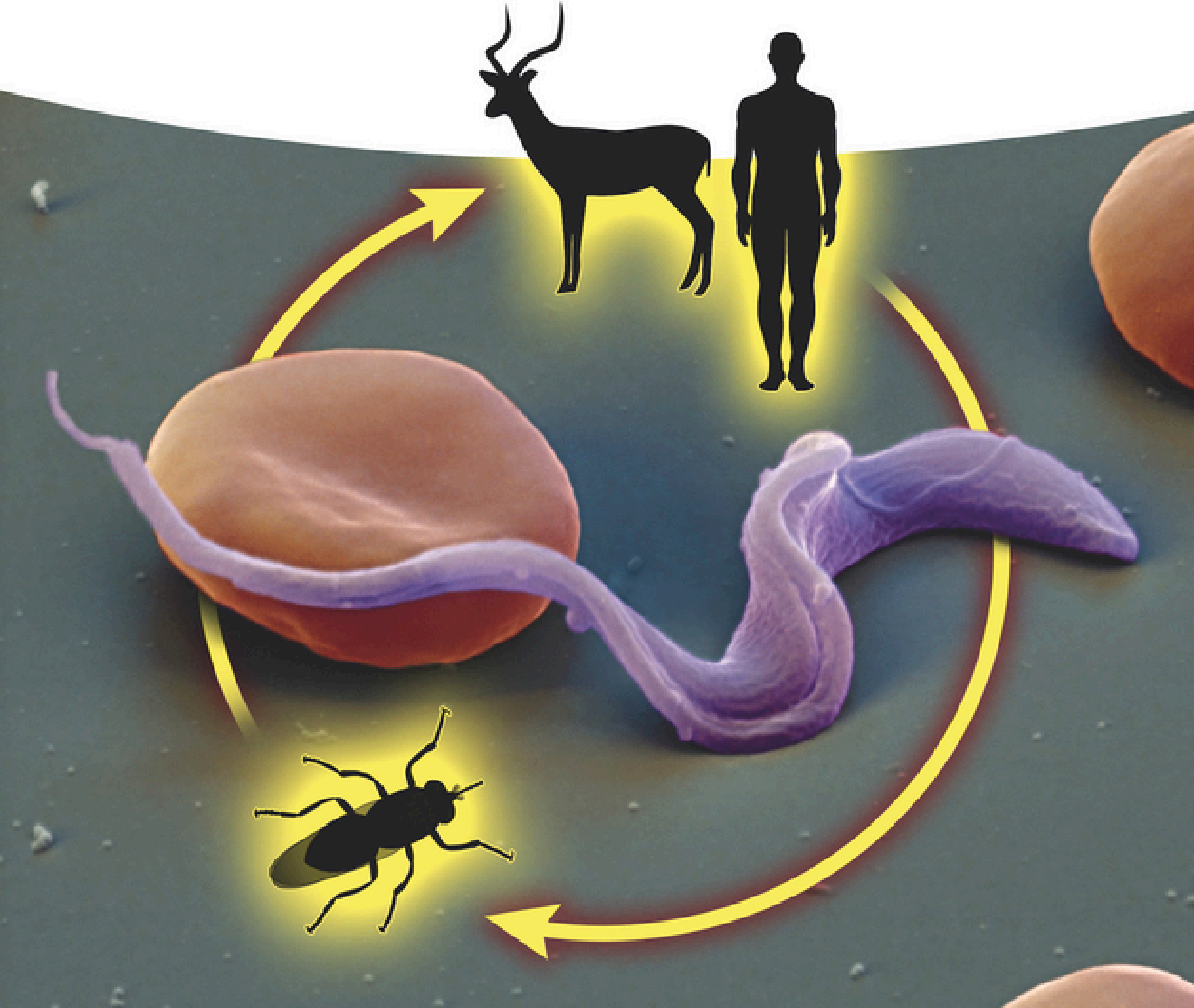
WILEY-VCH

R. Lucius, B. Loos-Frank, R. P. Lane, R. Poulin,
C. W. Roberts, and R. K. Grencis

The Biology of Parasites



Richard Lucius, Brigitte Loos-Frank,
Richard P. Lane, Robert Poulin,
Craig W. Roberts, and Richard K. Grencis

The Biology of Parasites

Richard Lucius, Brigitte Loos-Frank, Richard P. Lane,
Robert Poulin, Craig W. Roberts, and Richard K. Grencis

With contributions of guest authors
Nina Papavasiliou, Rockefeller University, New York, USA
John Boothroyd, Stanford University, Stanford, USA
Kai Matuschewski, Humboldt Universität zu Berlin, Berlin, Germany

The Biology of Parasites

Translated by Renate FitzRoy and Ron Shankland

WILEY-VCH
Verlag GmbH & Co. KGaA

Authors

Prof. Dr. Richard Lucius
Humboldt University
Institute of Biology
Philippstr. 13
10115 Berlin
Germany

Prof. Dr. Brigitte Loos-Frank
University of Hohenheim
Department of Parasitology
Emil Wolff-Straße 34
70599 Stuttgart
Germany

Prof. Dr. Richard P. Lane
Stonewall Holt
The Street
EX13 7RW Kilmington, Devon
United Kingdom

Prof. Dr. Robert Poulin
University of Otago
Zoology Department
Great King Sreet
Dunedin 9054
New Zealand

Prof. Dr. Craig W. Roberts
University of Strathclyde
Strathclyde Institute of Pharmacy and
Biomedical Sciences (SIPBS)
161 Cathedral Street
G4 0RE Glasgow
United Kingdom

Prof. Dr. Richard K. Grencis
University of Manchester
Life Sciences/AV Hill Building
Oxford Road
M13 9PT Manchester
United Kingdom

Translators

Renate FitzRoy
MSc Transl & Technology
26 Cairnhill Gardens
KY16 8QX St. Andrews
United Kingdom

Ron Shankland
Kevron Translations
Erlenweg 2
69509 Mörlenbach
Germany

Cover
Trypanosoma brucei SEM image © eye of science, Meckes & Ottawa GbR.

All books published by **Wiley-VCH** are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek
The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <http://dnb.d-nb.de>.

© 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-32848-2
ePDF ISBN: 978-3-527-69855-4
ePub ISBN: 978-3-527-69856-1
Mobi ISBN: 978-3-527-69857-8

Cover Design Formgeber, Mannheim, Germany
Typesetting SPi Global, Chennai, India
Printing and Binding

Printed on acid-free paper

This is a completely revised and updated version of the second edition of "R. Lucius and B. Loos-Frank: Biologie von Parasiten" (ISBN 978-3-540-37707-8, Springer-Verlag, Berlin, Heidelberg).

Contents

Preface

Parasitism is a specialized way of life, pursued by organisms that have evolved to thrive at the expense of a living host. Therefore, in a broad sense, all pathogens like viruses, bacteria, or eukaryotic infectious agents are parasites and thus share many common features. However, they also have important differences. For example, viruses and bacteria are genetically less complex and employ different strategies for exploiting a host, leading to different disease syndromes. As a consequence, different scientific fields have emerged, of which the discipline of parasitology is one that deals with eukaryotic pathogens, namely, protozoa, worms, and arthropods. Parasites, in this narrower sense, are a huge burden to mankind, with billions of infected people, mainly in tropical developing countries with relatively poor hygiene. Along with their medical and veterinary importance, parasites have a fascinating biology, which is the theme of this book. *The Biology of Parasites* is based on an earlier German book (Lucius & Loos-Frank (2008), Springer Verlag, Heidelberg), which has been extended and updated by the current team of authors.

The living host is a very particular niche; it is not a neutral place at all. Parasites are involved in a constant struggle with their hosts, who strive to rid themselves of the unwanted company, deploying all sorts of mechanisms against them. These range from defensive behavior to the effector molecules and cells of a complex immune system. In spite of such defenses, an extraordinary number of animals have adopted parasitism as a mode of life; some specialists believe that >50% of animal species are parasites or have at least a parasitic phase in their life cycle. It seems that the parasitic lifestyle is so rewarding that it has been worth the great effort parasites have made to develop most intriguing means of locating their hosts, survive within or on them, produce offspring, and ensure that the next generation reaches a new host. To exploit a host, parasites may change their morphology beyond all recognition: they may trick and cheat by disguising themselves or manipulate their host's cellular pathways or even their behavior. Because of these extraordinary, bizarre, or seemingly "otherworldly" abilities, parasites have always fascinated biologists and captured the attention of the general public.

The antagonistic relationship between pathogens and their hosts drives the evolution of both adversaries in a profound manner. This arms race has affected the evolution of some of the most important processes of life, for example, sexual reproduction and the immune system. It also shaped the genomes of both parties to a degree that we have only recently discovered. Indeed, new molecular techniques developed in past few decades have opened an extraordinary range of perspectives on the interplay between eukaryotic parasites and their hosts. Genome projects have cast light on the peculiarities of parasite genomes. For example, we have learned that many protozoans and worms have undergone a reductive evolution in their genomes, especially with regard to those functions they have appropriated from their host, while other areas have been expanded, such as those needed for the manipulation of the host. This explosion in genomic knowledge has also provided us with the tools to discover and describe precisely parasite-specific metabolic pathways. It has also facilitated the dissection of molecular mechanisms used by parasites to detect host cues, invade host cells, or cope with immune effector mechanisms. This information has already allowed and will hopefully further allow us to design specific measures against parasites and their vectors, ranging from strategies to prevent infection, such as vaccines and pesticides, to drug development. However, it is not the sole goal of parasitologists to fight diseases, as worthy as that is, but to understand the intricacies of the parasitic lifestyle and to put them into a broader biological context. This greatly contributes to our wider understanding of key biological processes, such as evolution, ecology, and generation of biodiversity. Last but not least, the simple wonder and awe the extraordinary biology of parasites instills in us makes their study worthwhile in its own right.

This book is designed to provide advanced information to students of biology, medicine, or veterinary medicine and to interested lay persons. An introductory chapter on general parasitology, addressing crosscutting topics of parasitology, is followed by specific chapters on the biology of protozoan parasites, parasitic worms, and parasitic arthropods. The focus is on parasites of medical or veterinary importance, as these are best known from intensive research and are of the widest interest, although we also highlight parasites with interesting biological adaptations to emphasize those traits most typical of the parasitic lifestyle. To be concise, we discuss particular species as representatives of their taxon, while related parasites are briefly mentioned or treated in tabular form. Inevitably, the book cannot cover the entire field of parasitology. It does not give detailed treatment of the therapy or control of parasitic infections, parasite ecology, or evolutionary parasitology. Likewise, we have sparingly mentioned marine parasites or parasitoids and their interesting biologies. To cover cutting-edge topics, we have invited three renowned guest authors to contribute concise information from their field of research, namely, John Boothroyd (parasite–host interplay of *Toxoplasma*), Kai Matuschewski (vaccine development against the malaria parasite *Plasmodium*), and Nina Papavasiliou (new developments in trypanosome research).

We are thankful to many colleagues from different fields of parasitology and beyond for their helpful discussions. We thank specifically those who provided images of parasites or illustrative research data, in particular Oliver Meckes and Nicole Ottawa from *eye of science* for fascinating electron microscope pictures, Prof. Egbert Tannich for images of amoebae, and Dr. Heiko Bellmann for photos

of arthropods. We gratefully acknowledge the permission of the Departments of Parasitology of University of Hohenheim and of Humboldt University to utlize pictures from their archives. The life cycles and other drawings are based on the painstaking work of Flavia Wolf, Dr. J. Gelnar, and Hanna Zeckau, which is gratefully acknowledged. A heartfelt thank-you goes to Christine Nowotny for her most professional help with the organization of the manuscript and illustrations. This work would not have been possible without the continuous support of Dr. Gregor Cicchetti and Dr. Andreas Sendtko and their team from the publisher Wiley-VCH, which is gratefully acknowledged.

September 2016 *Richard Lucius*
Berlin

1
General Aspects of Parasite Biology

Richard Lucius and Robert Poulin

The Biology of Parasites, First Edition. Richard Lucius, Brigitte Loos-Frank, Richard P. Lane, Robert Poulin, Craig W. Roberts, and Richard K. Grencis.
© 2017 Wiley-VCH Verlag GmbH & Co. KGaA. Published 2017 by Wiley-VCH Verlag GmbH & Co. KGaA.

1.1 Introduction to Parasitology and Its Terminology

1.1.1 Parasites

Parasites are organisms which live in or on another organism, drawing sustenance from the host and causing it harm. These include animals, plants, fungi, bacteria, and viruses, which live as host-dependent guests. Parasitism is one of the most successful and widespread ways of life. Some authors estimate that more than 50% of all eukaryotic organisms are parasitic, or have at least one parasitic phase during their life cycle. There is no complete biodiversity inventory to verify this assumption; it does stand to reason, however, given the fact that parasites live in or on almost every multicellular animal, and many host species are infected with several parasite species specifically adapted to them. Some of the most important human parasites are listed in Table 1.1.

The term parasite originated in Ancient Greece. It is derived from the Greek word “parasitos” (Greek *pará* = on, at, beside; *sítos* = food). The name parasite was first used to describe the officials who participated in sacrificial meals on behalf of the general public and wined and dined at public expense. It was later applied to minions who ingratiated themselves with the rich, paying them compliments and practicing buffoonery to gain entry to banquets where they would snatch some food.

Table 1.1 Occurrence and distribution of the more common human parasites.

Parasite	Infected people (in millions)	Distribution
Giardia lamblia	>200	Worldwide
Trichomonas vaginalis	173	Worldwide
Entamoeba histolytica	500*	Worldwide in warm climates
Trypanosoma brucei	0.01	Sub-Saharan Africa ("Tsetse Belt")
Trypanosoma cruzi	7	Central and South America
Leishmania spp.	2	Near + Middle East, Asia, Africa, Central and South America
Toxoplasma gondii	1500	Worldwide
Plasmodium spp.	>200	Africa, Asia, Central and South America
Paragonimus sp.	20	Africa, Asia, South America
Schistosoma sp.	>200	Asia, Africa, South America
Hymenolepis nana	75	worldwide
Taenia saginata	77	Worldwide
Trichuris trichiura	902	Worldwide in warm climates
Strongyloides stercoralis	70	Worldwide
Enterobius vermicularis	200	Worldwide
Ascaris lumbricoides	1273	Worldwide
Ancylostoma duodenale and *Necator americanus*	900	Worldwide in warm climates
Onchocerca volvulus	17	Sub-Saharan Africa, Central and South America
Wuchereria bancrofti	107	Worldwide in the tropics

Source: Compiled from various authors.
*many of those asymptomtic or infected with the morphologically identical *Entamoeba dispar*.

The result was a character figure, a type of Harlequin, who had a fixed role to play in the Greek comedy of classical antiquity (Figure 1.1). Later, "parasitus" also became an integral part of social life in Roman antiquity. It also reappeared in European theater in pieces such as Friedrich Schiller's "Der Parasit." In the seventeenth century, botanists were already describing parasitic plants such as mistletoe as parasites; in his 1735 standard work "Systema naturae," Linnaeus first used the term "specie parasitica" for tapeworms in its modern biological sense.

The delimitation of the term "parasite" to organisms which profit from a **heterospecific** host is very important for the definition itself. Interactions between individuals of the same species are thus excluded, even if the benefits of such interactions are very often unequally distributed in the colonies of social insects and naked mole rats, for instance, or in human societies. As a result, the interaction between parents and their offspring does not fall under this category, although the direct or indirect manner in which the offspring feed from their parent organism can at times be reminiscent of parasitism.

Figure 1.1 Parasitos mask, a miniature of a theater mask of Greek comedy; terracotta, around 100 B.C. (From Myrine (Asia Minor); antiquities collection of the Berlin State Museums. Image: Courtesy of Thomas Schmid-Dankward.)

The principle of one side (the parasite) taking advantage of the other (the host) applies to viruses, all pathogenic microorganisms, and multicellular parasites alike. This is why we often find that no clear distinction is made between prokaryotic and eukaryotic parasites. With regard to *parasites,* we usually do not differentiate between viruses, bacteria, and fungi on the one hand and animal parasites on the other; we tend to see only the common parasitic lifestyle. Even molecules to which a function in the organism cannot be assigned are sometimes described as parasitic, such as prions, for example, the causative agent of spongiform encephalopathy, or apparently functionless "selfish" DNA plasmids that are present in the genome of many plants. Many biologists are of the opinion that only parasitic protozoa, parasitic worms (helminths), and parasitic arthropods are parasites in the strict sense of the term. Parasitology, as a field, is concerned only with those groups, while viruses, bacteria, fungi, and parasitic plants are dealt with by other disciplines. This restriction clearly hampers cooperation with other disciplines, something that seems antiquated in today's modern biology, where all of life's processes are traced back to DNA; it is gratifying that the boundaries have relaxed in recent years. However, eukaryotic parasites are distinguished from viruses and bacteria by their comparatively higher complexity, which implies slower reproduction and less genetic flexibility. These traits typically drive eukaryotic parasites to establish long-standing connections with their hosts, using strategies different from the "hit-and-run" strategies used by many viruses and bacteria. For these reasons, and for the sake of clarity and tradition, only parasites in the stricter sense of the term, that is, parasitic protozoa, helminths, and parasitic arthropods are dealt with in this book.

1.1.2
Types of Interactions Between Different Species

The coexistence of different species of organisms involves interactions among them that take many different forms in which the benefits and costs are often very unevenly distributed. Both partners benefit from mutualistic relationships, while in antagonistic relationships the advantage lies with only one side. However, a direct relationship between two species is seldom completely neutral. Different types of interactions are not always easy to distinguish, such that transitions between them are often fluid and the differences subtle. The spectrum of the partnerships between different organisms can be best illustrated by the use of concrete examples.

1.1.2.1 Mutualistic Relationships

If different partners rely on their coexistence and are limited in their viability or even nonviable when separated, this close association is described as a **symbiosis** (Greek: *sym* = together, *bíos* = life). For example, Lichens – a combination of fungi and photosynthetically active algae – can only colonize completely new habitats in this combined form. Another example is the partnership of termites with cellulose-digesting protozoa, which live in the intestinal blind sacs of the hosts. The metabolites of the protozoa complement the hosts' rather unbalanced diet.

When the two partners benefit from coexistence without losing the ability to live independently, it is known as **mutualism**. A close mutualistic relationship exists between clown fish (anemone fish) and sea anemones: the fish can gain protection from predators by snuggling into the tentacles of the sea anemones without being attacked by the latter's poisonous stinging cells (Figure 1.2) and always returns to the anemone when danger threatens. The sea anemone benefits in turn

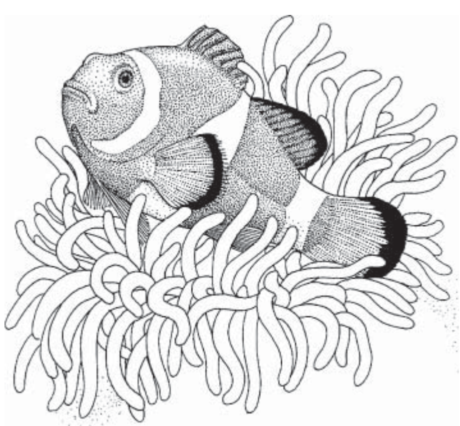


Figure 1.2 A clown fish in the tentacles of a sea anemone. The partners form a mutualistic symbiosis, but they can also survive independently. (Image: Richard Orr, courtesy of Random House Publishers, Munich.)

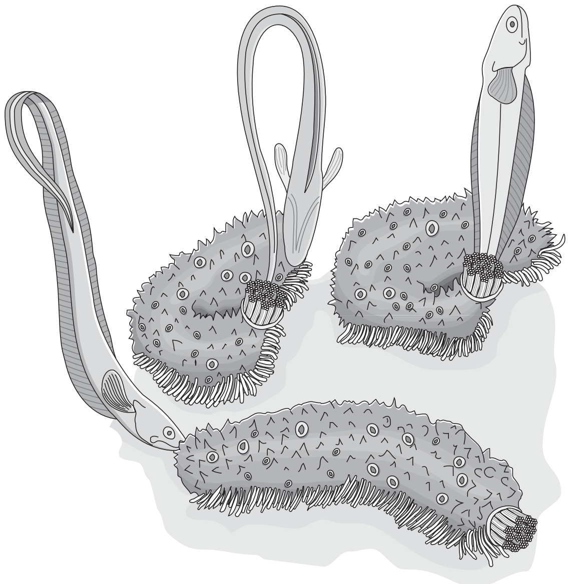


Figure 1.3 The pearlfish *Carapus* (syn. *Fierasfer*) *acus* lives in the water lungs of sea cucumbers. (Edited from Oche G. (1966) "The World of Parasites", Springer-Verlag Heidelberg.)

from the food remnants of the fish. Another example of a less intimate mutualistic association is the interaction between Cape buffalo and the cattle egret. While grazing, a buffalo flushes out insects, which are then snapped up by the egrets – and the danger-sensitive birds warn the buffalo by flying up when they spot big cats approaching.

Commensalism describes a feeding relationship, in which one partner benefits without providing any reciprocal benefits nor imposing any cost to the other. The commensal draws sustenance from the host's waste materials or from the components of the host's food, which are of no value to it. The flagellates that reside in the anal canals of arthropods provide an example, because these are areas of the digestive system where no more food absorption takes place.

However, there are symbiotic relationships in which a host is merely used as a living place. This involves organisms settling on the external surfaces of a different species (e.g., barnacles on crabs and shellfish), or even inside the host's body. One example of this is the pearlfish, a member of the cod family, which can grow to a length of approximately 20 cm. The fish lives in the water lungs of sea cucumbers into which it skillfully wriggles, pointed tail first (Figure 1.3). Pearlfish only leave their hosts to forage and reproduce.

1.1.2.2 Antagonistic Relationships

When a guest organism extracts nutrients from its host – and the host incurs a cost from the relationship – it is known as **parasitism**. Parasites can also cause damaging effects such as injury, inflammation, toxic metabolite, and other factors,

Figure 1.4 Coexistence of a typical parasite with its host. Tapeworms draw nourishment from their host and exploit the host in the long term – they are, however, only moderately pathogenic. (De bouche à Oreille by Claude Serre © Editions Glénat 2016)

and result in reduced evolutionary fitness of the host, even if the effects are only slight. Adult tapeworms may be regarded as typical examples here: they absorb nutrients from the digested food in the small intestine of the host, thereby harming the host, but do not attack its tissues. The host is thus weakened a little, but not killed, and the parasite lives of the interest without touching its capital. Claude Serre expresses all these qualities very aptly in his cartoon (Figure 1.4). Parasites are usually smaller and more numerous than their host, whereas predators are larger and less numerous than their prey. When one parasite settles on another, we call this **hyperparasitism**. *Nosema monorchis*, for example, a single-cell organism of the phylum Microspora, parasitizes the digenean *Monorchis parvus*, which is itself a parasite of fish.

We usually expect an intimate, physical relationship between parasite and host. Intimate contact like this exists in endoparasitism and (in many cases) ectoparasitism. There are also forms of parasitism in which the physical contact between the partners is less intimate, where the parasite does not exist as a pathogen, but exploits the host in other ways. The exploitation of interactions between members of social organisms is defined as **social parasitism**. In the case of social insects such as ants, the interactions of a host species are exploited by a parasitic species. The spectrum of social parasitism ranges from food theft to slavery and the targeted assassination of the queen, which is then replaced by the queen of a parasitic species. One specific form of social parasitism is the exploitation of a different species to rear one's own offspring, which is known as **brood parasitism**. A well-known representative of the brood parasites is the

Figure 1.5 Brood parasitism: A young cuckoo is fed by a warbler. (Image: Courtesy of Oldrich Mikulica.)

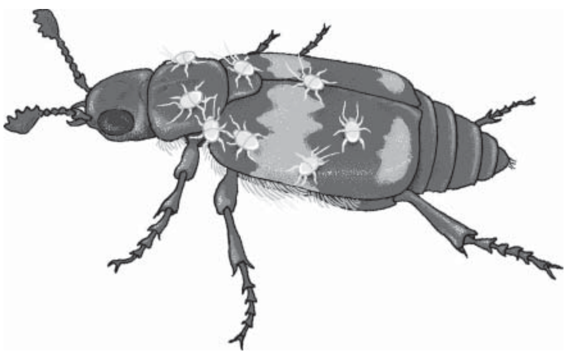


Figure 1.6 Phoresy: Mites latch on to a sexton beetle, "hitching a ride" to the nearest carrion. (Drawing from a photo by Frank Köhler.)

cuckoo (*Cuculus canorus*). The female of the species lays its eggs in the nests of smaller songbirds to have them raise its young ones (Figure 1.5). The cuckoo bee's behavior is very similar. Cuckoo bees account for 125 of a total of 547 species of bees in Germany – a fact that says much for the success of this form of parasitism. Not only food but also functions such as transportation can be exploited by parasites. For instance, some mites and certain nematodes latch on to insects for transportation. In this type of parasitism, **phoresy**, the carriers are referred to as transport hosts (Figure 1.6).

Parasitoidism occurs when the death of the host is almost inevitable following parasitic exploitation. One typical example of this involves ichneumon wasps, which lay their eggs on caterpillars. When the young wasps hatch, they feed on the host's tissues (Figure 1.7). The parasitic wasp larvae first devour the body fat, and then eat the muscle tissue and finally kill their hosts by consuming the neural

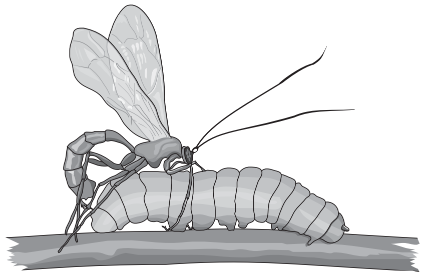


Figure 1.7 Parasitoidism: A parasitic wasp of the genus *Ichneumon* lays its eggs in a caterpillar. (From a photo in "The Animal Kingdom," courtesy of Marshall Cavendish Books Ltd.)

tissue. The larvae finally break out of the caterpillar and pupate. A parasitoid like this attacks the capital, rather than living of the interest. However, it does exploit the host for a relatively long period of time and only kills it when the parasitoid is finished with it.

The interaction between parasitoids and their host shows some similarities to **predator–prey relationships**, for example, between a lion and wildebeest (Figure 1.8). However, whereas the parasitoid only kills its host after eating most of it, the prey is immediately killed by the predator and then eaten. In addition, predators are typically larger than their prey, and consume more than one prey in their lifetime, two features that separate them from parasites.

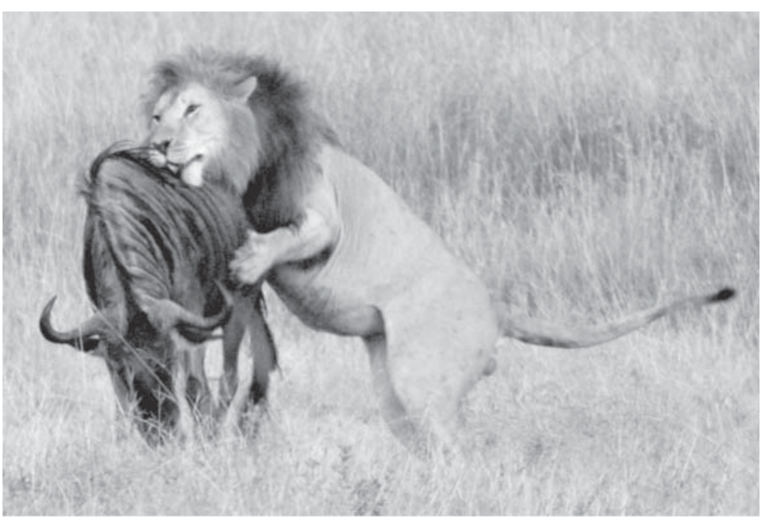


Figure 1.8 Predator–prey relationship: A lion attacks a wildebeest. (Image: Ingo Gerlach, www.tierphoto.de.)

1.1.3 Different Forms of Parasitism

Organisms, which can live as parasites, but are not necessarily dependent on the parasitic mode of life represent **facultative parasites**. One example is the bloodsucking kissing bug, *Triatoma infestans.* It can also live as a predator by sucking out the hemolymph of smaller insects. **Obligate parasites** have no alternative other than their way of life. In the case of some organisms, only one sex lives parasitically. In mosquitoes, for instance, only the females need a meal of blood to produce eggs; the male feeds on the sap of plants. **Permanent parasites** are parasitic in all stages of their development, while **temporary parasites** spend only certain phases of their life in a host.

An **ectoparasite** attaches to the skin or other external surfaces (e.g., the gills) of its host, where it subsists on hair or feathers, feeds on skin, or sucks blood or tissue fluid substance. Included among ectoparasites are numerous **temporary parasites** (sometimes called micropredators), which only seek out their hosts to feed (e.g., bloodsucking mosquitoes), and many **permanent parasites** that remain in constant contact with their hosts (e.g., lice, or the monogeneans parasitic on fish). Parasites that live inside their hosts are known as **endoparasites**. The worms living in the gut lumen of vertebrates illustrate the simplest form of endoparasitism. The difference between rotting substances in the outside world and the contents of the digestive tract is not particularly significant and it is relatively common to find organisms that have adapted to endoparasitism of this type. One example of these residents of the gut lumen is the nematode *Strongyloides stercoralis*, the life cycle of which illustrates that it has the option of either the free-living or the parasitic modes of life. Other endoparasites either live in organs (such as the great liver fluke *Fasciola hepatica*), live freely in the blood of their hosts (such as *Trypanosoma brucei*), or inhabit body tissue (such as the filarial nematode *Onchocerca volvulus*). **Intracellular parasites** induce very pronounced changes in the host cell: using these highly specific mechanisms, these parasites (e.g., *Leishmania* and *Plasmodium*) invade host cells, reorganize them to fit their own needs, and exploit this extreme ecological niche due to a multitude of adaptations.

As an adaptation to their modes of life, many parasites have evolved complex life cycles, which include switching between multiple hosts and sexual and asexual reproduction (Figure 1.9). In the simplest forms of parasitism, only one host is exploited; these parasites as referred to as **monoxenous** (Greek *mónos* = single, *xénos* = foreign). In this case, transmission from one host to the next takes place among members of the same host species, and is referred to as **direct transmission**. By contrast, **indirect transmission** occurs when the parasite switches between two or more host species. These parasites are known as **heteroxenous** (*hetero* = differing); their complex cycles require two or three, sometimes even four, host species, depending on the parasite. By switching hosts from one stage of their life cycle to the next, heteroxenous parasites achieve greater overall fitness, or transmission efficiency, than they would by utilizing a single host per generation. For example, the use of bloodsucking mosquitoes

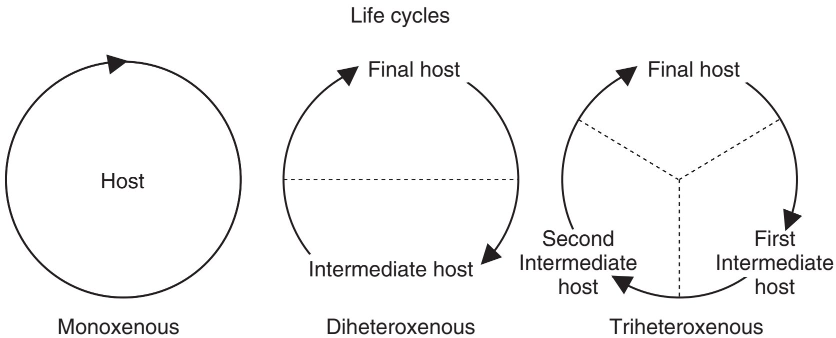


Figure 1.9 Life cycles of parasites. *Left*: Monoxenous cycle with one host, for example, *Ascaris lumbricoides*. *Center*: Heteroxenous cycle with final and intermediate hosts, for example, *Trypanosoma brucei*. Right: Heteroxenous cycle with final host and two intermediate hosts, for example, *Dicrocoelium dendriticum*.

as **vectors**, that is, carriers of the parasite between vertebrate hosts, results in a much higher level of efficiency in the transmission of malaria than has been measured in highly contagious viral diseases transmitted through direct transmission. The evolution of complex life cycles from what originally were simple ones has occurred in several unrelated parasite lineages, ranging from microorganisms to multicellular parasites, through the stepwise addition of a new host whenever this was favored by natural selection.

Modes of reproduction vary greatly among parasites, and many parasite species can switch from one reproduction mode to another during their life cycle. When a parasite alternates between sexual and asexual reproduction, this is known as **metagenesis**. The Apicomplexa, alternating between schizogony (asexual), gamogony (sexual), and sporogony (asexual), is a good example of metagenesis. Switching from sexual to asexual reproduction (i.e., parthenogenesis = virgin birth) is also seen in some intestinal nematodes, such as *Strongyloides stercoralis*, for instance; its life cycle illustrates a change between generations of parthenogenetically reproducing parasitic females and free-living sexually reproducing worms. Among sexually reproducing parasites, hermaphroditism is a common strategy, in which individual parasites possess both male and female reproductive organs. This is the case among platyhelminths such as tapeworms and flukes (except the blood flukes, or schistosomes). Hermaphrodites have the great advantage of being capable of reproduction even if they cannot find another member of their species in a host, by self-fertilization.

1.1.4
Parasites and Hosts

In heteroxenous life cycles a distinction is first made between the final host and intermediate host. Sexual reproduction takes place in the **final (definitive) host**. Some confusion in terminology can occasionally arise with this definition;

for plasmodia, for example, the more important host from an anthropocentric viewpoint is the human being. However, fertilization takes place in the mosquito, and hence the insect must be regarded as the definitive host. Another part of the life cycle of parasites takes place in the **intermediate host**, where significant developmental processes or asexual reproduction occur. This is the distinguishing factor between intermediate hosts and pure transmission agents (vectors), which transmit pathogens mechanically (e.g., through the stylets of bloodsucking insects). Several intermediate hosts may be exploited in succession during a life cycle, and these are known as first or second intermediate hosts. In some life cycles, a host individual plays the roles of the final and intermediate hosts simultaneously, as observed in the case of the nematode *Trichinella spiralis*. The trichina reproduces sexually in the gut of its host (final host function), and then forms resting stages in a completely different compartment, the muscle cell (intermediate host function). In many cases, transmission from intermediate to definitive hosts occurs by predation of the former by the latter. The larval stages of some parasites can also be transmitted from smaller to larger intermediate hosts through the food chain, without any significant morphological changes occurring. Such hosts, known as **paratenic hosts**, accumulate the larvae, and their insertion in the life cycle facilitates transmission of these larvae to the definitive host.

At each stage of their life cycle, many parasites are optimally adapted to a particular host species, which may represent their main host in fat, that is, the one they have coevolved with for a long time. On this host, growth and reproduction are optimal and the parasite enjoys a long life cycle. By contrast, living conditions are worse for the parasite in alternative host in fat that nonetheless allow the survival of the parasite, with the result that these hosts play a less significant role in the perpetuation of the life cycle. These alternative hosts, however, may serve as **reservoir hosts** in fat and be of major epidemiological importance – when control measures have been used on the main host, for example, chemotherapy on farm animals, the parasite cycle in wild reservoir hosts cannot be eradicated and a reinfection may take place via these hosts. By contrast, parasite development stages can sometimes occur in a **wrong host** or dead-end host, where no further transmission can take place (e.g., *Toxoplasma gondii* in humans).

One indispensable basis for the establishment of a host–parasite relationship is the **susceptibility** of the host. Susceptibility is essentially determined by the behavioral, physiological, and morphological characteristics of the host, and also by the host's innate and adaptive immune responses. Within a population, therefore, the host genotype often determines the individual degree of susceptibility – certain hosts may thus be predisposed for infection. Acquired characteristics, such as physical condition or age, can also affect an individual host's susceptibility to parasites.

Host **resistance** to a parasitic infection can depend on the immune responses of the host. This becomes clear when a host only becomes susceptible when elements of the immune system are disabled. For example, *Aotus* monkeys – used as experimental animals in malaria vaccine research – can only be reliably infected after splenectomy. However, resistance can also be defined by biochemical factors. *T. brucei,* for instance, is killed by a protein in human serum, which is associated with high-density lipoproteins. **Immunity** is the term used when a past infection leaves behind protective immune responses. In the case of parasitic infections, an existing infection often provides immunity to further infections. A **concomitant immunity** (premunition) like this permits already-established parasites to survive, but leads to the elimination of new infective stages trying to infect the host. This situation can cause parasite density to be downregulated to a tolerable level for the host. Hosts with defective immune systems are often more susceptible to parasites; these hosts may consequently be colonized by **opportunistic pathogens**, which are present only in low densities or not at all in immunocompetent individuals. Such opportunistic parasitic infections are common in AIDS patients – and in many cases, these infections are the direct cause of death. Examples of this are the frequent occurrence of *Toxoplasma gondii*, *Cryptosporidium parvum*, and *Leishmania* species in AIDS patients and other immunocompromised persons.

Parasites can specialize in varying degrees in the way they exploit their hosts. The degree of specialization is expressed in the **host specificity**, which combines the number of host species that can be used at any stage of the life cycle, and the relative prevalence and intensity of infection by the parasite on these hosts. For instance, parasites that can infect only one host species or infect a few host species but achieve high prevalence and intensity on only one of these species have a high degree of host specificity ("narrow host specificity"). Feather lice (Mallophaga, see Section 4.4.2) are one example of highly host specific parasites. They are not only adapted to a particular host species omit – they can only colonize certain parts of the host bird's body (Figure 1.10). Other highly host-specific parasites include omit the larval stages of digeneans (flukes) for their molluscan first intermediate host. By contrast, parasites with wide host specificity can colonize a wide range of hosts successfully, and often achieve high prevalence or intensity of infection on many of these hosts. For example, certain stages of *Trypanosoma cruzi* and *Toxoplasma gondii* exploit almost all mammals as hosts and invade almost all types of the hosts' nucleated cells. Relying on the **host range** combined with information on prevalence and intensity of infection as a measure of specialization can be, however, misleading. Let us consider two related parasite species, A and B, each using four host species and achieving almost equal prevalence and intensity in all their hosts. However, the hosts of parasite A belong to distantly related families, whereas those of parasite B all belong to the same genus. Therefore, we can easily argue that parasite B displays higher host specificity than A, since its hosts are restricted to a narrower phylogenetic spectrum. Host specificity is the outcome of colonization of new hosts and adaptation to these hosts over evolutionary time, and the more host-specific parasites are those that cannot make the large jump necessary to colonize animal species not closely related to their main host. In this context, several parasites have made the "jump" from wild or domestic animals to humans; diseases caused by parasites transmitted between vertebrates and humans under natural conditions are referred to as **zoonoses** (e.g.,

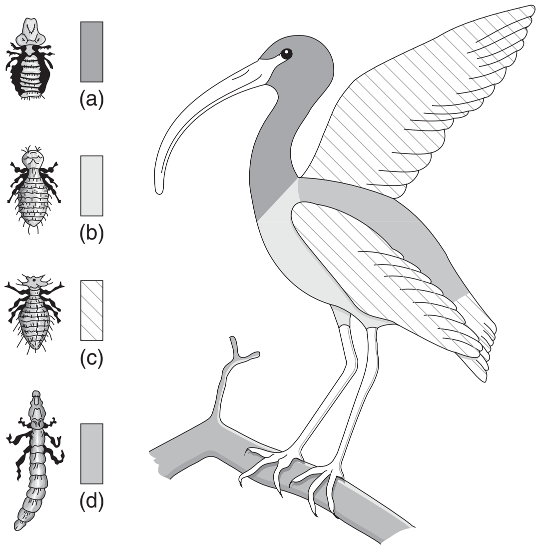


Figure 1.10 Distribution of various Mallophaga species on an Ibis (*Ibis falcinellus*), an example of high specificity for particular habitats on a host individual. (a) *Ibidoecus bisignatus*. (b) *Menopon plegradis*. (c) *Colpocephalum* and *Ferribia* species. (d) *Esthiopterum raphidium*. (From Dogiel, V.A. (1963) *Allgemeine Parasitologie (General Parasitology)*, VEB Gustav Fischer Verlag, Jena.)

T. spiralis, transmission between pigs and humans; and *Taenia saginata*, transmission between cattle and humans).

The establishment of parasites in a susceptible host results in an **infection**. In strict context, this term applies only if an increase in the number of parasites occurs by replication of the original parasite within the host, as in the case of protozoa. However, the term is now widely used in the case of helminths (worms) or arthropod parasites, too, where only one mature parasite develops from each infective larva. The term formerly used for these groups is "infestation." The period during which diagnostically relevant parasite stages appear, such as plasmodia in the blood, is known as **patency**. The period from infection to patency is called **prepatency** or the prepatent period, while the period until the onset of the first symptoms is known as the **incubation period**. For helminth parasites, prepatency corresponds to the period from initial infection of the host to the onset of egg production, when eggs start appearing in the feces or urine of the host; patency then corresponds to the adult life of the worm, from the onset of egg production to its death. In accordance with an international agreement, the infection and the resulting disease are known by the name of the parasite with the suffix -**osis**, for example, toxoplasmosis. However, for many diseases the suffix-iasis is in wide use.

The term used when an infection with the same pathogen occurs after a parasitosis has healed is **reinfection**. An infection contracted in addition to