**, 899–915.

Kummer, H. (1968). *Social organization of hamadryas baboons*. University of Chicago Press, Chicago, IL.

Kumm, H. W. and H. W. Laemmert Jr. (1950). The geographical distribution of immunity to yellow fever among the primates of Brazil. *American Journal of Tropical Medicine*, **30**, 733–748.

Kuntz, R. E. (1972). Trematodes of the intestinal tract and biliary passages. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 104–123. S. Karger, London.

Kuntz, R. E. (1982). Significant infections in primate parasitology. *Journal of Human Evolution*, **11**, 185–194.

Kuntz, R. E. and B. J. Myers (1966). Parasites of baboons (*Papio doguera* (Pucheran, 1856)) captured in Kenya and Tanzania, East Africa. *Primates*, **7**, 27–32.

Kuntz, R. E., B. J. Myers, J. Bergner, J. F., and D. E. Armstrong (1968). Parasites and commensals of the Taiwan macaque (*Macaca cyclopis*, Swinhoe, 1862). *Formosan Science*, **22**, 120–135.

Kunz, T. H. (1976). Observations on the winter ecology of the bat fly *Trichobius-corynorhini cockerell* (Diptera-Streblidae). *Journal of Medical Entomology*, **12**, 631–636.

Kuris, A. M., A. R. Blaustein, and J. Javier Alio (1980). Hosts as islands. *American Naturalist*, **116**, 570–586.

Kutsukake, N. and C. L. Nunn (in review). Comparative tests of reproductive skew in male primates: the roles of female mating behavior and incomplete control. *Behavioral Ecology and Sociobiology*.

Kyriazakis, I., B. J. Tolkamp, and M. R. Hutchings (1998). Towards a functional explanation for the occurrence of anorexia during parasitic infections. *Animal Behaviour*, **56**, 265–274.

Lacroix, R., W. R. Mukabana, L. C. Gouagna, and J. C. Koella (2005). Malaria infection increases attractiveness of humans to mosquitoes. *PLoS Biology*, **3**, e298.

Lafferty, K. and L. Gerber (2002). Good medicine for conservation biology: the intersection of epidemiology and conservation theory. *Conservation Biology*, **16**, 593–604.

Lafferty, K. D. (1992). Foraging on prey that are modified by parasites. *American Naturalist*, **140**, 854–867.

Laing, A. B. G., J. F. B. Edeson, and R. H. Wharton (1960). Studies on filariasis in Malaya: the vertebrate hosts of *Brugia malayi* and *B. pahangi*. *Annals of Tropical Medicine and Parasitology*, **54**, 92–97.

Lainson, R., R. R. Braga, A. A. A. Desouza, M. M. Povoa, E. A. Y. Ishikawa, and F. T. Silveira (1989). *Leishmania (Viannia) Shawi Sp-N*, a parasite of monkeys, sloths and procyonids in Amazonian Brazil. *Annales de Parasitologie Humaine et Comparee*, **64**, 200–207.

Lande, R. (1981). Models of speciation by sexual selection on polygenic traits. *Proceedings of the National Academy of Sciences USA*, **78**, 3721–3725.

Lande, R. and S. J. Arnold (1983). The measurement of selection on correlated characters. *Evoluiton*, **37**, 1210–1226.

Landsoud-Soukate, J., C. E. G. Tutin, and M. Fernandez (1995). Intestinal parasites of sympatric gorillas and chimpanzees in the Lope Reserve, Gabon. *Annals of Tropical Medicine and Parasitology*, **89**, 73–79.

Lasry, J. E. and B. W. Sheridan (1965). Chagas' myocarditis and heart failure in the red uakari. *International Zoo Yearbook*, **5**, 182–184.

Lathuilliere, M., N. Menard, A. Gautier-Hion, and B. Crouau-Roy (2001). Testing the reliability of noninvasive genetic sampling by comparing analyses of blood and fecal samples in Barbary macaques (*Macaca sylvanus*). *American Journal of Primatology*, **55**, 151–158.

Laurenson, K., C. Sillero-Zubiri, H. Thompson, F. Shiferaw, S. Thirgood, and J. Malcolm (1998). Disease as a threat to endangered species: Ethiopian wolves, domestic dogs and canine pathogens. *Animal Conservation*, **1**, 273–280.

Lawes, M. J., P. E. Mealin, and S. E. Piper (2000). Patch occupancy and potential metapopulation dynamics of three forest mammals in fragmented afromontane forest in South Africa. *Conservation Biology*, **14**, 1088–1098.

Lederberg, J. (2000). Infectious history. *Science*, **288**, 287–293.

Lederberg, J., R. E. Shope, and S. C. Oaks (1992). *Emerging Infections: Microbial Threats to Health in the United States*. National Academy Press, Washington, DC.

Lee, D. L. (2002). *The Biology of Nematodes*. London, Taylor and Francis.

Lee, P. (1999). *Comparative Primate Socioecology*. Cambridge University Press, Cambridge.

Leendertz, F. H., H. Ellerbrok, C. Boesch, E. Couacy-Hymann, K. Matz-Rensing, R. Hakenbeck, C. Bergmann et al. (2004). Anthrax kills wild chimpanzees in a tropical rainforest. *Nature*, **430**, 451–452.

Legesse, M. and B. Erko (2004). Zoonotic intestinal parasites in *Papio anubis* (baboon) and *Cercopithecus aethiops* (vervet) from four localities in Ethiopia. *Acta Tropica*, **90**, 231–236.

Lehane, M. (1991). *The Biology of Blood-Sucking Insects*. Harper-Collins, London.

Lehmann, T. (1993). Ectoparasites: direct impacts on host fitness. *Parasitology Today*, **9**, 8–13.

Leighton, D. R. (1987). Gibbons: territoriality and monogamy. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Stuhsaker), pp. 135–145. University of Chicago Press, Chicago, IL.

Lenski, M. and R. M. May (1994). The evolution of virulence in parasites and pathogens: reconciliation between two competing hypotheses. *Journal of Theoretical Biology*, **169**, 253–265.

Leroy, E. M., P. Rouquet, P. Formenty, S. Souquiere, A. Kilbourne, J.-M. Froment, M. Bermejo et al. (2004a). Multiple ebola virus transmission events and rapid decline of Central African wildlife. *Science*, **303**, 387–390.

Leroy, E. M., P. Telfer, B. Kumulungui, P. Yaba, P. Rouquet, P. Roques, J. P. Gonzalez et al. (2004b). A serological survey of Ebola virus infection in central African nonhuman primates. *Journal of Infectious Diseases*, **190**, 1895–1899.

Leroy, E. M., B. Kumulungui, X. Pourrut, P. Rouquet, A. Hassanin, P. Yaba, A. Delicat, J. T. Paweska, J. P. Gonzalez, and R. Swanepoel (2005). Fruit bats as reservoirs of Ebola virus. *Nature*, **438**, 575–576.

Levin, B. R. (1996). The evolution and maintenance of virulence in microparasites. *Emerging Infectious Diseases*, **2**, 93–102.

Levin, J. L., J. K. Hilliard, S. L. Lipper, T. M. Butler, and W. J. Goodwin (1988). A naturally-occurring epizootic of simian agent-8 in the baboon. *Laboratory Animal Science*, **38**, 394–397.

Levin, S. and D. Pimentel (1981). Selection of intermediate rates of increase in parasite-host systems. *American Naturalist*, **117**, 308–315.

Levine, N. D. (1963). Weather, climate and the bionomics of ruminant nematode larvae. *Advances in Veterinary Science*, **8**, 215.

Lewis, M., J. Gluck, J. Petitto, L. Hensley, and H. Ozer (2000). Early social deprivation in nonhuman primates: long-term effects on survival and cell-mediated immunity. *Biological Psychiatry*, **15**, 119–126.

Lim, M. M., A. D. Hammock, and L. J. Young (2004a). The role of vasopressin in the genetic and neural regulation of monogamy. *Journal of Neuroendocrinology*, **16**, 325–332.

Lim, M. M., Z. Wang, D. E. Olazabal, X. Ren, E. F. Terwilliger, and L. J. Young (2004b). Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. *Nature*, **429**, 754–757.

Lindenfors, P., L. Froberg, and C. L. Nunn (2004). Females drive primate social evolution. *Proceedings of the Royal Society B*: *Biological Sciences,* **271**, S101–S103.

Lindgren, E., L. Talleklint, and T. Polfeldt (2000). Impact of climatic change on the northern latitude limit and population density of the disease-transmitting European tick *Ixodes ricinus*. *Environmental Health Perspectives*, **108**, 119–123.

Lindstrom, K. M., J. Foufopoulos, H. Parn, and M. Wikelski (2004). Immunological investments reflect parasite abundance in island populations of Darwin's finches. *Proceedings of the Royal Society B*: *Biological Sciences,* **271**, 1513–1519.

Ling, B., P. Tefler, D. L. Robertson, and P. A. Marx (2004). A link between SIV_{sm} in sooty mangabeys (SM) in wild-living monkeys in Sierra Leone and SIV_{sm} in an American-based SM colony. *AIDS Research and Human Retroviruses*, **20**, 1348–1351.

Lipsitch, M. and M. Nowak (1995). The evolution of virulence in sexually transmitted HIV/AIDS. *Journal of Theoretical Biology*, **174**, 427–440.

Lipsitch, M., E. A. Herre, and M. A. Nowak (1995a). Host population structure and the evolution of virulence: a law of diminishing returns. *Evolution*, **49**, 743–748.

Lipsitch, M., M. Nowak, D. Ebert, and R. May (1995b). The population dynamics of vertically and horizontally transmitted parasites. *Proceedings of the Royal Society B*: *Biological Sciences*, **260**, 321–327.

Lipsitch, M., T. Cohen, B. Cooper, J. M. Robins, S. Ma, L. James, G. Gopalakrishna et al. (2003). Transmission dynamics and control of severe acute respiratory syndrome. *Science*, **300**, 1966–1970.

Liu, H. F., P. Goubau, M. Van Brussel, K. Van Laethem, Y. C. Chen, J. Desmyter, and A. M. Vandamme (1996). The three human T-lymphotropic virus type I subtypes arose from three geographically distinct simian reservoirs. *Journal of General Virology*, **77**, 359–368.

Lively, C. M. (1992). Parthenogenesis in a freshwater snail: reproductive assurance versus parasitic release. *Evolution*, **46**, 907–913.

Lively, C. M. (1999). Migration, virulence, and the geographic mosaic of adaptation by parasites. *American Naturalist*, **153**, S34–S47.

Lively, C. M. and M. F. Dybdahl (2000). Parasite adaptation to locally common host genotypes. *Nature*, **405**, 679–681.

Lloyd, S. (1995). Environmental influences on host immunity. In *Ecology of Infectious Diseases in Natural Populations* (eds. B. T. Grenfell and A. P. Dobson), pp. 327–361. Cambridge University Press, Cambridge.

Lloyd, S. S. (1983). Immunosuppression during pregnancy and lactation. *Irish Veterinary Journal*, **37**, 64–67.

Lloyd-Smith, J. O., W. M. Getz, and H. V. Westerhoff (2004). Frequency-dependent incidence in models of sexually transmitted diseases: portrayal of pair-based transmission and effects of illness on contact behaviour. *Proceedings of the Royal Society B*: *Biological Sciences,* **271**, 625–634.

Lloyd-Smith, J., P. Cross, C. Briggs, M. Daugherty, W. Getz, J. Latto, M. Sanchez et al. (2005). Should we expect population thresholds for wildlife disease? *Trends in Ecology and Evolution*, **20**, 511–519.

Lochmiller, R. L. and C. Deerenberg (2000). Trade-offs in evolutionary immunology: just what is the cost of immunity? *Oikos*, **88**, 87–98.

Lockhart, A. B., P. H. Thrall, and J. Antonovics (1996). Sexually transmitted diseases in animals: ecological and evolutionary implications. *Biological Reviews of the Cambridge Philosophical Society*, **71**, 415–471.

Loehle, C. (1995). Social barriers to pathogen transmission in wild animal populations. *Ecology*, **76**, 326–335.

Loehle, C. (1997). The pathogen transmission avoidance theory of sexual selection. *Ecological Modelling*, **103**, 231–250.

Loftin, R. (1995). Captive breeding of endangered species. In *Ethics of the Ark* (eds. B. G. Norton, M. Hutchins, E. F. Stevens, and T. L. Maple), pp. 164–180. Smithsonian Institution Press, Washington, DC.

Logiudice, K. (2003). Trophically transmitted parasites and the conservation of small populations: raccoon roundworm and the imperiled Allegheny woodrat. *Conservation Biology*, **17**, 258–266.

Longino, J. T. (1984). True anting by the capuchin, *Cebus capucinus*. *Primates*, **25**, 243–245.

Lourenco de Oliveira, R. and L. M. Deane (1995). Simian malaria at two sites in the Brazilian Amazon. 1. the infection rates of *Plasmodium brasilianum* in nonhuman primates. *Memorias do Instituto Oswaldo Cruz*, **90**, 331–339.

Low, B. S. (1987). Pathogen stress and polygyny in humans. In *Human Reproductive Behaviour: A Darwinian Perspective* (eds. L. Betzig, M. Borgerhoff Mulder, and P. W. Turke), pp. 115–127. Cambridge University Press, Cambridge.

Low, B. S. (1990). Marriage systems and pathogen stress in human societies. *American Zoologist*, **30**, 325–339.

Lowen, C. and R. I. M. Dunbar (1994). Territory size and defendability in primates. *Behavioral Ecology and Sociobiology*, **35**, 347–354.

Lozano, G. A. (1991). Optimal foraging theory: a possible role for parasites. *Oikos*, **60**, 391–395.

Lozano, G. A. (1998). Parasitic stress and self-medication in wild animals. *Advances in the Study of Behavior*, **27**, 291–317.

Lukas, D., B. J. Bradley, A. M. Nsubuga, D. Doran-Sheehy, M. M. Robbins, and L. Vigilant (2004). Major histocompatibility complex and microsatellite variation in two populations of wild gorillas. *Molecular Ecology*, **13**, 3389–3402.

Lukas, D., V. Reynolds, C. Boesch, and L. Vigilant (2005). To what extent does living in a group mean living with kin? *Molecular Ecology*, **14**, 2181–2196.

Lyles, A. M. and A. P. Dobson (1993). Infectious disease and intensive management: population dynamics, threatened hosts, and their parasites. *Journal of Zoo and Wildlife Medicine*, **24**, 315–326.

Macdonald, G. (1957). *The Epidemiology and Control of Malaria*. Oxford University Press, Oxford.

Macfie, L. (1996). Case report on scabies infection in Bwindi gorillas. *Gorilla Journal*, **13**, 19–20.

MacKinnon, J. (1974). The behaviour and ecology of wild orang-utans (*Pongo pygmaeus). Animal Behaviour*, **22**, 3–74.

Mackinnon, M. J. and A. F. Read (2004). Immunity promotes virulence evolution in a malaria model. *PLOS Biology*, **2**, 1286–1292.

Mackinnon, M. J., D. J. Gaffney, and A. F. Read (2002). Virulence of malaria parasites: host genotype by parasite genotype interactions. *Infection, Genetics and Evolution*, **1**, 287–296.

MacPhee, R. D. E. and P. A. Marx (1997). The 40,000-Year Plague. In *Natural Change and Human Impact in Madagascar* (eds. S. M. Goodman and B. D. Patterson), pp. 169–217. Smithsonian Institution Press, Washington, DC.

Maddison, W. P. (1990). A method for testing the correlated evolution of two binary characters: are gains or losses concentrated on certain branches of a phylogenetic tree. *Evolution*, **44**, 539–557.

Maggenti, A. (1981). *General Nematology*. Springer-Verlag, New York.

Mahaney, W. C., D. P. Watts, and R. G. V. Hancock (1990). Geophagia by mountain gorillas (*Gorilla gorilla beringei*) in the Virunga Mountains, Rwanda. *Primates*, **31**, 113–120.

Mahaney, W. C., R. G. V. Hancock, and M. Inoue (1993). Geochemistry and clay mineralogy of soils eaten by Japanese macaques. *Primates*, **34**, 85–91.

Mahaney, W. C., J. Zippin, M. W. Milner, K. Sanmugadas, R. G. V. Hancock, S. Aufreiter, S. Campbell et al. (1999). Chemistry, mineralogy and microbiology of termite mound soil eaten by the chimpanzees of the Mahale Mountains, Western Tanzania. *Journal of Tropical Ecology*, **15**, 565–588.

Maier, S. F., L. R. Watkins, and M. Fleshner (1994). Psychoneuroimmunology—the interface between behavior, brain, and immunity. *American Psychologist*, **49**, 1004–1017.

Mak, J. W., W. H. Cheong, P. K. F. Yen, P. K. C. Lim, and W. C. Chan (1982). Studies on the epidemiology of subperiodic *Brugia malayi* in Malaysia—problems in its control. *Acta Tropica*, **39**, 237–245.

Makuwa, M., S. Souquiere, P. Telfer, E. M. Leroy, O. Bourry, P. Rouquet, S. Clifford et al. (2003). Occurrence of hepatitis viruses in wild-born non-human primates: a three year (1998–2001) epidemiological survey in Gabon. *Journal of Medical Primatology*, **32**, 307–314.

Manga-Gonzalez, M. Y., C. Gonzalez-Lanza, E. Cabanas, and R. Campo (2001). Contributions to and review of dicrocoeliosis, with special reference to the intermediate hosts of *Dicrocoelium dendriticum*. *Parasitology*, **123** (suppl.), S91–S114.

Manson, J. H., S. Perry, and A. R. Parish (1997). Nonconceptive sexual behavior in bonobos and capuchins. *International Journal of Primatology*, **18**, 767–786.

Marlowe, F. (2000). Paternal investment and the human mating system. *Behavioural Processes*, **51**, 45–61.

Marr, J. S. and C. H. Calisher (2003). Alexander the Great and West Nile virus encephalitis. *Emerging Infectious Diseases*, **9**, 1599–1603.

Martens, W. J. M., T. H. Jetten, J. Rotmans, and L. W. Niessen (1995). Climate change and vector borne diseases: a global modeling perspective. *Global Environmental Change, Part A*, **5**, 195–209.

Martens, W. J. M., L. W. Niessen, J. Rotmans, T. H. Jetten, and A. J. McMichael (1997). Potential impact of global climate change on malaria risk. *Environmental Health Perspectives*, **103**, 458–465.

Martin, R. D., D. J. Chivers, A. M. MacLarnon, and C. M. Hladik (1985). Gastrointestinal allometry in primates and other mammals. In *Size and Scaling in Primate Biology* (ed. W. L. Jungers), pp. 61–89. Plenum, New York.

Martins, E. P. (1996) *Phylogenies and the Comparative Method in Animal Behavior*. New York, Oxford University Press.

Mason, W. A. (1966). Social organization of the South American monkey, *Callicebus moloch*: a preliminary report. *Tulane Studies in Zoology*, **13**, 23–28.

Matsumoto, J., S. Kawai, K. Terao, M. Kirinoki, Y. Yasutomi, M. Aikawa, and H. Matsuda (2000). Malaria infection induces rapid elevation of the soluble fas ligand level in serum and subsequent T lymphocytopenia: possible factors responsible for the differences in susceptibility of two species of *Macaca* monkeys to *Plasmodium coatneyi* infection. *Infection and Immunity*, **68**, 1183–1188.

Matsumura, S. (1999). The evolution of "egalitarian" and "despotic" social systems among macaques. *Primates*, **40**, 23–31.

May, R. M. (1983). Parasitic infections as regulators of animal populations. *American Scientist*, 36–45.

May, R. M. and R. M. Anderson (1978). Regulation and stability of host parasite population interactions. II. Destabilising processes. *Journal of Animal Ecology*, **47**, 249–267.

May, R. M. and R. M. Anderson (1979). Population biology of infectious diseases: Part II. *Nature*, **280**, 455–461.

McCabe, P., J. Sheridan, J. Weiss, J. Kaplan, B. Natelson, and W. Pare (2000). Animal models of disease. *Physiological Behaviour*, **68**, 501–507.

McCallum, H. (1994). Quantifying the impact of disease on threatened species. *Pacific Conservation*, **1**, 107–117.

McCallum, H., N. Barlow, and J. Hone (2001). How should pathogen transmission be modeled? *Trends in Ecology and Evolution*, **16**, 295–300.

McCallum, H. and A. Dobson (1995). Detecting disease and parasite threats to endangered species and ecosystems. *Trends in Ecology and Evolution*, **10**, 190–194.

McCallum, H. and A. Dobson (2002). Disease, habitat fragmentation and conservation. *Proceedings of the Royal Society B: Biological Sciences*, **269**, 2041–2049.

McConnell, E. E., P. A. Basson, V. de Vos, B. J. Myers, and R. E. Kuntz (1974). A survey of diseases among 100 free-ranging baboons (*Papio ursinus*) from the Kruger National Park. *Onderstpoort Journal of Veterinary Research*, **41**, 97–168.

McDade, T. and C. Worthman (1999). Evolutionary process and the ecology of human immune function. *American Journal of Human Biology*, **11**, 705–717.

McDade, T. W. (2003). Life history theory and the immune system: steps toward a human ecological immunology. *Yearbook of Physical Anthropology*, **46**, 100–125.

McGrew, W. C. (1998). Culture in nonhuman primates? *Annual Review of Anthropology*, **27**, 301–328.

McGrew, W. C., C. E. G. Tutin, D. A. Collins, and S. K. File (1989a). Intestinal parasites of sympatric *Pan troglodytes* and *Papio spp*. at two sites: Gombe (Tanzania) and Mt. Assirik (Senegal). *American Journal of Primatology*, **17**, 147–155.

McGrew, W. C., C. E. G. Tutin, and S. K. File (1989b). Intestinal parasites of two species of free-living monkeys in far Western Africa, *Cercopithecus* (*aethiops*) *sabaeus* and *Erythrocebus patas patas*. *African Journal of Ecology*, **27**, 261–262.

McKenna, J. J., S. Mosko, and C. Richard (1999). Breast-feeding and mother-infant cosleeping in relation to SIDS prevention. In *Evolutionary Medicine* (eds. W. R. Trevathan, E. O. Smith, and J. J. McKenna), pp. 53–74. Oxford University Press, Oxford.

McMichael, A. J. (2004). Environmental and social influences on emerging infectious diseases: past, present and future. *Philosophical Transactions of The Royal Society B: Biological Sciences*, **359**, 1049–1058.

McMichael, A. J., D. H. Campbell-Lendrum, C. F. Corvalán, K. L. Ebi, A. Githeko, J. D. Scheraga, and A. Woodwa (2003). *Climate Change and Human Health—Risks and Responses*. World Health Organization.

McNeill, W. H. (1977). *Plagues and Peoples*. Anchor Books, New York.

McPeek, M. A. (1996). Trade-offs, food web structure, and the coexistence of habitat specialists and generalists. *American Naturalist*, **148**, S124–S138.

Meade, B. J. (1984). Host-parasite dynamics among Amboseli baboons. Ph.D. thesis, Virginia Polytechnic Institute and State University, Blacksburg, VA.

Meade, M. S., J. W. Flori, and W. M. Gesler (1988). *Medical Geography*. The Guilford Press, New York.

Medley, K. E. (1993). Primate conservation along the Tana River, Kenya—an examination of the forest habitat. *Conservation Biology*, **7**, 109–121.

Mellor, P. S., J. Boorman, and M. Baylis (2000). *Culicoides* biting midges: their role as arbovirus vectors. *Annual Review of Entomology*, **45**, 307–340.

Melnick, D. J., and M. C. Pearl (1987). Cercopithecines in multimale groups: genetic diversity and population structure. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Stuhsaker), pp. 578. University of Chicago Press, Chicago, IL.

Ménard, N. and D. Vallet (1993). Dynamics of fission in a wild barbary macaque group (*Macaca sylvanus*). *International Journal of Primatology*, **14**, 479–500.

Mescas, J. and E. J. Strass (1996). Molecular mechanisms of bacterial virulence. Type III secretions and virulence islands. *Emerging Infectious Diseases*, **2**, 271–288.

Migot-Nabias, F., B. Ollomo, G. Dubreuil, A. Morelli, O. Domarle, R. Nabias, A. J. Georges et al. (1999). *Plasmodium coatneyi*: differential clinical and immune responses of two populations of *Macaca fascicularis* from different origins. *Experimental Parasitology*, **91**, 30–39.

Mikota, S. K. and R. F. Aguilar (1996). Management protocols for animals in captive propagation and reintroduction programmes. *Revue Scientifique et Technique de L Office International des Epizooties*, **15**, 191–208.

Milinski, M. and T. C. M. Bakker (1990). Female sticklebacks use male coloration in mate choice and hence avoid parasitized males. *Nature*, **344**, 330–333.

Miller, J. H. (1960). *Papio doguera* (dog face baboon), a primate reservoir host of *Schistosoma mansoni* in East Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **54**, 44 – 46.

Miller, M. A., I. A. Gardner, A. Packham, J. K. Mazet, K. D. Hanni, D. Jessup, J. Estes et al. (2002). Evaluation of an indirect fluorescent antibody test (IFAT) for demonstration of antibodies to *Toxoplasma gondii* in the sea otter (*Enhydra lutris*). *Journal of Parasitology*, **88**, 594–599.

Miller, P. S. and P. Hedrick (1991). MHC polymorphism and the design of captive breeding programs: simple solutions are not the answer. *Conservation Biology*, **5**, 556–558.

Milton, K. (1996). Effects of bot fly (*Alouattamyia baeri*) parasitism on a free-ranging howler monkey (*Alouatta palliata*) population in Panama. *Journal of Zoology*, **239**, 39–63.

Milton, K. and M. L. May (1976). Body weight, diet and home range area in primates. *Nature*, **259**, 459–462.

Min-Oo, G. and P. Gros (2005). Erythrocyte variants and the nature of their malaria protective effect. *Cellular Microbiology*, **7**, 753–763.

Minette, H. P. (1966). Leptospirosis in primates other than man. *American Journal of Tropical Medicine and Hygiene*, **15**, 190–198.

Misra, S., K. Tyagi, and R. K. Chatterjee (1997). Experimental transmission of nocturnally periodic *Wuchereria bancrofti* to Indian leaf monkey (*Presbytis entellus*). *Experimental Parasitology*, **86**, 155–157.

Mitani, J. C. and P. S. Rodman (1979). Territoriality: the relation of ranging pattern and home range size to defendability, with an analysis of territoriality among primate species. *Behavioral Ecology and Sociobiology*, **5**, 241–251.

Mitani, J. C. and D. P. Watts (1999). Demographic influences on the hunting behavior of chimpanzees. *American Journal of Physical Anthropology*, **109**, 439–454.

Mitani, J. C., J. Gros-Louis, and J. H. Manson (1996a). Number of males in primate groups: comparative tests of competing hypotheses. *American Journal of Primatology*, **38**, 315–332.

Mitani, J. C., J. Gros-Louis, and A. F. Richards (1996b). Sexual dimorphism, the operational sex ratio, and the intensity of male competition in polygynous primates. *American Naturalist*, **147**, 966–980.

Mitchell, C. L., S. Boinski, and C. P. van Schaik (1991). Competitive regimes and female bonding in two species of squirrel monkeys (*Saimiri oerstedi* and *S. sciureus*). *Behavioral Ecology and Sociobiology*, **28**, 55–60.

Mitter, C., B. Farrell, and D. J. Futuyma (1991). Phylogenetic studies of insect plant interactions—insights into the genesis of diversity. *Trends in Ecology and Evolution*, **6**, 290–293.

Mittermeier, R. and D. Cheney (1987). Conservation of primates and their habitats. In *Primate Societies* (eds. D. Cheney, R. Seyfarth, R. Wrangham, and T. Struhsaker), pp. 477–490. Chicago University Press, Chicago, IL.

Mittermeier, R. A., W. R. Konstant, A. B. Rylands, J. Ganzhorn, J. F. Oates, T. M. Butynski et al. (2002). *Primates in Peril*: *The World's Top 25 Most Endangered Primates*. Conservation International, Margo Marsh Biodiversity Foundation, IUCN/SSC, International Primatological.

Mohr, C. O. and W. A. Stumpf (1964). Relation of tick and chigger infestations to home areas of California meadow mice. *Journal of Medical Entomology*, **1**, 73–77.

Molineaux, L. (1985). The pros and cons of modelling malaria transmission. *Transactions of the Royal Society for Tropical Medicine and Hygiene*, **79**, 743–747.

Møller, A. P. (1993). A fungus infecting domestic flies manipulates sexual behavior of its host. *Behavioral Ecology and Sociobiology*, **33**, 403–407.

Møller, A. P. (1998). Evidence of larger impact of parasites on hosts in the tropics: investment in immune function within and outside the tropics. *Oikos*, **82**, 265–270.

Møller, A. P. and N. Saino (1994). Parasites, immunology of hosts, and host sexual selection. *Journal of Parasitology*, **80**, 850–858.

Møller, A. P. and J. Erritzoe (1996). Parasite virulence and host immune defense: host immune response is related to nest reuse in birds. *Evolution*, **50**, 2066–2072.

Møller, A. P. and M. Petrie (2002). Condition dependence, multiple sexual signals, and immunocompetence in peacocks. *Behavioral Ecology*, **13**, 248–253.

Møller, A. P., R. Dufva, and K. Allander (1993). Parasites and the evolution of host social behavior. *Advances in the Study of Behavior*, **22**, 65–102.

Møller, A. P., R. Dufva, and J. Erritzoe (1998a). Host immune function and sexual selection in birds. *Journal of Evolutionary Biology*, **11**, 703–719.

Møller, A. P., G. Sorci, and J. Erritzoe (1998b). Sexual dimorphism in immune defense. *American Naturalist*, **152**, 605–619.

Møller, A. P., P. Christe, and E. Lux (1999). Parasitism, host immune function, and sexual selection. *Quarterly Review of Biology*, **74**, 3–20.

Møller, A. P., S. Merino, C. R. Brown, and R. J. Robertson (2001). Immune defense and host sociality: a comparative study of swallows and martins. *American Naturalist*, **158**, 136–145.

Moore, C. and M. E. J. Newman (2000). Epidemics and percolation in small-world networks. *Physical Review E*, **61**, 5678–5682.

Moore, J. (1984). Female transfer in primates. *International Journal of Primatology*, **5**, 537–589.

Moore, J. (1995). The behavior of parasitized animals. *Bioscience*, **45**, 89–96.

Moore, J. (2002). *Parasites and the Behavior of Animals*. Oxford University Press, Oxford.

Moore, S. E. (1998). Nutrition, immunity and the fetal and infant origins of disease hypothesis in developing countries. *Proceedings of the Nutrition Society*, **57**, 241–247.

Moore, S. L. and K. Wilson (2002). Parasites as a viability cost of sexual selection in natural populations of mammals. *Science*, **297**, 2015–2018.

Mooring, M. S. and B. L. Hart (1992). Animal grouping for protection from parasites: selfish herd and encounter-dilution effects. *Behaviour*, **123**, 173–193.

Moran, N. and P.-. Baumann (1994). Phylogenetics of cytoplasmically inherited microorganisms of arthropods. *Trends in Ecology and Evolution*, **9**, 15–20.

Morand, S. (2000). Wormy world: comparative tests of theoretical hypotheses on parasite species richness. In *Evolutionary Biology of Host-Parasite Relationships* (eds. R. Poulin, S. Morand, and A. Skorping), pp. 63–79. Elsevier, Amsterdam.

Morand, S. and P. H. Harvey (2000). Mammalian metabolism, longevity and parasite species richness. *Proceedings of the Royal Society B*: *Biological Sciences,* **267**, 1999–2003.

Morand, S. and R. Poulin (2000). Nematode parasite species richness and the evolution of spleen size in birds. *Canadian Journal of Zoology*, **78**, 1356–1360.

Morand, S., S. D. Manning, and M. E. J. Woolhouse (1996). Parasite-host coevolution and geographic patterns of parasite infectivity and host susceptibility. *Proceedings of the Royal Society B*: *Biological Sciences,* **263**, 119–128.

Morand, S., M. S. Hafner, R. D. M. Page, and D. L. Reed (2000). Comparative body size relationships in pocket gophers and their chewing lice. *Biological Journal of the Linnean Society*, **70**, 239–249.

Morell, V. (1995). Emerging viruses—chimpanzee outbreak heats up search for Ebola origin. *Science*, **268**, 974–975.

Moreno, J., J. J. Sanz, S. Merino, and E. Arriero (2001). Daily energy expenditure and cell-mediated immunity in pied flycatchers while feeding nestlings: interaction with moult. *Oecologia*, **129**, 492–497.

Morens, D., G. Folkers, and A. S. Fauci (2004). The challenge of emerging and re-emerging infectious diseases. *Nature*, **430**, 242–249.

Moret, Y. and P. Schmid-Hempel (2000). Survival for immunity: the price of immune system activation for bumblebee workers. *Science*, **290**, 1166–1168.

Morgan, J. A. T., R. J. Dejong, S. D. Snyder, G. M. Mkoji, and E. S. Loker (2001). *Schistosoma mansoni* and *Biomphalaria*: past history and future trends. *Parasitology*, **123**, S211-S228.

Morin, P., K. Chambers, C. Boesch, and L. Vigilant (2001). Quantitative polymerase chain reaction analysis of DNA from noninvasive samples for accurate microsatellite genotyping of wild chimpanzees (*Pan troglodytes verus*). *Molecular Ecology*, **10**, 1835–1844.

Morris, W., D. Doak, M. Groom, P. Karieva, J. Fieberg, L. Gerber, P. Murphy et al. (1999). *A Practical Handbook for Population Viability Analysis*, The Nature Conservancy. http://training.fws.gov/EC/Resources/Advanced_Sec_7/June_2005/Scientific_References/TNC_Morris_etal_1999.pdf

Morris, W. F. and D. F. Doak (2002). *Quantitative Conservation Biology*. Sinauer Associates Inc., Sunderland, MA.

Morrow-Tesch, J., J. McGlone, and R. Norman (1993). Consequences of restraint stress on natural killer cell activity, behavior, and hormone levels in rhesus macaques (*Macaca mulatta*). *Psychoneuroendocrinology*, **18**, 383–395.

Morse, S. S. (1995). Factors in the emergence of infectious diseases. *Emerging Infectious Diseases*, **1**, 7–15.

Morse, S. S. (1996). *Emerging Viruses*. Oxford University Press, Oxford.

Mostowy, S., D. Cousins, J. Brinkman, A. Aranaz, and M. Behr (2002). Genomic deletions suggest a phylogeny for the *Mycobacterium tuberculosis* complex. *The Journal of Infectious Diseases*, **186**, 74–80.

Mudikikwa, A. B., M. R. Cranfield, J. M. Sleeman, and U. Eilenberger (2001). Clinical medicine, preventative health care and research on mountain gorillas in the Virunga Volcanoes region. In *Mountain Gorillas: Three Decades of Research at Karisoke* (eds. M. M. Robbins, P. Sicotte, and K. J. Stewart), pp. 341–360. Cambridge University Press.

Müller-Graf, C. D. M., D. A. Collins, and M. E. J. Woolhouse (1996). Intestinal parasite burden in five troops of olive baboons (*Papio cynocephalus anubis*) in Gombe Stream National Park, Tanzania. *Parasitology*, **112**, 489–497.

Müller-Graf, C. D. M., D. A. Collins, C. Packer, and M. E. J. Woolhouse (1997). *Schistosoma mansoni* infection in a natural population of olive baboons (*Papio cynocephalus anubis*) in Gombe Stream National Park, Tanzania. *Parasitology*, **115**, 621–627.

Müller-Graf, C. D. M., M. E. J. Woolhouse, and C. Packer (1999). Epidemiology of an intestinal parasite (*Spirometra* spp.) in two populations of African lions (*Panthera leo*). *Parasitology*, **118**, 407–415.

Munene, E., M. Otsyula, D. A. N. Mbaabu, W. T. Mutahi, S. M. K. Muriuki, and G. M. Muchemi (1998). Helminth and protozoan gastrointestinal tract parasites in captive and wild-trapped African non-human primates. *Veterinary Parasitology*, **78**, 195–201.

Munger, J. and W. Krasnov (1991). Sublethal parasites of white-footed mice: effects on survival and reproduction. *Canadian Journal of Zoology*, **69**, 398–404.

Muriuki, S. M. K., R. K. Murugu, E. Munene, G. M. Karere, and D. C. Chai (1998). Some gastro-intestinal parasites of zoonotic (public health) importance commonly observed in old world non-human primates in Kenya. *Acta Tropica*, **71**, 73–82.

Murphy, F. A. (1998). Emerging zoonoses. *Emerging Infectious Diseases*, **4**, 429–435.

Murphy, F. A., C. M. Fauquet, D. H. L. Bishop, S. A. Ghabrial, A. W. Jarvis, G. P. Martelli, M. A. Mayo et al. (1995). *The Classification and Nomenclature of Viruses*. Springer-Verlag, Wien.

Murray, D. L., C. A. Kapke, J. F. Evermann, and T. K. Fuller (1999). Infectious disease and the conservation of free-ranging large carnivores. *Animal Conservation*, **2**, 241–254.

Murray, J. D., E. A. Stanley, and D. L. Brown (1986). On the spatial spread of rabies among foxes. *Proceedings of the Royal Society B*: *Biological Sciences,* **229**, 111–150.

Murray, M. J. and A. B. Murray (1979). Anorexia of infection as a mechanism of host defense. *American Journal of Clinical Nutrition*, **32**, 593–596.

Murray, S., C. Stem, B. Boudreau, and J. Goodall (2000). Intestinal parasites of baboons (*Papio cynocephalus anubis*) and chimpanzees *(Pan troglodytes*) in Gombe National Park. *Journal of Zoo and Wildlife Medicine*, **31**, 176–178.

Myers, B. J. and R. E. Kuntz (1965). A checklist of parasites reported for the baboon. *Primates*, **6**, 137–194.

Myers, B. J. and R. E. Kuntz (1967). Parasites of baboons taken by the Cambridge Mwanza Expedition (Tanzania, 1965). *East African Medical Journal*, **44**, 322–324.

Myers, B. J. and R. E. Kuntz (1968). Intestinal protozoa of the baboon *Papio doguera* Pucheran, 1856. *Journal of Protozoology*, **15**, 363–365.

Myers, N., R. A. Mittermeier, C. G. Mittermeier, G. A. B. da Fonseca, and J. Kent (2000). Biodiversity hotspots for conservation priorities. *Nature*, **403**, 853–858.

Ménard, N. and D. Vallet (1993). Dynamics of fission in a wild Barbary macaque group (*Macaca sylvanus*). *International Journal of Primatology*, **14**, 479–500.

Nadler, R. D. (1977). Sexual-behavior of captive orangutans. *Archives of Sexual Behavior*, **6**, 457–475.

Naiff, R. D., T. V. Barrett, M. F. Naiff, L. C. L. Ferreira, and J. R. Arias (1996). New records of *Histoplasma capsulatum* from wild animals in the Brazilian Amazon. *Review of Institute of Medicine Tropical Sao Paulo*, **38**, 273–277.

Nakamichi, M. and N. Koyama (1997). Social relationships among ring-tailed lemurs (*Lemur catta*) in two free-ranging troops at Berenty Reserve, Madagascar. *International Journal of Primatology*, **18**, 73–93.

Nakamichi, M., E. Kato, Y. Kojima, and N. Itoigawa (1998). Carrying and washing of grass roots by free-ranging Japanese macaques at Katsuyama. *Folia Primatologia*, **69**, 35–40.

Naug, D. and S. Camazine (2002). The role of colony organization on pathogen transmission in social insects. *Journal of Theoretical Biology*, **215**, 427–439.

Nei, M. and A. L. Hughes (1991). Polymorphism and evolution of the major histocompatibility compex loci in mammals. In *Evolution at the Molecular Level* (eds. R. K. Selander, A. Clark, and S. Thomas), pp. 222–247. Sinauer, Sunderland, MA.

Nelson, G. S. (1960). Schistosome infections as zoonoses in Africa. *Transactions of the Royal Society of Tropical Medicine and Hygeine*, **54**, 301–314.

Nelson, G. S. (1965). The parasitic helminths of baboons with particular reference to species transmissible to man. In *The Baboon in Medical Research. Proceedings of the First International Symposium on the Baboon and its Use as an Experimental Animal* (ed. H. Vagtborg), pp. 441–447. University of Texas Press, Austin, TX.

Nelson, G. S., F. R. N. Pester, and R. Rickman (1965). The significance of wild animals in the transmission of cestodes of medical importance in Kenya. *Transactions of the Royal Society of Tropical Medicine and Hygeine*, **59**, 507–524.

Nelson, R. J. (2004). Seasonal immune function and sickness responses. *Trends in Immunology*, **25**, 187–192.

Nelson, R. J., G. E. Demas, S. L. Klein, and L. J. Kriegsfeld (2002). *Seasonal Patterns of Stress, Immune Function, and Disease*. Cambridge University Press, New York.

Nerrienet, E., X. Amouretti, M. C. Muller-Trutwin, V. Poaty-Mavoungou, I. Bedjebaga, H. T. Nguyen, G. Dubreuil et al. (1998). Phylogenetic analysis of SIV and STLV type I in mandrills (*Mandrillus sphinx*): indications that intracolony transmissions are predominantly the result of male-to-male aggressive contacts. *AIDS Research and Human Retroviruses*, **14**, 785–796.

Nerrienet, E., M. L. Santiago, Y. Foupouapouognigni, E. Bailes, N. I. Mundy, B. Njinku, A. Kfutwah et al. (2005). Simian immunodeficiency virus infection in wild-caught chimpanzees from cameroon. *Journal of Virology*, **79**, 1312–1319.

Nesse, R. M. and G. C. Williams (1996). *Why We Get Sick*. Vintage Books, New York.

Newey, S. and S. Thirgood (2004). Parasite-mediated reduction in fecundity of mountain hares. *Biology Letters*, **6**, S413–S415.

Newman, M. E. J. (2002). Mixing patterns in networks: empirical results and models. *Physical Review E*, **67**, DOI:10.1103/Phys-RevE.1166.016128.

Newton, P. (1991). The use of medicinal-plants by primates—a missing link. *Trends in Ecology and Evolution*, **6**, 297–299.

Newton, P. N. and T. Nishida (1990). Possible buccal administration of herbal drugs by wild chimpanzees, *Pan troglodytes*. *Animal Behaviour*, **39**, 798–801.

Nieberding, C., S. Morand, R. Libois, and J. Michaux (2004). A parasite reveals cryptic phylogeographic history of its host. *Proceedings of the Royal Society B*: *Biological Sciences,* **27**, 2559–2568.

Nishi, J. S., B. T. Elkin, and T. R. Ellsworth (2002). The Hook Lake Wood Bison Recovery Project—can a disease-free captive wood bison herd be recovered from a wild population infected with bovine tuberculosis and brucellosis? *Annals of the New York Academy of Sciences*, **969**, 229–235.

Nishida, T. and M. Hiraiwa-Hasegawa (1987). Chimpanzees and bonobos: cooperative relationships among males. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Stuhsaker). University of Chicago Press, Chicago, IL.

Nizeyi, J. B., R. Mwebe, A. Nanteza, M. R. Cranfield, G. R. N. N. Kalema, and T. K. Graczyk (1999). *Cryptosporidium sp* and *Giardia sp* infections in mountain gorillas (*Gorilla gorilla beringei*) of the Bwindi Impenetrable National Park, Uganda. *Journal of Parasitology*, **85**, 1084–1088.

Nizeyi, J. B., R. B. Innocent, J. Erume, G. R. N. N. Kalema, M. R. Cranfield, and T. K. Graczyk (2001). Campylobacteriosis, salmonellosis, and shigellosis in free-ranging human-habituated mountain gorillas of Uganda. *Journal of Wildlife Diseases*, **37**, 239–244.

Nordling, D., M. Andersson, S. Zohari, and L. Gustafsson (1998). Reproductive effort reduces specific immune response and parasite resistance. *Proceedings of the Royal Society B*: *Biological Sciences,* **265**, 1291–1298.

Norley, S., B. Beer, S. Holzammer, J. zur Megede, and R. Kurth (1999). Why are the natural hosts of SIV resistant to AIDS? *Immunology Letters*, **66**, 47–52.

Norris, K. and M. R. Evans (2000). Ecological immunology: life history trade-offs and immune defense in birds. *Behavioral Ecology*, **11**, 19–26.

Nunn, C. L. (1999). The number of males in primate social groups: a comparative test of the socioecological model. *Behavioral Ecology and Sociobiology*, **46**, 1–13.

Nunn, C. L. (2002a). A comparative study of leukocyte counts and disease risk in primates. *Evolution*, **56**, 177–190.

Nunn, C. L. (2002b). Spleen size, disease risk and sexual selection: a comparative study in primates. *Evolutionary Ecology Research*, **4**, 91–107.

Nunn, C. L. (2003). Behavioural defences against sexually transmitted diseases in primates. *Animal Behaviour*, **66**, 37–48.

Nunn, C. L. and S. Altizer (2004). Sexual selection, behaviour and sexually transmitted diseases. In *Sexual Selection in Primates: New and Comparative Perspectives* (eds. P. M. Kappeler, and C. P. van Schaik), pp. 117–130. Cambridge University Press, Cambridge.

Nunn, C. L. and S. Altizer (2005). The Global Mammal Parasite Database: an online resource for infectious disease records in wild primates. *Evolutionary Anthroplogy*, **14**, 1–2.

Nunn, C. L. and R. A. Barton (2000). Allometric slopes and independent contrasts: a comparative test of Kleiber's law in primate ranging patterns. *American Naturalist*, **156**, 519–533.

Nunn, C. L. and R. A. Barton (2001). Comparative methods for studying primate adaptation and allometry. *Evolutionary Anthroplogy*, **10**, 81–98.

Nunn, C. L. and A. T. W. Dokey. (in review). Territoriality and parasitism in primates. *Biology Letters*.

Nunn, C. L. and E. W. Heymann (2005). Malaria infection and host behaviour: a comparative study of Neotropical primates. *Behavioral Ecology and Sociobiology*, **59**, 30–37.

Nunn, C. L. and C. P. van Schaik (2000). Intersexual conflict and ecological factors in primate social evolution. In *Infanticide by Males and Its Implications* (eds. C. P. van Schaik, and C. Janson). Cambridge University Press, Cambridge.

Nunn, C. L. and C. P. van Schaik (2001). Reconstructing the behavioral ecology of extinct primates. In *Reconstructing Behavior in the Fossil Record* (eds. J. M. Plavcan, R. F. Kay, W. L. Jungers, and C. P. van Schaik), pp. 159–216. Kluwer Academic/ Plenum, New York.

Nunn, C. L., J. L. Gittleman, and J. Antonovics (2000). Promiscuity and the primate immune system. *Science*, **290**, 1168–1170.

Nunn, C. L., C. P. van Schaik and D. Zinner (2001). Do exaggerated sexual swellings function in female mating competition in primates? A comparative test of the reliable indicator hypothesis. *Behavioral Ecology*, **12**, 646–654.

Nunn, C. L., S. Altizer, K. E. Jones, and W. Sechrest (2003a). Comparative tests of parasite species richness in primates. *American Naturalist*, **162**, 597–614.

Nunn, C. L., J. L. Gittleman, and J. Antonovics (2003b). A comparative study of white blood cell counts and disease risk in carnivores. *Proceedings of the Royal Society B*: *Biological Sciences,* **270**, 347–356.

Nunn, C. L., S. Altizer, W. Sechrest, K. E. Jones, R. A. Barton, and J. L. Gittleman (2004). Parasites and the evolutionary diversification of primate clades. *American Naturalist*, **164**, S90–S103.

Nunn, C. L., S. M. Altizer, W. Sechrest, and A. Cunningham (2005). Latitudinal gradients of disease risk in primates. *Diversity and Distributions*, **11**, 249–256.

Nunn, C. L., P. H. Thrall, A. H. Harcourt, and K. Stewart (in review a.). Emerging infectious diseases and animal mating and social systems. *Evolutionary Ecology.*

Nunn, C. L., B. M. Rothschild, and J. L. Gittleman (in review b.). Arthritis increases with body size in mammals.

Nurnberg, P., U. Sauermann, M. Kayser, C. Lanfer, E. Manz, A. Widdig, J. Berard et al. (1998). Paternity assessment in rhesus macaques (*Macaca mulatta*): multilocus DNA fingerprinting and PCR marker typing. *American Journal of Primatology*, **44**, 1–18.

Nygard, K., Y. Andersson, J. A. Rottingen, A. Svensson, J. Lindback, T. Kistemann, and J. Giesecke (2004). Association between environmental risk factors and campylobacter infections in Sweden. *Epidemiology and Infection*, **13**, 317–325.

O'Brien, S. and J. Evermann (1988). Interactive influence of infectious disease and genetic diversity in natural populations. *Trends in Ecology and Evolution*, **3**, 254–259.

O'Brien, S. J., M. E. Roelke, L. Marker, A. Newman, C. A. Winkler, D. Meltzer, L. Colly et al. (1985). Genetic-basis for species vulnerability in the cheetah. *Science*, **227**, 1428–1434.

O'Keefe, K. J. and J. Antonovics (2002). Playing by different rules: the evolution of virulence in sterilizing pathogens. *American Naturalist*, **159**, 597–605.

O'Leary, H. and J. E. Fa (1993). Effects of tourists on Barbary macaques at Gibraltar. *Folia Primatologica*, **61**, 77–91.

O'Lorcain, P. and C. V. Holland (2000). The public health importance of *Acaris lumbricoides*. *Parasitology*, **121**, S51–S71.

O'Sullivan, B. M. and A. D. Donald (1970). A field study of nematode parasite populations in the lactating ewe. *Parasitology*, **61**, 301–315.

Oates, J. F. (1978). Water, plant and soil consumption by guereza monkeys (*Colobus* guereza)—relationship with minerals and toxins in the diet. *Biotropica*, **10**, 241–253.

Ohsawa, H. (1979). The local gelada population and environment of the Gich area. In *Ecological and Sociological Studies of Gelada Baboons* (ed. M. Kawai), pp. 4–45. Karger, Basel.

Ohsawa, H. and R. I. M. Dunbar (1984). Variations in the demographic structure and dynamics of gelada baboon populations. *Behavioral Ecology and Sociobiology*, **15**, 231–240.

Oldstone, M. (1998). *Viruses, Plagues and History*. Oxford University Press, New York.

Olson, M. E. and A. G. Buret (2001). Giardia and giardiasis. In *Parasitic Diseases of Wild Mammals* (eds. W. M. Samuel, M. J. Pybus, and A. A. Kocan), pp. 399–416. Iowa State University Press, Ames, IA.

Olupot, W., C. A. Chapman, P. M. Waser, and G. Isabirye-Basuta (1997). Mangabey (*Cercocebus albigena*) ranging patterns in relation to fruit availability and the risk of parasite infection in Kibale National Park, Uganda. *American Journal of Primatology*, **43**, 65–78.

Oriel, J. D. and A. H. S. Hayward (1974). Sexually transmitted diseases in animals. *British Journal of Veterinary diseases*, **50**, 412–420.

Orihel, T. C. and H. R. Seibold (1972). Nematodes of the bowel and tissues. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 76–103. S. Karger, London.

Ostfeld, R. S., G. E. Glass, and F. Keesing (2005). Spatial epidemiology: an emerging (or reemerging) discipline. *Trends in Ecology and Evolution*, **20**, 328–336.

Ostrow, R. S., R. C. McGlennen, M. K. Shaver, B. E. Kloster, and D. Houser (1990). A rhesus monkey model for sexual transmission of a papillomavirus isolated from a squamous cell carcinoma. *Proceedings of the National Academy of Sciences USA*, **87**, 8170–8174.

Overdorff, D. J. (1993). Similarities, differences, and seasonal patterns in the diets of *Eulemur rubriventer* and *Eulemur fulvus rufus* in the Ranomafana National Park, Madagascar. *International Journal of Primatology*, **14**, 721–753.

Pacala, S. W. and A. P. Dobson (1988). The relation between the number of parasites/host and host age: population-dynamic causes and maximum-likelihood estimation. *Parasitology*, **96**, 197–210.

Packer, C., S. Altizer, M. Appel, E. Brown, J. Martenson, S. J. O'Brien, M. Roelke-Parker et al. (1999). Viruses of the Serengeti: patterns of infection and mortality in African lions. *Journal of Animal Ecology*, **68**, 1161–1178.

Padgett, D. and R. Glaser (2003). How stress influences the immune response. *Trends in Immunology*, **24**, 444 – 448.

Padgett, D., R. MacCallum, and S. JF. (1998a). Stress exacerbates age-related decrements in the immune response to an experimental influenza viral infection. *Journal of Gerontology Series A: Biological Sciences and Medical Science*, **53**, B347–B353.

Padgett, D., J. Sheridan, J. Dorne, G. Berntson, J. Candelora, and R. Glaser (1998b). Social stress and the reactivation of latent herpes simplex virus type 1. *Proceedings of the National Academy Sciences USA*, **95**, 7231–7235.

Page, J. E., M. A. Huffman, V. Smith, and G. H. N. Towers (1997). Chemical basis for *Aspilia* leaf-swallowing by chimpanzees: A reanalysis. *Journal Of Chemical Ecology*, **23**, 2211–2226.

Page, L. K., R. K. Swihart, and K. R. Kazacos (1999). Implications of raccoon latrines in the epizootiology of Baylisascariasis. *Journal of Wildlife Diseases*, **35**, 474–480.

Page, R. D. M. (2003a). Introduction. In *Tangled Trees: Phylogenies, Cospeciation and Coevolution* (ed. R. D. M. Page), pp. 1–21. University of Chicago Press, Chicago, IL.

Page, R. D. M. (2003b). *Tangled Trees: Phylogenies, Cospeciation and Coevolution*. University of Chicago Press, Chicago, IL.

Page, R. D. M. and M. A. Charleston (1998). Trees within trees: phylogeny and historical associations. *Trends in Ecology and Evolution*, **13**, 356–359.

Page, R. D. M. and E. C. Holmes (1998). *Molecular Evolution: A Phylogenetic Approach*. Blackwell Science, Oxford.

Pagel, M. (1994a). Detecting correlated evolution on phylogenies: a general method for the comparative analysis of discrete characters. *Proceedings of the Royal Society B*: *Biological Sciences,* **255**, 37–45.

Pagel, M. (1994b). The evolution of conspicuous oestrous advertisement in Old World monkeys. *Animal Behaviour*, **47**, 1333–1341.

Pagel, M. and W. Bodmer (2003). A naked ape would have fewer parasites. *Proceedings of the Royal Society B*: *Biological Sciences,* **270** (Suppl. 1), S117–S119.

Palombit, R. A. (1992). *Pair bonds and monogamy in wild siamang* (Hylobates syndactylus) *and white-handed gibbon* (Hylobates lar) *in northern Sumatra*. Ph.D. thesis, University of California, Davis, California.

Palombit, R. A. (1994). Extra-pair copulations in a monogamous ape. *Animal Behaviour*, **47**, 721–723.

Palombit, R. A. (2000). Infanticide and the evolution of male-female bonds in animals. In *Infanticide by Males and Its Implications* (eds. C. van Schaik, and C. Janson), pp. 239–268. Cambridge University Press, Cambridge.

Palombit, R. A., R. M. Seyfarth, and D. L. Cheney (1997). The adaptive value of "friendships" to female baboons: experimental and observational evidence. *Animal Behaviour*, **54**, 599–614.

Pålsson, K., T. G. T. Jaenson, F. Dias, T. Laugen, and A. Bjorkman (2004). Endophilic *Anopheles* mosquitoes in Guinea Bissau, West Africa, in relation to human housing conditions. *Journal of Medical Entomology*, **41**, 746–752.

Palumbi, S. R. (2001). *The Evolution Explosion: How Humans Cause Rapid Evolutionary Change*. Norton, New York.

Pandya, I. J. and J. Cohen (1985). The leukocytic reaction of the human uterine cervix to spermatozoa. *Fertility and Sterility*, **43**, 417–421.

Panhuis, T. M., R. Butlin, M. Zuk, and T. Tregenza (2001). Sexual selection and speciation. *Trends in Ecology and Evolution*, **16**, 364–371.

Parham, P. (2005). *The Immune System*. Garland Publishing, New York.

Parham, P. and T. Ohta (1996). Population biology of antigen presentation by MHC class I molecules. *Science*, **272**, 67–74.

Park, A. W., S. Gubbins, and C. A. Gilligan (2002). Extinction times for closed epidemics: the effects of host spatial structure. *Ecology Letters*, **5**, 747–755.

Parrish, S. W. K., A. E. Brown, P. Chanbancherd, M. Gettayacamin, and J. H. Parrish (2004). Transmission of STLV in a closed colony of macaques. *American Journal of Primatology*, **63**, 103–109.

Pascual, M., M. J. Bouma, and A. Dobson (2002). Cholera and climate: revisiting the quantitative evidence. *Microbes and Infection*, **4**, 237–245.

Paterson, S., K. Wilson, and J. M. Pemberton (1998). Major histocompatibility complex (MHC) variation associated with juvenile survival and parasite resistance in a large ungulate population (*Ovis aries* L.). *Proceedings of the National Academy of Sciences USA*, **95**, 3714–3719.

Patterson, B. D., J. W. O. Ballard, and R. L. Wenzel (1998). Distributional evidence for cospeciation between neotropical bats and their bat fly ectoparasites. *Studies on Neotropical Fauna and Environment*, **33**, 76–84.

Patz, J. A. (2002). A human disease indicator for the effects of recent global climate change. *Proceedings of the National Academy of Sciences USA*, **99**, 12506–12508.

Patz, J. A., T. K. Graczyk, N. Geller, and A. Y. Vittor (2000). Effects of environmental change on emerging parasitic diseases. *International Journal for Parasitology*, **30**, 1395–1405.

Paul, A. (2002). Sexual selection and mate choice. *International Journal of Primatology*, **23**, 877–904.

Paul, A. and J. Kuester (1988). Life-history patterns of Barbary macaques (*Macaca sylvanus*) at Affenberg Salem. In *Ecology and Behavior of Food-Enhanced Primate Groups* (eds. J. E. Fa, and C. H. Southwick), pp. 199–228. Alan R. Liss, Inc., New York.

Pedersen, A., M. Poss, C. L. Nunn, C. A. and S. Altizer (2005). Patterns of host specificity and transmission among parasites of free-living primates. *International Journal for Parasitology*, 35, 647–657.

Peeters, M. (2004). Cross-species transmissions of simian retroviruses in Africa and risk for human health. *Lancet*, **363**, 911–912.

Peeters, M., V. Courgnaud, B. Abela, P. Auzel, X. Pourrut, F. Bibollet-Ruche, S. Loul et al. (2002). Risk to human health from a plethora of simian immunodeficiency viruses in primate bushmeat. *Emerging Infectious Diseases*, **8**, 451–457.

Penn, D. and W. K. Potts (1998). Chemical signals and parasite-mediated sexual selection. *Trends in Ecology and Evolution*, **13**, 391–396.

Penn, D., G. Schneider, K. White, P. Slev, and W. Potts (1998). Influenza infection neutralizes the attractiveness of male odour to female mice (*Mus musculus*). *Ethology*, **104**, 685–694.

Penn, D. J., K. Damjanovich, and W. K. Potts (2002). MHC heterozygosity confers a selective advantage against multiple-strain infections. *Proceedings of the National Academy of Sciences USA*, **99**, 11260–11264.

Percy, D., R. Page, and Q. Cronk (2004). Plant-insect interactions: double-dating associated insect and plant lineages reveals asynchronous radiations. *Systematic Biology*, **53**, 120–127.

Pereira, M. E. and M. L. Weiss (1991). Female mate choice, male migration, and the threat of infanticide in ringtailed lemurs. *Behavioral Ecology and Sociobiology*, **28**, 141–152.

Peres, C. (1990a). Effects of hunting on western Amazonian primate communities. *Biological Conservation*, **54**, 47–59.

Peres, C. (1990b). A harpy eagle successfully captures an adult male red howler monkey. *Wilson Bulletin*, **102**, 560–561.

Peres, C. (2000). Effects of subsistence hunting on vertebrate community structure in Amazonian forests. *Conservation Biology*, **14**, 240–253.

Perkins, S. E., I. M. Cattadori, V. Tagliapietra, A. Rizzoli, and P. J. Hudson (2003a). Empirical evidence for key hosts in persistence of a tick-borne disease. *International Journal for Parasitology*, **33**, 909–917.

Perkins, S. E., I. M. Cattadori, V. Tagliapietra, A. P. Rizzoli, and P. J. Hudson (2003b). Empirical evidence for key hosts in persistence of a tick-borne disease. *International Journal for Parasitology*, **33**, 909–917.

Perlman, S. J. and J. Jaenike (2003). Infection success in novel hosts: an experimental and phylogenetic study of *Drosophila*-parasitic nematodes. *Evolution*, **57**, 544–557.

Perry, J. M., M. K. Izard, and P. A. Fail (1992). Observations on reproduction, hormones, copulatory behavior, and neonatal mortality in captive *Lemur mongoz* (mongoose lemur). *Zoo Biology*, **11**, 81–97.

Peterson, D. and K. Ammann (2003). *Eating Apes*. University of California Press, Berkeley, CA.

Pettifer, H. L. (1984). The helminth fauna of the digestive tracts of chacma baboons, *Papio ursinus*, from different localities in the Transvaal. *Onderstepoort Journal of Veterinary Research*, **51**, 161–170.

Pfenning, D. W. (2000). Effect of predator-prey phylogenetic similarity on the fitness consequences of predation: a trade-off between nutrition and disease? *American Naturalist*, **155**, 335–345.

Phillips, D. M. and S. Mahler (1977). Phagocytosis of spermatozoa by the rabbit vagina. *Anatomical Record*, **189**, 61–72.

Phillips, R. (2002). Immunology taught by Darwin. *Nature Immunology*, **3**, 987–989.

Phillips-Conroy, J., C. J. Jolly, P. Nystrom, and H. A. Hemmalin (1992). Migration of male hamadryas baboons into anubis groups in the Awash National Park, Ethiopia. *International Journal of Primatology*, **13**, 455–476.

Phillips-Conroy, J. E. (1986). Baboons, diet and disease: food plant selection and schistosomiasis. In *Current Perspectives in Primate Social Dynamics* (eds. D. M. Taub, and F. A. King), pp. 287–304. Van Nostrand Reinhold, New York.

Phillips-Conroy, J. E. and P. M. Knopf (1986). The effects of ingesting plant hormones on schistosomiasis in mice—an experimental-study. *Biochemical Systematics and Ecology*, **14**, 637–645.

Phillips-Conroy, J. E. and C. J. Jolly (1999). Collaboration between field primatologists and biomedical researchers. *Laboratory Primate Newsletter*, **38**, 10.

Phillips-Conroy, J. E. C. F. Hildebolt, J. Altmann, C. J. Jolly, and P. Muruthi (1993). Periodontal health in free-ranging baboons of Ethiopia and Kenya. *American Journal of Physical Anthropology*, **90**, 359–371.

Phillips-Conroy, J. E., C. J. Jolly, B. Petros, J. S. Allan, and R. C. Desrosiers (1994). Sexual transmission of SIV(Agm) in wild grivet monkeys. *Journal of Medical Primatology*, **23**, 1–7.

Pickering, J. and C. A. Norris (1996). New evidence concerning the extinction of the endemic murid *Rattus macleari* from Christmas Island, Indian Ocean. *Australian Mammalogy*, **19**, 19–25.

Pie, M. R., R. B. Rosengaus, and J. F. Traniello (2004). Nest architecture, activity pattern, worker density and the dynamics of disease transmission in social insects. *Journal of Theoretical Biology*, **226**, 45–51.

Pinzon, J., J. Wilson, C. Tucker, R. Arthur, P. Jahrling, and P. Formenty (2004). Trigger events: enviroclimatic coupling of ebola hemorrhagic fever outbreaks. *American Journal of Tropical Medicine and Hygiene*, **71**, 664–674.

Pitchford, R. J. and P. S. Visser (1975). Excretion of *Schistosoma mattheei* eggs from man, baboons and cattle living in their normal environment. *Journal of Helminthology*, **49**, 137–142.

Pontier, D., E. Fromont, F. Courchamp, M. Artois, and N. G. Yoccoz (1998). Retroviruses and sexual size dimorphism in domestic cats (*Felis catus* L.). *Proceedings of the Royal Society B*: *Biological Sciences,* **265**, 167–173.

Pope, T. R. (1998). Effects of demographic change on group kin structure and gene dynamics of populations of red howling monkeys. *Journal of Mammalogy*, **79**, 692–712.

Port, G. R., P. F. L. Boreham, and J. H. Bryan (1980). The relationship of host size to feeding by mosquitos of the *Anopheles gambiae* Giles Complex (Diptera, Culicidae). *Bulletin of Entomological Research*, **70**, 133–144.

Potkay, S. (1992). Diseases of the callitrichidae—a review. *Journal of Medical Primatology*, **21**, 189–236.

Potts, W. K., C. J. Manning, and E. K. Wakeland (1994). The role of infectious disease, inbreeding and mating preferences in maintaining MHC genetic diversity: an experimental test. *Philosophical Transactions of the Royal Society B: Biological Sciences,* **346**, 369–378.

Poulin, R. (1992). Determinants of host-specificity in parasites of freshwater fishes. *International Journal for Parasitology*, **22**, 753–758.

Poulin, R. (1994). The evolution of parasite manipulation of host behavior—a theoretical-analysis. *Parasitology*, **109**, S109–S118.

Poulin, R. (1995). Phylogeny, ecology, and the richness of parasite communities in vertebrates. *Ecological Monographs*, **65**, 283–302.

Poulin, R. (1998a). *Evolutionary Ecology of Parasites*. Chapman and Hall, New York.

Poulin, R. and S. Morand (2000). The diversity of parasites. *Quarterly Review of Biology*, **75**, 277–293.

Poulin, R. and S. Morand (2004). *Parasite Biodiversity*. Smithsonian Institution Press, Washington, DC.

Poulin, R., J. Brodeur, and J. Moore (1994). Parasite manipulation of host behaviour: should hosts always lose? *Oikos*, **70**, 479–484.

Poulin, R. A. (1998b). *Evolutionary Ecology of Parasites*. Chapman and Hall, London.

Powell, M. L. and D. C. Cook. 2005. *The Myth of Syphilis: The Natural History of Treponematosis in North America*, pp. 532. Gainesville, University Press of Florida.

Power, A. G. and C. E. Mitchell (2004). Pathogen spillover in disease epidemics. *American Naturalist*, **164**, S79–S89.

Prescott, L., J. Harley, and D. Klein (2001). *Microbiology*. McGraw-Hill.

Preston, R. (1995). *The Hot Zone: A Terrifying True Story*. Anchor Books, New York.

Price, P. W. (1980). *Evolutionary Biology of Parasites*. Princeton University Press, Princeton, NJ.

Price, P. W. and K. M. Clancy (1983). Patterns in number of helminth parasite species in freshwater fishes. *Journal of Parasitology*, **69**, 449–454.

Price, T., D. Schluter, and N. E. Heckman (1993). Sexual selection when the female directly benefits. *Biological Journal of the Linnean Society*, **48**, 187–211.

Prier, J. E., R. M. Sauer, and H. C. Fegley (1964). Zoonoses associated with captive monkeys. *Laboratory Animal Care*, **14**, 48–57.

Printes, R. C. and K. B. Strier (1999). Behavioral correlates of dispersal in female muriquis (*Brachyteles arachnoides*). *International Journal of Primatology*, **20**, 941–960.

Pryor, W. H., J. Bergner, J. F., and G. L. Raulston (1970). Leech (*Dinobdella ferox*) infection of a Taiwan monkey (*Macaca cyclopis*). *Journal of the American Veterinary Medical Association*, **157**, 1926–1927.

Pullen, S. L., S. K. Bearder, and A. F. Dixson (2000). Preliminary observations on sexual behavior and the mating system in free-ranging lesser galagos (*Galago moholi*). *American Journal of Primatology*, **51**, 79–88.

Purvis, A. (1995). A composite estimate of primate phylogeny. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **348**, 405–421.

Purvis, A., P. M. Agapow, J. L. Gittleman, and G. M. Mace (2000). Nonrandom extinction and the loss of evolutionary history. *Science*, **288**, 328–330.

Pusey, A. E. (1992). The primate perspective on dispersal. In *Animal Dispersal: Small Mammals as a Model* (eds. N. C. Stenseth and W. Z. Lidicker), pp. 243–257. Chapman and Hall, London.

Pusey, A. E. and C. Packer (1987). Dispersal and philopatry. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Struhsaker), pp. 250–266. University of Chicago Press, Chicago, IL.

Pybus, M. J. (2001). Liver flukes. In *Parasitic Diseases of Wild Mammals* (eds. W. M. Samuel, M. J. Pybus, and A. A. Kocan), pp. 121–149. Iowa State University Press, Ames, IA.

Pybus, O. G., M. A. Charleston, S. Gupta, A. Rambaut, E. C. Holmes, and P. H. Harvey (2001). The epidemic behavior of the hepatitis C virus. *Science*, **292**, 2323–2325.

Raibaut, A., C. Combes, and F. Benoit (1998). Analysis of the parasitic copepod species richness among Mediterranean fish. *Journal of Marine Systems*, **15**, 185–206.

Ralley, W. E., T. D. Galloway, and G. H. Crow (1993). Individual and group-behavior of pastured cattle in response to attack by biting flies. *Canadian Journal of Zoology*, **71**, 725–734.

Rand, D. A., M. J. Keeling, and W. G. Wilson (1995). Invasion, stability and evolution to criticality in spatially extended artificial host-pathogen ecologies. *Proceedings of the Royal Society B*: *Biological Sciences,* **259**, 55–63.

Ransom, T. W. (1981). *Beach Troop of the Gombe*. Bucknell University Press, Lewisburg, PA.

Rasa, O. A. E. (1983). A case of invalid care in wild dwarf mongooses. *Zeitschrift fur Tierpsychologie*, **62**, 235–240.

Rau, M. E. (1983). Establishment and maintenance of behavioral dominance in male mice infected with *Trichinella spiralis*. *Parasitology*, **86**, 319–322.

Rea, J. G. and S. W. B. Irwin (1994). The ecology of host-finding behaviour and parasite transmission: past and future perspectives. *Parasitology*, 109 (Supp.), S31–S39.

Read, A. F. (1990). Parasites and the evolution of host sexual behaviour. In *Parasitism and Host Behaviour* (eds. C. J. Barnard and J. M. Behnke), pp. 117–157. Taylor and Francis, London.

Read, A. F. and J. E. Allen (2000). The economics of immunity. *Science*, **290**, 1104–1105.

Read, A. F., M. J. Mackinnon, M. A. Anwar, and L. H. Taylor (2002). Kin selection models as evolutionary explanations of malaria. In *Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management* (ed. U. Dieckmann, Metz, J.A.J., Sabelis, M.A., Sigmund, K.), pp. 140–153. Cambridge University Press, Cambridge.

Read, A. F. and L. H. Taylor (2001). The ecology of genetically diverse infections. *Science*, **292**, 1099–1102.

Read, J. M. and M. J. Keeling (2003). Disease evolution on networks: the role of contact structure. *Proceedings of the Royal Society B*: *Biological Sciences,* **270**, 699–708.

Reeder, M. M. and P. E. S. Palmer (2001). *The Imaging of Tropical Diseases*. Springer-Verlag, New York.

Regan, G. (1998). *The Evolution of Pelage Colouration in Primates*. Ph.D. thesis, University of Durham, Durham, UK.

Reichard, U. (1995). Extra-pair copulation in a monogamous gibbon (*Hylobates lar*). *Ethology*, **100**, 99–112.

Reichard, U. and V. Sommer (1994). Grooming site preferences in wild white-handed gibbons (*Hylobates lar*). *Primates*, **35**, 369–374.

Reichert, K. E., M. Heistermann, J. K. Hodges, C. Boesch, and G. Hohmann (2002). What females tell males about their reproductive status: are morphological and behavioural cues reliable signals of ovulation in bonobos (*Pan paniscus*)? *Ethology*, **108**, 583–600.

Rey-Cuille, M. A., J. L. Berthier, M. C. Bomsel-Demontoy, Y. Chaduc, L. Montagnier, A. G. Hovanessian, and L. A. Chakrabarti (1998). Simian immunodeficiency virus replicates to high levels in sooty mangabeys without inducing disease. *Journal of Virology*, **72**, 3872–3886.

Reynolds, S. J., M. E. Shepherd, A. R. Risbud, R. R. Gangakhedkar, R. S. Brookmeyer, A. D. Divekar, S. M. Mehendale, et al. (2004). Male circumcision and risk of HIV-1 and other sexually transmitted infections in India. *Lancet*, **363**, 1039–1040.

Rhodes, R. (1997). *Deadly Feasts: Tracking the Secrets of a Terrifying New Plague*. Simon and Schuster, New York.

Rice, P. A. and H. H. Handsfield (1999). Arthritis associated with sexually transmitted diseases. In *Sexually Transmitted Diseases* (eds. K. K. Holmes, P. F. Sparling, P.-A. Mardh, S. M. Lemon, W. E. Stamm, P. Piot, and J. N. Wasserheit), pp. 921–935. McGraw-Hill, New York.

Richard, A. (1970). A comparative study of the activity patterns and behavior of *Alouatta villosa* and *Ateles geoffroyi*. *Folia Primatologia*, **12**, 241–263.

Richard, A. F., S. J. Goldstein, and R. E. Dewar (1989). Weed macaques—the evolutionary implications of macaque feeding ecology. *International Journal of Primatology*, **10**, 569–597.

Ridley, M. (1996). *Evolution*. Blackwell Science, Cambridge, MA.

Ritchie, B. G. and D. M. Fragaszy (1988). Capuchin monkey (*Cebus apella*) grooms her infants wound with tools. *American Journal of Primatology*, **16**, 345–348.

Ritter, R. C. and A. N. Epstein (1974). Saliva lost by grooming: a major item in the rat's water economy. *Behavioral Biology*, **11**, 581–585.

Roberts, C. (2005). Genital herpes in young adults: changing sexual behaviours, epidemiology and management. *Herpes*, **12**, 10–14.

Roberts, L. and J. Janovy (1999). *Foundations of Parasitology*. McGraw-Hill, Boston.

Roberts, M. G., A. P. Dobson, P. Arneberg, G. A. de Leo, R. C. Krecek, M. T. Manfredi, P. Lanfranchi et al. (2002). Parasite community ecology and biodiversity. In *The Ecology of Wildlife Diseases* (eds. P. J. Hudson, A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. Dobson), pp. 63–82. Oxford University Press, Oxford.

Roberts, M. L., K. L. Buchanan, and M. R. Evans (2004). Testing the immunocompetence handicap hypothesis: a review of the evidence. *Animal Behaviour*, **68**, 227–239.

Roberts, S. C., A. C. Little, L. Morris Gosling, D. I. Perrent, V. Carter, B. C. Jones, I. Penton-Voak et al. (2005). MHC heterozygosity and human facial attractiveness. *Evolution and Human Behavior*, **26**, 213–226.

Robertson, S., B. Hull, O. Tomori, O. Bele, J. LeDuc, and K. Esteves (1996). Yellow fever: a decade of reemergence. *JAMA*, **276**, 1157–1162.

Robinson, J., M. J. Waller, P. Parham, N. G. de Groot, R. E. Bontrop, L. J. Kennedy, P. Stoehr et al. (2003). IMGT/HLA and IMGT/MHC: sequence databases for the study of the major histocompatibility complex. *Nucleic Acids Research*, **31**, 311–314.

Rode, K. D., C. A. Chapman, L. J. Chapman, and L. R. McDowell (2003). Mineral resource availability and consumption by *Colobus* in Kibale National Park, Uganda. *International Journal of Primatology*, **24**, 541–573.

Roelke-Parker, M. E., L. Munson, C. Packer, R. Kock, S. Cleaveland, M. Carpenter, S. J. OBrien et al. (1996). A canine distemper virus epidemic in Serengeti lions (*Panthera leo*). *Nature*, **379**, 441–445.

Rogers, D. J. and S. E. Randolph (2003). Studying the global distribution of infectious diseases using GIS and RS. *Nature Reviews Microbiology*, **1**, 231–236.

Rogers, D. J. S. E. Randolph, R. W. Snow, and S. I. Hay (2002). Satellite imagery in the study and forecast of malaria. *Nature*, **415**, 710–715.

Rohani, P., D. J. Earn, and B. T. Grenfell (2000). Impact of immunisation on pertussis transmission in England and Wales. *Lancet*, **355**, 285.

Rohde, K. (1978). Latitudinal gradients in species diversity and their causes. I. A review of the hypotheses explaining the gradients. *Biologisches Zentralblatt*, **97**, 393–403.

Roitt, I. M., J. Brostoff, and D. K. Male (1998). *Immunology*. Gower Medical Publishing, London.

Rolland, R. M., G. Hausfater, B. Marshall, and S. B. Levy (1985). Antibiotic-resistant bacteria in wild primates—increased prevalence in baboons feeding on human refuse. *Applied and Environmental Microbiology*, **49**, 791–794.

Romero, L. M. (2004). Physiological stress in ecology: lessons from biomedical research. *Trends in Ecology and Evolution*, **19**, 249–255.

Rosenberg, C. E. (1962). *The Cholera Years: The United States in 1832, 1849 and 1866*. The University of Chicago Press, Chicago, IL.

Ross, C. and K. E. Jones (1999). Socioecology and the evolution of primate reproductive rates. In *Comparative Primate Socioecology* (ed. P. C. Lee), pp. 73–110. Cambridge University Press, Cambridge.

Ross, R. (1911). *The Prevention of Malaria*. Murray, London.

Rothman, J. and D. D. Bowman (2003). A review of the endoparasites of mountain gorillas. In *Companion and Exotic Animal Parasitology* (ed. D. D. Bowman). International Veterinary Information Service, Ithaca, NY.

Rothschild, B. (2005). History of syphilis. *Clinical Infectious Diseases*, **40**, 1454–1463.

Rothschild, B. M. and R. J. Woods (1989). Spondyloarthropathy in gorillas. *Seminars in Arthritis and Rheumatism*, **18**, 267–276.

Rothschild, B. M. and R. J. Woods (1991a). Reactive erosive arthritis in chimpanzees. *American Jounral of Primatology*, **25**, 49–56.

Rothschild, B. M. and R. J. Woods (1991b). Spondyloarthropathy: erosive arthritis in representative defleshed bones. *American Journal of Physical Anthropology*, **85**, 125–134.

Rothschild, B. M. and R. J. Woods (1992). Spondyloarthropathy as an Old World phenomenon. *Seminars in Arthritis and Rheumatism*, **21**, 306–316.

Rothschild, B. M. and R. J. Woods (1993). Arthritis in New World monkeys—osteoarthritis, calcium pyrophosphate deposition disease, and spondyloarthropathy. *International Journal of Primatology*, **14**, 61–78.

Rothschild, B. M. and R. J. Woods (1996). Inflammatory arthritis in *Pongo*. *Journal of Medical Primatology*, **25**, 414–418.

Rothschild, B. M., X. Wang, and R. Cifelli (1993). Spondyloarthropathy in Ursidae: a sexually-transmitted disease? *Research and Exploration*, **9**, 382–384.

Rouquet, P., J. M. Froment, M. Bermejo, A. Kilbourn, W. Karesh, P. Reed, B. Kumulungui et al. (2005). Wild animal mortality monitoring and human Ebola outbreaks, Gabon and Republic of Congo, 2001–2003. *Emerging Infectious Diseases*, **11**, 283–290.

Routman, E., R. D. Miller, J. Phillips-Conroy, and D. L. Hartl (1985). Antibiotic-resistance and population structure in *Escherichia coli* from free-ranging African yellow baboons. *Applied and Environmental Microbiology*, **50**, 749–754.

Rowell, T. E., C. Wilson, and M. Cords (1991). Reciprocity and partner preference in grooming of female blue monkeys. *International Journal of Primatology*, **12**, 319–336.

Roy, A. D. and H. M. Cameron (1972). *Rhinophycomycosis entomophthorae* occurring in a chimpanzee in the wild in East Africa. *The American Journal of Tropical Medicine and Hygiene*, **21**, 234–237.

Roy, B. A. (2001). Patterns of association between crucifers and their flower-mimic pathogens: host jumps are more common than coevolution or cospeciation. *Evolution*, **55**, 41–53.

Rubenstein, D. I. and M. E. Hohmann (1989). Parasites and social behavior of island feral horses. *Oikos*, **55**, 312–320.

Rudolf, V. H. W. and J. Antonovics (2005). Species coexistence and pathogens with frequency-dependent transmission. *American Naturalist*, **166**, 112–118.

Rudran, R. and E. Fernandez-Duque (2003). Demographic changes over thirty years in a red howler population in Venezuela. *International Journal of Primatology*, **24**, 925–947.

Rupprecht, C. E., T. J. Wiktor, D. J. Johnson, A. N. Hamir, B. Tietzschold, W. H. Wunner, L. T. Glickman et al. (1986). Oral immunization and protection of raccoons (*Procyon lotor*) with a vaccinia-rabies glycoprotein recombinant virus vaccine. *Proceedings of the National Academy of Sciences USA*, **83**, 7947–7950.

Rushton, S. P., P. W. W. Lurz, J. Gurnell, and R. Fuller (2000). Modelling the spatial dynamics of parapoxvirus disease in red and grey squirrels: a possible cause of the decline in the red squirrel in the UK? *Journal of Applied Ecology*, **37**, 997–1012.

Russell, C., D. Smith, L. Waller, and et al. (2004). *A priori* prediction of disease invasion dynamics in a novel environment. *Proceedings of the Royal Society B*: *Biological Sciences*, **1534**, 21–25.

Russell, C. A., D. L. Smith, J. E. Childs, and L. A. Real (2005). Predictive spatial dynamics and strategic planning for raccoon rabies emergence in Ohio. *PLoS Biology*, **3**, 382–388.

Rutberg, A. T. (1987). Horse fly harassment and the social-behavior of feral ponies. *Ethology*, **75**, 145–154.

Ryan, S. J. and S. D. Thompson (2001). Disease risk and inter-institutional transfer of specimens in cooperative breeding programs: herpes and the elephant species survival plans. *Zoo Biology*, **20**, 89–101.

Rylands, A. B. and A. Keuroghlian (1988). Primate populations in continuous forest and forest fragments in central Amazonia. *Acta Amazonica*, **18**, 291–307.

Saino, N., L. Canova, M. Fasola, and R. Martinelli (2000). Reproduction and population density affect humoral immunity in bank voles under field experimental conditions. *Oecologia*, **124**, 358–366.

Salman, M. D. (2003). *Animal Disease Surveillance and Survey Systems*. Iowa State Press, Ames, IA.

Samuel, W. M., M. J. Pybus, and A. A. Kocan (2001). *Parasitic Diseases of Wild Mammals*. Iowa State Press, Ames, IA.

Sanchez, A., T. G. Ksiazek, P. E. Rollin, C. J. Peters, S. T. Nichol, A. S. Khan, and B. W. J. Mahy (1995). Reemergence of Ebola virus in Africa. *Emerging Infectious Diseases*, **1**, 96–97.

Sanchez-Villagra, M. R., T. R. Pope, and V. Salas (1998). Relation of intergroup variation in allogrooming to group social structure and ectoparasite loads in red howlers (*Alouatta seniculus*). *International Journal of Primatology*, **19**, 473–491.

Santiago, M. L., C. M. Rodenburg, S. Kamenya, F. Bibollet-Ruche, F. Gao, E. Bailes, S. Meleth et al. (2002). SIVcpz in wild chimpanzees. *Science*, **295**, 465–465.

Sapolsky, R. M. (1994). Fallible instinct—a dose of skepticism about the medicinal knowledge of animals. *Sciences-New York*, **34**, 13–15.

Sapolsky, R. M. and J. G. Else (1987). Bovine tuberculosis in a wild baboon population—epidemiologic aspects. *Journal of Medical Primatology*, **16**, 229–235.

Sapolsky, R. M. and L. J. Share (1998). Darting terrestrial primates in the wild: a primer. *American Journal of Primatology*, **44**, 155–167.

Sapolsky, R. M. and L. J. Share (2004). A pacific culture among wild baboons: its emergence and transmission. *PLoS Biology*, **2**, 534–541.

Sapolsky, R. M., L. M. Romero, and A. U. Munck (2000). How do glucocorticoids infuence stress responses. Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrinology Review*, 21, 55–89.

Sapolsly, R. (2003). Bugs in the brain. *Scientific American*, **288**, 94–97.

Sato, K., H. Matsuda and A. Sasaki (1994). Pathogen invasion and host extinction in lattice structured populations. *Journal of Mathematical Biology*, **32**, 251–268.

Sattenspiel, L. (2000). Tropical environmental, human activities and the transmission of infectious diseases. *Yearbook of Physical Anthropology*, **43**, 3–31.

Sauermann, U., C. Stahl-Hennig, N. Stolte, T. Muhl, M. Krawczak, M. Spring, D. Fuchs et al. (2000). Homozygosity for a conserved MHC class II DQ-DRB haplotype is associated with rapid disease progression in simian immunodeficiency virus-infected macaques: results from a prospective study. *Journal of Infectious Diseases*, **182**, 716–724.

van Schaik, C. P. (1983). Why are diurnal primates living in groups? *Behaviour*, **87**, 120–143.

van Schaik, C. P. (1989). The ecology of social relationships amongst female primates. In *Comparative Socioecology* (eds. V. Standen and R. A. Foley), pp. 195–218. Blackwell, Oxford.

van Schaik, C. P. (1996). Social evolution in primates: the role of ecological factors and male behaviour. *Proceedings of the British Academy*, **88**, 9–31.

van Schaik, C. P. and R. I. M. Dunbar (1990). The evolution of monogamy in large primates—a new hypothesis and some crucial tests. *Behaviour*, **115**, 30–62.

van Schaik, C. P. and C. Janson (2000). *Infanticide by Males and Its Implications*. Cambridge University Press, Cambridge.

van Schaik, C. P. and P. M. Kappeler (1997). Infanticide risk and the evolution of male-female association in primates. *Proceedings of the Royal Society B*: *Biological Sciences,* **264**, 1687–1694.

van Schaik, C. P., and P. M. Kappeler (2003). *Sexual Selection in Primates*. Cambridge, Cambridge University Press.

van Schaik, C. P. and J. A. R. A. M. Van Hooff (1983). On the ultimate causes of primate social systems. *Behaviour*, **85**, 91–117.

van Schaik, C. P., M. A. van Noordwijk, B. Warsono, and E. Sutriono (1983). Party size and early detection of predators in Sumatran forest primates. *Primates*, **24**, 211–221.

van Schaik, C. P., M. A. van Noordwijk, and C. L. Nunn (1999). Sex and social evolution in primates. In *Comparative Primate Socioecology* (ed. P. C. Lee), pp. 204-240. Cambridge University Press, Cambridge.

Schiermeier, Q. (2003). Primatologist rocks Gibraltar by quitting over macaque cull. *Nature*, **426**, p. 111.

Schmid-Hempel, P. (1998). *Parasites in Social Insects*. Princeton University Press, Princeton, NJ.

Schmid-Hempel, P. and D. Ebert (2003). On the evolutionary ecology of specific immune defence. *Trends in Ecology & Evolution*, **18**, 27–32.

Schmidt, G., L. Roberts, J. J. Jr, and J. Janovy (2000). *Foundations of Parasitology*. McGraw-Hill, Boston.

Schmidt, G. D. (1972). *Acanthocephala* of captive primates. In *Pathology of Simian Primates. Part II. Infectious and Parasitic Diseases* (ed. R. N. T. W. Fiennes), pp. 144–156. S. Karger, London.

Schrag, S. J. and P. Wiener (1995). Emerging infectious disease—what are the relative roles of ecology and evolution? *Trends in Ecology and Evolution*, **10**, 319–324.

Schultes, R. E. and S. Von Reis (1995). *Ethnobotany: Evolution of a Discipline*. Dioscorides Press, Portland, Or.

Schwartlander, B., G. Garnett, N. Walker, and R. Anderson (2000). AIDS special report—AIDS in a new millennium. *Science*, **289**, 64–67.

Scott, G. R. (1981). Rinderpest. In *Infectious Diseases of Wild Mammals* (eds. J. W. Davis, L. Karstad, and D. O. Trainer), pp. 18–30. Iowa State University Press, Ames, IA.

Scott, M. E. (1987a). Regulation of mouse colony abundance by *Heligmosomoides polygyrus*. *Parasitology*, **95**, 111–124.

Scott, M. E. (1987b). Temporal changes in aggregation: a laboratory study. *Parasitology*, **94**, 583–595.

Scott, M. E. (1988). The impact of infection and disease on animal populations: implications for conservation biology. *Conservation Biology*, **2**, 40–56.

Scott, M. E. and A. Dobson (1989). The role of parasites in regulating host abundance. *Parasitology Today*, **5**, 176–183.

Seal, U. S. (1986). Goals of captive propagation programmes for the conservation of endangered species. *International Zoo Yearbook*, **24/25**, 174–179.

Seger, J. and W. D. Hamilton (1988). Parasites and sex. In *Evolution of Sex: An Examination of Current Ideas* (eds. R. E. Michod, and B. R. Levin), pp. 176–193. Sinauer, Sunderland, MA.

Segerstråle, U. (2000). *Defenders of the Truth*. Oxford University Press, Oxford.

Semple, S., G. Cowlishaw, and P. M. Bennett (2002). Immune system evolution among anthropoid primates: parasites, injuries and predators. *Proceedings of the Royal Society B*: *Biological Sciences,* **269**, 1031–1037.

Sessa, R., C. Palagiano, M. G. Scifoni, M. Di Pietro, and M. Del Piano (1999). The major epidemic infections: a gift from the Old World to the New? *Panminerva Medica*, **41**, 78–84.

Shahabuddin, M., S. Cocianicich, and H. Zieler (1998). The search for novel malaria transmission-blocking targets in the mosquito midgut. *Parasitology Today*, **14**, 493–497.

Sharman, M. J. (1981). Feeding, ranging and social organisation of the Guinea baboon, University of St Andrews, St Andrews.

Shaw, D. J. and A. P. Dobson (1995). Patterns of macroparasite abundance and aggregation in wildlife populations: a quantitative review. *Parasitology*, **111**, S111–S133.

Shaw, D. J., B. T. Grenfell, and A. P. Dobson (1998). Patterns of macroparasite aggregation in wildlife host populations. *Parasitology*, **117**, 597–610.

Sheldon, B. C. (1993). Sexually-transmitted disease in birds—occurrence and evolutionary significance. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **339**, 491–497.

Sheldon, B. C. and S. Verhulst (1996). Ecological immunology: costly parasite defences and trade-offs in evolutionary ecology. *Trends in Ecology and Evolution*, **11**, 317–321.

Sherman, P. W., T. D. Seeley, and H. K. Reeve (1988). Parasites, pathogens, and polyandry in social hymenoptera. *American Naturalist*, **131**, 602–610.

Shields, W. M. and J. R. Crook (1987). Barn swallow coloniality—a net cost for group breeding in the Adirondacks. *Ecology*, **68**, 1373–1386.

Shigesada, N. and K. Kawasaki (1997). *Biological Invasions: Theory and Practice*. Oxford University Press, New York.

Shipman, P., W. Bosler, and K. L. Davis (1981). Butchering of giant geladas at an Acheulian site. *Current Anthropology*, **22**, 257–268.

Sholley, C. and B. Hastings (1989). Outbreak of illness among Rwanda's gorillas. *Gorilla Conservation News*, **3**, 7.

Sibley, L. D. (2003). Recent origins among ancient parasites. *Veterinary Parasitology*, **115**, 185.

Silk, J. B. (1987). *Social Behavior in Evolutionary Perspective*. Chicago University Press, Chicago, IL.

Simberloff, D., J. A. Farr, J. Cox, and D. W. Mehlman (1992). Movement corridors—conservation bargains or poor investments. *Conservation Biology*, **6**, 493–504.

Simon, J. H. M., D. L. Miller, R. A. M. Fouchier, M. A. Soares, K. W. C. Peden, and M. H. Malim (1998). The regulation of primate immunodeficiency virus infectivity by Vif is cell

species restricted: a role for Vif in determining virus host range and cross-species transmission. *Embo Journal*, **17**, 1259–1267.

Singh, M., M. Singh, M. Ananda Kumar, H. N. Kumara, A. K. Sharma, and W. Kaumanns (2002). Distribution, population structure, and conservation of lion-tailed macaques (*Macaca silenus*) in the Anaimalai Hills, Western Ghats, India. *American Journal of Primatology*, **57**, 91–102.

Slattery, J., G. Franchini, and A. Gessain (1999). Genomic evolution, patterns of global dissemination, and interspecies transmission of human and simian T-cell leukemia/lymphotropic viruses. *Genome Research*, **9**, 525–540.

Sleeman, J. M., K. Cameron, A. B. Mudakikwa, J. B. Nizeyi, S. Anderson, J. E. Cooper, H. M. Richardson, et al. (2000). Field anesthesia of free-living mountain gorillas (*Gorilla gorilla beringei*) from the Virunga Volcano Region, Central Africa. *Journal of Zoo and Wildlife Medicine*, **31**, 9–14.

Small, M. F. (1989). Female choice in nonhuman-primates. *Yearbook of Physical Anthropology*, **32**, 103–127.

Smith, C. C. (1977). Feeding behaviour and social organization in howling monkeys. In *Primate Ecology* (ed. T. H. Clutton-Brock), pp. 97–126. Academic Press, London.

Smith, D. L., B. Lucey, L. A. Waller, J. E. Childs, and L. A. Real (2002). Predicting the spatial dynamics of rabies epidemics on heterogeneous landscapes. *Proceedings of the National Academy of Sciences USA*, **99**, 3668–3672.

Smith, G. (1990). The population biology of the free-living phase of *Haemonchus contortus*. *Parasitology*, **101**, 309–316.

Smith, G. and A. P. Dobson (1992). Sexually transmitted diseases in animals. *Parasitology Today*, **8**, 159–166.

Smith, K., S. Alberts, M. Bayes, M. Bruford, J. Altmann, and C. Ober (2000). Cross-species amplification, non-invasive genotyping, and non-Mendelian inheritance of human STRPs in savannah baboons. *American Journal of Primatology*, **51**, 219–227.

Smith, R. and S. Blower (2004). Could disease-modifying HIV vaccines cause population-level perversity? *Lancet Infectious Diseases*, **4**, 636–639.

Smith, R. J. and J. M. Cheverud (2002). Scaling of sexual dimorphism in body mass: a phylogenetic analysis of Rensch's rule in primates. *International Journal of Primatology*, **23**, 1095–1135.

Smuts, B. B. (1985). *Sex and Friendship in Baboons*. Aldine, New York.

Smuts, B. B. and R. W. Smuts (1993). Male aggression and sexual coercion of females in nonhuman primates and other mammals: evidence and theoretical implications. *Advances in the Study of Behavior*, **22**, 1–63.

Smuts, B. B., D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Struhsaker (1987). *Primate Societies*. Chicago University Press, Chicago, IL.

Solomon, G. B. (1969). Host hormones and parasitic infection. *International Review of Tropical Medicine*, **3**, 101–158.

Soltis, J. (2002). Do primate females gain nonprocreative benefits by mating with multiple males? Theoretical and empirical considerations. *Evolutionary Anthroplogy*, **11**, 187–197.

Soper, H. E. (1929). The interpretation of periodicity and disease prevalence. *Journal of the Royal Statistical Society: Series A*, **92**, 34–73.

Sorci, G., F. Skarstein, S. Morand, and J. P. Hugot (2003). Correlated evolution between host immunity and parasite life histories in primates and oxyurid parasites. *Proceedings of the Royal Society B*: *Biological Sciences,* **270**, 2481–2484.

Sousa, O. E., R. N. Rossan, and D. C. Baerg (1974). The prevalence of trypanosomes and microfilariae in Panamanian monkeys. *American Journal of Tropical Medicine and Hygiene*, **23**, 862–867.

Southwood, T. R. E. (1987). Species-time relationships in human parasites. *Evolutionary Ecology*, **1**, 245–246.

Stammbach, E. (1987). Desert, forest, and montane baboons: multilevel societies. In *Primate Societies* (ed. D. L. C. B.B. Smuts, R.M. Seyfarth, R.W. Wrangham, and T.T. Struhsaker), pp. 112–120. University of Chicago Press, Chicago, IL.

Stanberry, L. and S. Rosenthal (1999). The epidemiology of herpes simplex virus infections in adolescents. *Herpes*, **6**, 12–15.

Stanford, C. B., J. Wallis, H. Matama, and J. Goodall (1994). Patterns of predation by chimpanzees on red colobus monkeys in Gombe National Park, 1982–1991. *American Journal of Physical Anthropology*, **94**, 213–228.

Stearns, S. C. 1999. *Evolution in Health and Disease*. New York, Oxford.

Steklis, H. D., C. N. Gerald, and S. Madry (1996/1997). The mountain gorilla: conserving an endangered primate in conditions of extreme political instability. *Primate Conservation*, **17**, 145–151.

Stephens, J. C., D. E. Reich, D. B. Goldstein, H. D. Shin, M. W. Smit, M. Carrington, C. Winkler et al. (1998). Dating the origin of the CCR5-Delta32 AIDS-resistance allele by the coalescence of haplotypes. *American Journal of Human Genetics*, **62**, 1507–1515.

Sterck, E. H. M., D. P. Watts, and C. P. van Schaik (1997). The evolution of female social relationships in nonhuman primates. *Behavioral Ecology and Sociobiology*, **41**, 291–309.

Stewart, P. D., D. W. Macdonald, C. Newman, and F. H. Tattersall (2002). Behavioural mechanisms of information transmission and reception by badgers, *Meles meles*, at latrines. *Animal Behaviour*, **63**, 999–1007.

Stien, A., R. J. Irvine, E. Ropstad, O. Halvorsen, R. Langvatn, and S. D. Albon (2002). The impact of gastrointestinal nematodes on wild reindeer: experimental and cross-sectional studies. *Journal of Animal Ecology*, **71**, 937–945.

Stockwell, C. A., A. P. Hendry, and M. T. Kinnison (2003). Contemporary evolution meets conservation biology. *Trends in Ecology and Evolution*, **18**, 94–101.

Stoner, K. E. (1993). *Habitat preferences, foraging patterns, intestinal parasite infections, and diseases in mantled howler monkeys*, Alouatta palliata (*Mammalia: Primates: Cebidae*), *in a rainforest in Northeastern Costa Rica*, Ph. D Thesis, University of Kansas, Lawrence, KS.

Stoner, K. E. (1996). Prevalence and intensity of intestinal parasites in mantled howling monkeys (*Alouatta palliata*) in northeastern Costa Rica: Implications for conservation biology. *Conservation Biology*, **10**, 539–546.

Strier, K. B. (1992). *Faces in the Forest*. Oxford University Press, New York.

Strier, K. B. (1993). Menu for a monkey. *Natural History*, **102**, 34–42.

Strier, K. B. (1997). Mate preferences of wild muriqui monkeys (*Brachyteles arachnoides*)—reproductive and social correlates. *Folia Primatologica*, **68**, 120–133.

Struhsaker, T. T. (1967). Social structure among vervet monkeys (*Cercopithecus aethiops*). *Behaviour*, **29**, 83–121.

Struhsaker, T. T. (1969). Correlates of ecology and social organization among African cercopithecines. *Folia Primatologica*, **11**, 80–118.

Struhsaker, T. T. and J. S. Gartlan (1970). Observations on the behaviour and ecology of the patas monkey (*Erythrocebus patas*) in the Waza Reserve, Cameroon. *Journal of Zoology,* **161**, 49–63.

Struhsaker, T. T. and L. Leland (1987). Colobines: infanticide by adult males. In *Primate Societies* (eds. D. L. C. B.B. Smuts, R.M. Seyfarth, R.W. Wrangham, and T.T. Struhsaker). University of Chicago Press, Chicago, IL.

Stuart, M., V. Pendergast, S. Rumfelt, S. Pierberg, L. Greenspan, K. Glander, and M. Clarke (1998). Parasites of wild howlers (*Alouatta* spp.). *International Journal of Primatology*, **19**, 493–512.

Stuart, M. D., L. L. Greenspan, K. E. Glander, and M. R. Clarke (1990). A coprological survey of parasites of wild mantled howling monkeys, *Alouatta palliata palliata*. *Journal of Wildlife Diseases*, **26**, 547–549.

Stuart, M. D. and K. B. Strier (1995). Primates and parasites—a case for a multidisciplinary approach. *International Journal of Primatology*, **16**, 577–593.

Stuart, M. D., K. B. Strier, and S. M. Pierberg (1993). A coprological survey of parasites of wild muriquis, *Brachyteles arachnoides*, and brown howling monkeys, *Alouatta fusca*. *Journal of the Helminthological Society of Washington*, **60**, 111–115.

Stumpf, R. M. and C. Boesch (2005). Does promiscuous mating preclude female choice? Female sexual strategies in chimpanzees (*Pan troglodytes verus*) of the Taï National Park, Cote d'Ivoire. *Behavioral Ecology and Sociobiology*, **57**, 511–524.

Su, C. D. E., R. H. Cole, J. C. Kissinger, J. W. Ajioka, L. D. Sibley (2003). Recent expansion of *Toxoplasma* through enhanced oral transmission. *Science*, **299**, 414–416.

Sugiyama, Y. (1971). Characteristics of the social life of bonnet macaques (*Macaca radiata*). *Primates*, **12**, 247–266.

Summers, R., D. Elliott, J. J. Urban, R. Thompson, and J. Weinstock (2005). *Trichuris suis* therapy in Crohn's disease. *Gut*, **54**, 6–8.

Sumner, J. (2000). *The Natural History of Medicinal Plants*. Timber Press, Portland, Oregon.

Swinton, J., J. Harwood, B. T. Grenfell, and C. A. Gilligan (1998). Persistence thresholds for phocine distemper virus infection in harbour seal *Phoca vitulina* metapopulations. *Journal of Animal Ecology*, **67**.

Swinton, J., M. Woolhouse, M. Begon, A. Dobson, E. Ferroglio, B. Grenfell, et al. (2002). Microparasite transmission and persistence. In *The Ecology of Wildlife Diseases* (eds. P. J. Hudson, A. Rizzoli, B. Grenfell, H. Heesterbeek, and A. P. Dobson), pp. 83–101. Oxford University Press, New York.

Switzer, W. M., M. Salemi, V. Shanmugam, F. Gao, M. Cong, C. Kuiken, V. Bhullar, et al. (2005). Ancient co-speciation of simian foamy viruses and primates. *Nature*, **434**, 376–380.

Symons, L. E. A. (1985). Anorexia—occurrence, patho-physiology, and possible causes in parasitic infections. *Advances in Parasitology*, **24**, 103–133.

Takasaki, H. and K. Hunt (1987). Further medicinal plant consumption in wild chimpanzees? *African Study Monographs*, **8**, 125–128.

Tantalean, M., A. Gozalo, and E. Montoya (1990). Notes on some helminth parasites from Peruvian monkeys. *Laboratory Primate Newsletter*, **29**, 6–9.

Tarara, R., M. A. Suleman, R. Sapolsky, M. J. Wabomba, and J. G. Else (1985). Tuberculosis in wild olive baboons, *Papio cynocephalus anubis* (Lesson), in Kenya. *Journal of Wildlife Diseases*, **21**, 137–140.

Taub, D. M. (1980). Female choice and mating strategies among wild Barbary macaques (*Macaca sylvanus* L.). In *The Macaques: Studies in Ecology, Behavior and Evolution* (ed. D. G. Lindburg), pp. 287–344. van Nostrand, New York.

Taylor, L. H., S. M. Latham, and M. E. J. Woolhouse (2001). Risk factors for human disease emergence. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **356**, 983–989.

Temple, S. A. (1987). Do predators always capture substandard individuals disproportionately from prey populations? *Ecology*, **68**, 669–674.

Templeton, A. R. (1982). Adaptation and the integration of evolutionary forces. In *Perspectives on Evolution* (ed. R. Milkman), pp. 15–31. Sinauer Associates, Inc., Sunderland, MA.

Thomas, F., F. Renaud, and J. Guegan (2004a). *Parasitism and Ecosystems*. Oxford University Press, Oxford, UK.

Thomas, F., A. T. Teriokhin, E. V. Budilova, S. P. Brown, F. Renaud, and J. F. Guegan (2004b). Human birthweight evolution across contrasting environments. *Journal of Evolutionary Biology*, **17**, 542–553.

Thompson, J. N. (1989). Concepts of coevolution. *Trends in Ecology and Evolution*, **4**, 179–183.

Thompson, J. N. (1994a). *The Coevolutionary Process*. University of Chicago Press, Chicago, IL.

Thompson, J. N. (2005). *The Geographic Mosaic of Coevolution*. University of Chicago Press, Chicago, IL.

Thompson, S. N. (1994b). Physiological alterations during parasitism and their effects on host behaviour. In *Parasitism and Host Behaviour* (eds. C. J. Barnard and J. M. Behnke), pp. 64–94. Taylor and Francis, London.

Thorne, E. T. and E. S. Williams (1988). Disease and endangered species: the black-footed ferret as a recent example. *Conservation Biology*, **2**, 66–74.

Thrall, M. A., D. C. Baker, and E. D. Lassen (2004). *Veterinary Hematology and Clinical Chemistry*. Lippincott, Williams and Wilkins, London.

Thrall, P. H. and J. Antonovics (1997). Polymorphism in sexual versus non-sexual disease transmission. *Proceedings of the Royal Society B*: *Biological Sciences,* **264**, 581–587.

Thrall, P. H. and J. J. Burdon (1997). Host pathogen dynamics in a metapopulation context: the ecological and evolutionary consequences of being spatial. *Journal of Ecology*, **85**, 743–753.

Thrall, P. H., J. Antonovics, and D. W. Hall (1993a). Host and pathogen coexistence in sexually-transmitted and vector-borne diseases characterized by frequency-dependent disease transmission. *American Naturalist*, **142**, 543–552.

Thrall, P. H., A. Biere, and J. Antonovics (1993b). Plant life-history and disease susceptibility—the occurrence of *Ustilago violacea* on different species within the Caryophyllaceae. *Journal of Ecology*, **81**, 489–498.

Thrall, P. H., J. Antonovics, and W. G. Wilson (1998). Allocation to sexual versus nonsexual disease transmission. *American Naturalist*, **151**, 29–45.

Thrall, P. H., J. Antonovics, and J. D. Bever (1997). Sexual transmission of disease and host mating systems: within-season reproductive success. *American Naturalist*, **149**, 485–506.

Thrall, P. H., J. Antonovics, and A. P. Dobson (2000). Sexually transmitted diseases in polygynous mating systems: prevalence and impact on reproductive success. *Proceedings of the Royal Society B*: *Biological Sciences*, **267**, 1555–1563.

Thursz, M. R., D. Kwiatkowski, C. E. Allsopp, B. M. Greenwood, H. C. Thomas, and A. V. Hill (1995). Association between an MHC class II allele and clearance of hepatitis B virus in the Gambia. *New England Journal of Medicine*, **332**, 1065–1069.

Tishkoff, S. and B. Verrelli (2003). Patterns of human genetic diversity: implications for human evolutionary history and disease. *Annual Review of Genomics and Human Genetics*, **4**, 293–340.

Tompkins, D. M. and M. Begon (1999). Parasites can regulate wildlife populations. *Parasitology Today*, **15**, 311–313.

Tompkins, D. M., J. V. Greenman, and P. J. Hudson (2001). Differential impact of a shared nematode parasite on two gamebird hosts: implications for apparent competition. *Parasitology*, **122**, 187–193.

Tompkins, D. M., A. Dobson, P. Arneberg, M. E. Begon, I. M. Cattadori, J. V. Greenman, J. A. P. Heesterbeek, et al. (2002). Parasites and host population dynamics. In *The Ecology of Wildlife Diseases* (eds. P. J. Hudson, A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. Dobson), pp. 45–62. Oxford University Press, New York.

Torrey, E. F. and R. H. Yolken (2003). *Toxoplasma gondii* and schizophrenia. *Emerging Infectious Diseases*, **9**, 1375–1380.

Trevathan, W. R., E. O. Smith, and J. J. McKenna (1999). *Evolutionary Medicine*. Oxford University Press, New York.

Treves, A. and C. A. Chapman (1996). Conspecific threat, predation avoidance, and resource defense: implications for grouping in langurs. *Behavioral Ecology and Sociobiology*, **39**, 43–53.

Trivers, R. (1985). *Social Evolution*. The Benjamin/Cummings Publishing Company, Inc., Menlo Park, CA.

Turelli, M., N. H. Barton, and J. A. Coyne (2001). Theory and speciation. *Trends in Ecology and Evolution*, **16**, 330–343.

Turner, G. F. and T. J. Pitcher (1986). Attack abatement—a model for group protection by combined avoidance and dilution. *American Naturalist*, **128**, 228–240.

Tutin, C. E. G. (2000). Ecologie et organisation des primates de la foret tropicale Africaine: aide a la comprehension de la transmission des retrovirus. *Forets Tropicales et Emergences Virales*, **93**, 157–161.

Tutin, C. E. G. and M. Fernandez (1984). Nationwide census of gorilla (*Gorilla gorilla*) and chimpanzee (*Pan troglodytes*) populations in Gabon. *American Journal of Primatology*, **6**, 313–336.

Tutin, C. E. G. and P. R. McGinnis (1981). Chimpanzee reproduction in the wild. In *Reproductive Biology of the Great Apes: Comparative and Biomedical Perspectives* (ed. C. E. Graham), pp. 239–264. Academic Press, New York.

Uehara, S. and R. Nyundo (1983). One observed case of temporary adoption of an infant by unrelated nulliparous females among wild chimpanzees in the Mahale Mountains, Tanzania. *Primates*, **24**, 456–466.

Upham, J. and P. Holt (2005). Environment and development of atopy. *Current Opinion in Clinical Immunology*, **5**, 167–172.

Valderrama, X., J. G. Robinson, A. B. Attygalle, and T. Eisner (2000). Seasonal anointment with millipedes in a wild primate: a chemical defense against insects? *Journal of Chemical Ecology*, **26**, 2781–2790.

Valladares-Padua, C. B., J. D. Ballou, C. S. Martins, and L. Cullen (2002). Metapopulation management for the conservation of black lion tamarins. In *Lion Tamarins* (eds. D. G. Kleiman and A. B. Rylands), pp. 301–314. Smithsonian Institution Press, Washington, DC.

Van Baalen, M. (2001). Contact networks and the evolution of virulence. In *Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management* (eds. U. Dieckmann, J. A. J. Metz, M. W. Sabelis, and K. Sigmund), pp. 85–103. Cambridge University Press, Cambridge.

Van Baalen, M. and M. W. Sabelis (1995). The dynamics of multiple infection and the evolution of virulence. *American Naturalist*, 146, 881–910.

Van Blerkom, L. M. (2003). Role of viruses in human evolution. In *Yearbook of Physical Anthropology: Vol 46*, pp. 14–46.

Van Brussel, M., M. Salemi, H. F. Liu, J. Gabriels, P. Goubau, J. Desmyter, and A. M. Vandamme (1998). The simian T-lymphotropic virus STLV-PP1664 from *Pan paniscus* is distinctly related to HTLV-2 but differs in genomic organization. *Virology*, **243**, 366–379.

van Regenmortel, M. and B. Mahy (2004). Emerging issues in virus taxonomy. *Emerging Infectious Diseases*, **10**, 8–13.

Van Riper, C., S. G. Van Riper, M. L. Goff, and M. Laird (1986). The epizootiology and ecological significance of malaria in Hawaiian land birds. *Ecological Monographs*, **56**, 327–344.

Verschoor, E. J., K. S. Warren, H. Niphuis, Heriyanto, R. A. Swan, and J. L. Heeney (1998). Characterization of a simian T-lymphotropic virus from a wild-caught orangutan (*Pongo pygmaeus*) from Kalimantan, Indonesia. *Journal of General Virology*, **79**, 51–55.

Vick, L. G. and J. M. Conley (1976). An ethogram for *Lemur fulvus*. *Primates*, **17**, 125–144.

Vie, J. C. and C. Richard-Hansen (1997). Primate translocations in French Guiana—a preliminary report. *Neotropical Primates*, **5**, 1–3.

Vine, I. (1971). Risk of visual detection and pursuit by a predator and the selective advantage of flocking behaviour. *Journal of Theoretical Biology*, **30**, 405–422.

Vine, I. (1973). Detection of prey flocks by predators. *Journal of Theoretical Biology*, **40**, 207–210.

Vitone, N. D., S. M. Altizer, and C. L. Nunn (2004). Body size, diet and sociality influence the species richness of parasitic worms in anthropoid primates. *Evolutionary Ecology Research*, **6**, 1–17.

Voros, J., W. C. Mahaney, M. W. Milner, R. Krishnamani, S. Aufreiter, and R. G. V. Hancock (2001). Geophagy by the bonnet macaques (*Macaca radiata*) of southern India: a preliminary analysis. *Primates*, **42**, 327–344.

Voss, G. and G. Hunsmann (1993). Cellular immune response to SIVmac and HIV-2 in macaques: model for the human HIV-1 infection. *Journal of Acquired Immune Deficiency Syndromes*, **6**, 969–976.

Vrigenhoek, R. C. and P. L. Leberg (1991). Let's not throw the baby out with the bathwater: a comment on management for MHC diversity in captive populations. *Conservation Biology*, **5**, 252–253.

Waage, J. K. (1981). How the zebra got its stripes—biting flies as selective agents in evolution of zebra coloration. *Journal of Entomological Society of South Africa*, **44**, 351–358.

Waitt, C., A. C. Little, S. Wolfensohn, P. Honess, A. P. Brown, H. M. Buchanan-Smith, and D. I. Perrett (2003). Evidence from rhesus macaques suggests that male coloration plays a role in female primate mate choice. *Proceedings of the Royal Society B*: *Biological Sciences,* **270**, S144–S146.

Wakelin, D. (1996). *Immunity to Parasites: How Parasitic Infections are Controlled*. Cambridge University Press, Cambridge.

Wakibara, J. V., M. A. Huffman, M.Wink, S. Reich, S. Aufreiter, R. G. V. Hancock, R. Sodhi, and et al. (2001). The Adaptive significance of geophagy for Japanese macaques (*Macaca fuscata*) at Arashiyama, Japan. *International Journal of Primatology*, **22**, 495–520.

Wallis, J. (2000). Prevention of disease transmission in primate conservation. *Annals of the New York Academy of Sciences*, **916**, 691–693.

Wallis, J. and D. R. Lee (1999). Primate conservation: the prevention of disease transmission. *International Journal of Primatology*, **20**, 803–826.

Walsh, E. C., K. A. Mather, S. F. Schaffner, L. Farwell, M. J. Daly, N. Patterson, M. Cullen, and et al. (2003a). An integrated haplotype map of the human major histocompatibility complex. *American Journal of Human Genetics*, **73**, 580–590.

Walsh, P. D., K. A. Abernethy, M. Bermejo, R. Beyersk, P. De Wachter, M. E. Akou, B. Huljbregis, and et al. (2003b). Catastrophic ape decline in western equatorial Africa. *Nature*, **422**, 611–614.

Walsh, P. D., R. Biek, and L. A. Real (2005). Wave-like spread of Ebola Zaire. *PLoS Biology*, **3**, e371.

Walsh, P. D., T. Breuer, C. Sanz, D. Morgan, and D. Doran-Sheehy (unpublished manuscript). Potential for Ebola transmission between gorilla and chimpanzee social groups.

Walther, B. A. and S. Morand (1998). Comparative performance of species richness estimation methods. *Parasitology*, **116**, 395–405.

Walther, B. A., D. H. Clayton, and R. D. Gregory (1999). Showiness of Neotropical birds in relation to ectoparasite abundance and foraging stratum. *Oikos*, **87**, 157–165.

Walther, B. A., P. Cotgreave, R. D. Price, R. D. Gregory, and D. H. Clayton (1995). Sampling effort and parasite species richness. *Parasitology Today*, **11**, 306–310.

Wandeler, A. I. (1994). Oral immunization of wildlife. In *The Natural History of Rabies* (ed. G. Baer), pp. 485–503. CRC Press, Boca Raton, FL.

Warner, R. E. (1968). The role of introduced diseases in the extinction of the endemic Hawaiian avifauna. *Condor*, **70**, 101–120.

Waser, P. M. (1976). *Cercocebus albigena*: site attachment, avoidance, and intergroup spacing. *American Naturalist*, **110**, 911–935.

Waser, P. M. (1987). Interactions among primate species. In *Primate Societies* (eds. B. B. Smuts, D. L. Cheney, R. M. Seyfarth, R. W. Wrangham, and T. T. Struhsaker), pp. 210–226. The University of Chicago Press, Chicago and London.

Wasser, S., K. Hunt and C. Clarke (2002). Assessing stress and population genetics through noninvasive means. In *Conservation Medicine: Ecological Health in Practice* (eds. A. Aguirre, R. Ostfeld, G. Tabor, C. House, and M. Pearl), pp. 130–144. Oxford University Press, Oxford, UK.

Wasserman, S. and K. Faust (1994). *Social Network Analysis: Methods and Applications*. Cambridge University Press, Cambridge.

Watanabe, K. (1994). Precultural behavior of Japanese macaques: longitudinal studies of the Koshima troops. In *The Ethological Roots of Culture* (eds. R. Gardner, B. Gardner, B. Chiarelli, and F. Plooij), pp. 81–94. Kluwer Dordrecht, The Netherlands.

Watanabe, K., A. Mori, and M. Kawai (1992). Characteristic features of the reproduction of Koshima monkeys, *Macaca fuscata fuscata*: a summary of thirty-four years of observation. *Primates*, **33**, 1–32.

Watanabe, M. (2004). Origins of HIV: the interrelationship between nonhuman primates and the virus. *BioScience*, **54**, 810–814.

Watts, D. P. (1990). Ecology of gorillas and its relation to female transfer in mountain gorillas. *International Journal of Primatology*, **11**, 21–45.

Watts, D. P. (1998). Seasonality in the ecology and life histories of mountain gorillas (*Gorilla gorilla beringei*). *International Journal of Primatology*, **19**, 929–948.

Watve, M. G. and M. M. Jog (1997). Epidemic diseases and host clustering: an optimum cluster size ensures maximum survival. *Journal of Theoretical Biology*, **184**, 167–171.

Watve, M. G. and R. Sukumar (1997). Asian elephants with longer tusks have lower parasite loads. *Current Science*, **72**, 885–889.

Weber, D., K. Danielson, S. Wright, and J. Foley (2002). Hematology and serum biochemistry values of dusky-footed wood rat (*Neotoma fuscipes*). *Journal of Wildlife Diseases*, **38**, 576–582.

Webster, J. P. and M. E. J. Woolhouse (1999). Cost of resistance: relationship between reduced fertility and increased resistance in a snail-schistosome host-parasite system. *Proceedings of the Royal Society B*: *Biological Sciences,* **266**, 391–396.

Wedekind, C., T. Seebeck, F. Bettens, and A. J. Paepke (1995). MHC-dependent mate preferences in humans. *Proceedings of the Royal Society B*: *Biological Sciences,* **260**, 245–249.

Weinstock, J., R. Summers, and D. Elliott (2005). Role of helminths in regulating mucosal inflammation. *Spring Seminars in Immunopathology*, **27**, 249–271.

Weiss, R. (2001). The Leeuwenhoek Lecture 2001. Animal origins of human infectious disease. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **356**, 957–977.

Weldon, P. J., J. R. Aldrich, J. A. Klun, J. E. Oliver, and M. Debboun (2003). Benzoquinones from millipedes deter mosquitoes and elicit self-anointing in capuchin monkeys (*Cebus spp*.). *Naturwissenschaften*, **90**, 301–304.

White, P. C. L., S. Harris, and G. C. Smith (1995). Fox contact behaviour and rabies spread: a model for the estimation of contact probabilities between urban foxes at different densities and its implication for rabies control in Britain. *Journal of Applied Ecology*, **32**, 693–706.

Whitlock, M. C. (1996). The red queen beats the jack-of-all-trades: the limitations on the evolution of phenotypic plasticity and niche breadth. *American Naturalist*, **148**, S65–S77.

Whitten, A. J. (1982). The role of ants in selection of night trees by gibbons. *Biotropica*, **14**, 237–238.

Whitten, P. L., D. K. Brockman, and R. C. Stavisky (1998). Recent advances in noninvasive techniques to monitor hormone-behavior interactions. In *Yearbook of Physical Anthropology,* **41**, 1–23.

WHO (2000). *WHO Report on Global Surveillance of Epidemic-prone Infectious Diseases*, World Health Organization: Department of Communicable Disease Surveillance and Response.

WHO (2005). *Communicable Disease Surveillance and Response: Ebola Hemorrhagic Fever*, World Health Organization. http://www.who.int/csr/don/archive/disease/ebola_haemorrhagic_fever/en/.

Wickler, W. (1968). *Mimicry in Plants and Animals*. McGraw-Hill, New York.

Wilkie, D. S. and J. F. Carpenter (1999). Bushmeat hunting in the Congo Basin: an assessment of impacts and options for mitigation. *Biodiversity and Conservation*, **8**, 927–955.

Wilkinson, G. S. (1985). The social-organization of the common vampire bat.1. Pattern and cause of association. *Behavioral Ecology and Sociobiology*, **17**, 111–121.

Williams, E. S. and I. K. Barker (2001). *Infectious Diseases of Wild Mammals*. Iowa State Press, Ames, IA.

Willig, M. R., D. M. Kaufman, and R. D. Stevens (2003). Latitudinal gradients of biodiversity: pattern, process, scale, and synthesis. *Annual Review Ecology and Evolutionary Systems*, **34**, 273–309.

Wilson, E. O. (1975). *Sociobiology*. Belknap Press, Cambridge.

Wilson, K., R. Knell, M. Boots, and J. Koch-Osborne (2003). Group living and investment in immune defence: an interspecific analysis. *Journal of Animal Ecology*, **72**, 133–143.

Wilson, M. L., M. D. Hauser, and R. W. Wrangham (2001). Does participation in intergroup conflict depend on numerical assessment, range location, or rank for wild chimpanzees? *Animal Behaviour*, **61**, 1203–1216.

Wimberger, P. H. (1984). The use of green plant material in bird nests to avoid ectoparasites. *Auk*, **101**, 615–618.

Wimsatt, W. C. and Jeffrey C. Schank (1988). Two constraints on the evolution of complex adaptations and the means for their avoidance. In *Evolutionary Progress* (ed. M. H. Nitecki), pp. 231–273. The University of Chicago Press, Chicago, IL.

Windsor, D. A. (1990). Heavenly hosts. *Nature*, **348**, 104.

Windsor, D. A. (1995). Equal-rights for parasites. *Conservation Biology*, **9**, 1–2.

Windsor, D. A. (1998). Most of the species on earth are parasites. *International Journal for Parasitology*, **28**, 1939–1941.

Wobeser, G. (2002a). Disease management strategies for wildlife. *Revue Scientifique et Technique de L Office International des Epizooties*, **21**, 159–178.

Wobeser, G. (2002b). New and emerging diseases: the wildlife interface. *Canadian Veterinary Journal*, **43**, 798.

Wolfe, N. D., A. A. Escalante, W. B. Karesh, A. Kilbourn, A. Spielman, and A. A. Lal (1998). Wild primate populations in emerging infectious disease research: the missing link? *Emerging Infectious Diseases*, **4**, 149–158.

Wolfe, N. D., W. Heneine, J. K. Carr, A. D. Garcia, V. Shanmugam, U. Tamoufe, J. N. Torimiro, and et al. (2005). Emergence of unique primate T-lymphotropic viruses among central African bushmeat hunters. *PNAS*, **102**, 7994–7999.

Wolfe, N. D., W. M. Switzer, J. K. Carr, V. B. Bhullar, V. Shanmugam, U. Tamoufe, A. T. Prosser, and et al. (2004). Naturally acquired simian retrovirus infections in central African hunters. *Lancet*, **363**, 932–937.

Wolff, P. L. and U. S. Seal (1993). Implications of infectious-disease for captive propagation and reintroduction of threatened species. *Journal of Zoo and Wildlife Medicine*, **24**, 229–230.

Woodford, M. H. and P. Rossiter (1994). Disease risks associated with wildlife translocation projects. In *Creative Conservation: Interactive Management of Wild and Captive Animals* (eds. P. J. S. Olney, G. M. Mace, and A. T. C. Feistner), pp. 178–200. Chapman and Hall, London.

Wooding, S., A. Stone, D. Dunn, S. Mummidi, L. Jorde, R. Weiss, S. Ahuja, and et al. (2005). Contrasting effects of natural selection on human and chimpanzee CC chemokine receptor 5. *American Journal of Human Genetics*, **76**, 291–301.

Woodroffe, R. (1999). Managing disease threats to wild mammals. *Animal Conservation*, **2**, 185–193.

Woolhouse, M. E. J., L. H. Taylor, and D. T. Hayden (2001). Population biology of multihost pathogens. *Science*, **292**, 1109–1112.

Wrangham, R. (1977). Feeding behavior of chimpanzees in Gombe National Park, Tanzania. In *Primate Ecology* (ed. T. H. Clutton-Brock). Academic Press, New York.

Wrangham, R. W. (1979). On the evolution of ape social systems. *Social Science Information*, **18**, 335–368.

Wrangham, R. W. (1980). An ecological model of female-bonded primate groups. *Behaviour*, **75**, 262–299.

Wrangham, R. W. (1993). The evolution of sexuality in chimpanzees and bonobos. *Human Nature*, **4**, 47–79.

Wrangham, R. W. (1995). Relationship of chimpanzee leaf-swallowing to a tapeworm infection. *American Journal of Primatology*, **37**, 297–303.

Wrangham, R. W. and T. Nishida (1983). *Aspilia spp*. leaves: a puzzle in the feeding behavior of wild chimpanzees. *Primates*, **24**, 276–282.

Wrangham, R. W., M. Wilson, B. Hare, and N. D. Wolfe (2000). Chimpanzee predation and the ecology of microbial exchange. *Microbial Ecology in Health and Disease*, **12**, 186–188.

Wright, A., L. Simpson, and J. Oliver (1981). Role of iron in the pathogenesis of *Vibrio vulnificus* infections. *Infection and Immunity*, **34**, 503–507.

Yeager, C. P. (1990). Proboscis monkey (*Nasalis larvatus*) social organization: group structure. *American Journal of Primatology*, **20**, 95–106.

Yeager, C. P. (1991). Proboscis monkey (*Nasalis larvatus*) social organization: intergroup patterns of association. *American Journal of Primatology*, **23**, 73–86.

Yezerinac, S. M. and P. J. Weatherhead (1995). Plumage coloration, differential attraction of vectors and hematozoa infections in birds. *Journal of Animal Ecology*, **64**, 528–537.

Young, T. P. (1994). Natural die-offs of large mammals—implications for conservation. *Conservation Biology*, **8**, 410–418.

Yuhki, N., T. Beck, R. M. Stephens, Y. Nishigaki, K. Newmann, and S. J. O'Brien (2003). Comparative genome organization of human, murine, and feline MHC class II region. *Genome Research*, **13**, 1169–1179.

Yuill, T. M. and C. Seymour (2001). Arbovirus infections. In *Infectious Diseases of Wild Mammals* (eds. E. S. Williams and I. K. Barker), pp. 98–118. Iowa State University Press, Ames, IA.

Yusim, K., M. Peeters, O. G. Pybus, T. Bhattacharya, E. Delaporte, C. Mulanga, M. Muldoon, et al. (2001). Using human immunodeficiency virus type 1 sequences to infer historical features of the aquired immune deficiency syndrome epidemic and human immunodeficiency virus evolution. *Philosophical Transactions of the Royal Society B*: *Biological Sciences,* **356**, 855–866.

Zamma, K. (2002). Grooming site preferences determined by lice infection among Japanese macaques in Arashiyama. *Primates*, **43**, 41–49.

Ziegler, P. (1969). *The Black Death*. Collins, London.

Zimmer, C. (2000). Do parasites rule the world? *Discover*, **21**, 78–85.

Zito, M., S. Evans, and P. J. Weldon (2003). Owl monkeys (*Aotus* spp.) self-anoint with plants and millipedes. *Folia Primatologica*, **74**, 159–161.

Zuk, M. and K. A. McKean (1996). Sex differences in parasite infections: patterns and processes. *International Journal for Parasitology*, **26**, 1009–1023.

Zuk, M. and A. Stoehr (2002). Immune defense and host life history. *American Naturalist*, **160**, S9–S22.

This page intentionally left blank

Index