Modern Parasitology

A TEXTBOOK OF PARASITOLOGY

EDITED BY F. E. G. COX

SECOND EDITION

BLACKWELL
SCIENCE

MODERN PARASITOLOGY

Modern Parasitology

A TEXTBOOK OF PARASITOLOGY

EDITED BY

F. E. G. COX
Professor of Parasite Immunology
King's College London

SECOND EDITION

Blackwell
Science

© 1982, 1993 by
Blackwell Science Ltd
Editorial Offices:
Osney Mead, Oxford OX2 0EL
25 John Street, London WC1N 2BL
23 Ainslie Place, Edinburgh EH3 6AJ
238 Main Street, Cambridge
Massachusetts 02142, USA
54 University Street, Carlton
Victoria 3053, Australia

Other Editorial Offices:
Arnette Blackwell SA
1, rue de Lille
75007 Paris
France

Blackwell Wissenschafts-Verlag GmbH
Kurfürstendamm 57
10707 Berlin
Germany

Feldgasse 13
A-1238 Wien
Austria

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the copyright owner.

First published 1982
Reprinted 1987
Second edition 1993
Reprinted 1994, 1996
Transferred to digital print 2004

Set by Excel Typesetters Company, Hong Kong
Printed and bound in Great Britain by
Marston Book Services Limited, Oxford

DISTRIBUTORS

Marston Book Services Ltd
PO Box 87
Oxford OX2 0DT
(*Orders*: Tel: 01865 791155
Fax: 01865 791927
Telex: 837515)

USA
Blackwell Science, Inc.
238 Main Street
Cambridge, MA 02142
(*Orders*: Tel: 800 215-1000
617 876-7000
Fax: 617 492-5263)

Canada
Oxford University Press
70 Wynford Drive
Don Mills
Ontario M3C 1J9
(*Orders*: Tel: 416 441–2941)

Australia
Blackwell Science Pty Ltd
54 University Street
Carlton, Victoria 3053
(*Orders*: Tel: 03 347-0300
Fax: 03 349–3016)

A catalogue record for this title
is available from the British Library

ISBN 0-632-02585-9

Library of Congress
Cataloging in Publication Data

Modern parasitology: a textbook of parasitology/
edited by F.E.G. Cox. – 2nd ed.
p. cm.
Includes bibliographical references.
ISBN 0-632-02585-9
1. Medical parasitology. I. Cox, Francis E. G.
[DNLM: 1. Parasitic Diseases – drug
therapy. 2. Parasitic Diseases – prevention &
control. 3. Parasites – physiology.
4. Host – Parasite Relations.
QX 4 M6895 1993]
QR251.M66 1993
616.9′6 – dc20

Contents

List of contributors, ix

Introduction, x

1 PARASITIC PROTOZOA, 1
F.E.G. Cox
1.1 Introduction
1.2 Structure and function of protozoa
1.3 Classification of the protozoa
1.4 Kinetoplastid flagellates
1.4.1 Trypanosomes of humans in South America
1.4.2 Trypanosomes of humans in Africa
1.4.3 Trypanosomes of domesticated animals
1.4.4 Other trypanosomes of mammals
1.4.5 *Leishmania*
1.5 Intestinal and related flagellates
1.5.1 Intestinal and related forms in humans
1.5.2 Intestinal and related forms in domesticated animals
1.5.3 Other flagellates
1.6 Parasitic amoebae
1.6.1 *Entamoeba histolytica*
1.6.2 Other intestinal amoebae of humans
1.6.3 Facultative amoebae of humans
1.7 Coccidia
1.7.1 Coccidiosis in domesticated animals
1.7.2 *Toxoplasma* and related coccidia
1.7.3 *Cryptosporidium*
1.8 Malaria parasites
1.8.1 Malaria parasites of humans
1.8.2 Other malaria parasites
1.9 Piroplasms
1.9.1 *Babesia*
1.9.2 *Theileria*
1.10 Microsporidia
1.11 Ciliophora
1.11.1 *Balantidium coli*
1.12 *Pneumocystis*

2 PARASITIC HELMINTHS, 24
P.J. Whitfield
2.1 Introduction
2.2 Structure and function of helminths
2.3 Classification of parasitic helminths
2.4 Platyhelminth parasites of vertebrates
2.4.1 Cestodes
2.4.2 Human cestodiasis
2.4.3 Other cestodes
2.4.4 Digeneans
2.4.5 Human schistosomiasis
2.4.6 Other digeneans
2.5 Nematode parasites of vertebrates
2.5.1 Human intestinal nematodes
2.5.2 Human filariasis
2.5.3 Other human nematode diseases
2.5.4 Other nematodes

3 VECTORS, 53
D.H. Molyneux
3.1 Introduction to vectors
3.2 Flies: Order Diptera
3.2.1 Mosquitoes: Family Culicidae
3.2.2 Blackflies: Family Simuliidae
3.2.3 Sandflies: Family Psychodidae
3.2.4 Tsetse flies: Family Glossinidae
3.2.5 Biting midges: Family Ceratopogonidae
3.2.6 Deer flies: Family Tabanidae
3.3 Bugs: Order Hemiptera
3.4 Ectoparasitic insects
3.4.1 Lice: Order Anoplura
3.4.2 Fleas: Order Siphonaptera
3.5 Ticks: Class Arachnida
3.5.1 Soft ticks: Family Argasidae
3.5.2 Hard ticks: Family Ixodidae
3.6 Molluscs: intermediate hosts of digeneans
3.7 Vector identification and species complexes

4 EPIDEMIOLOGY, 75
R.M. Anderson
4.1 Introduction
4.2 Units of study

4.2.1 The population as a unit of study
4.2.2 Parasitic infection as a unit of study
4.2.3 Measurement of infection within the host population
4.3 Frequency distribution of parasite numbers per host
4.4 Transmission between hosts
4.4.1 Transmission by contact between hosts
4.4.2 Transmission by an infective agent
4.4.3 Transmission by ingestion
4.4.4 Transmission by a biting arthropod
4.5 Regulation of parasite abundance within the host population
4.5.1 The host as the basic unit of study
4.5.2 The parasite as the basic unit of study
4.6 Population dynamics
4.6.1 Transmission thresholds
4.6.2 Microparasites: direct transmission
4.6.3 Microparasites: vector-borne diseases
4.6.4 Macroparasites: direct transmission
4.6.5 Macroparasites: indirect transmission
4.6.6 Breakpoints in parasite transmission
4.7 Climatic factors
4.8 The epidemiological significance of the basic reproductive rate *R*

5 BIOCHEMISTRY, 117
C. Bryant
5.1 Introduction
5.2 Energy metabolism
5.2.1 Environments and life cycles
5.2.2 Energy stores
5.2.3 Regulation of energy metabolism
5.3 Energy metabolism in parasitic protozoa
5.3.1 Electron transport in parasitic protozoa
5.4 Energy metabolism in parasitic helminths
5.4.1 Homolactate fermentation
5.4.2 Malate dismutation
5.4.3 Electron transport in helminths
5.5 Lipids
5.6 Metabolism of nitrogen compounds
5.6.1 Amino acid metabolism
5.6.2 Purines, pyrimidines and their salvage
5.6.3 Nucleic acid metabolism
5.7 Other processes
5.8 Envoi

6 MOLECULAR BIOLOGY AND MOLECULAR GENETICS, 137
D.T. Hart and F.E.G. Cox
6.1 Introduction
6.2 DNA and RNA technology
6.2.1 Introduction to recombinant techniques
6.2.2 Gene cloning
6.2.3 Site-specific mutagenesis
6.2.4 DNA sequencing
6.2.5 DNA amplification
6.3 Gene expression and regulation
6.3.1 Antigenic variation in trypanosomes
6.3.2 Telomeric gene expression
6.3.3 Discontinuous transcription of mRNA
6.3.4 RNA editing in kinetoplastid flagellates
6.3.5 Transfection systems in kinetoplastid flagellates
6.3.6 Homologous gene recombination
6.3.7 Genetic exchange in malaria parasites and trypanosomes
6.4 Chromosomes and gene mapping
6.5 Polypeptide isolation and identification
6.6 Monoclonal antibodies
6.7 Rational drug design
6.7.1 Antiglycosomal drug design
6.7.2 Antitrypanothione metabolism drug design
6.7.3 Mechanisms of drug resistance
6.8 Vaccine development
6.9 Molecular diagnosis and taxonomy
6.9.1 Diagnosis
6.9.2 Taxonomic and systematic relationships
6.10 The future of molecular parasitology

7 PHYSIOLOGY AND NUTRITION, 157
L.H. Chappell
7.1 Introduction
7.2 Survival outside the body of the host and transmission
7.2.1 Cystic stages of parasites
7.2.2 Helminth eggs
7.2.3 Mechanisms for locating the host
7.2.4 Entry mechanisms

7.2.5 Heat shock proteins
7.2.6 Circadian rhythms and parasite transmission
7.3 Establishment and survival within the host
7.3.1 Transformation of digenean cercariae
7.3.2 Hatching and excystation
7.3.3 The role of bile salts in parasite establishment
7.3.4 Hypobiosis
7.3.5 Migration and site selection
7.3.6 Invasion of tissues
7.4 Reproductive physiology
7.4.1 Asexual mechanisms
7.4.2 Sexual reproduction
7.4.3 Reproductive synchrony
7.5 Chemical communication
7.6 Neurophysiology of helminth parasites
7.6.1 Helminth nervous systems
7.6.2 Sense organs and sensory biology
7.6.3 Neurotransmission and neurosecretion
7.6.4 The neuromuscular junction in helminths
7.7 Locomotory physiology
7.7.1 Helminth locomotion for drug assays
7.8 Nutrition of parasites
7.8.1 Nutrient requirements and *in vitro* culture
7.8.2 Nutrient acquisition by parasites
7.8.3 The parasite surface and its role in nutrition
7.8.4 Excretory physiology
7.9 Parasite physiology in a wider context

8 IMMUNOLOGY, 193
F.E.G. Cox
8.1 Introduction
8.2 The immune response
8.2.1 Antibodies
8.2.2 Cell-mediated immunity
8.2.3 Hypersensitivity
8.2.4 Regulation of the immune response
8.3 Immunity to microorganisms
8.4 Animal models and *in vitro* systems
8.5 Immunity to protozoa
8.5.1 Intestinal protozoa
8.5.2 Leishmaniasis
8.5.3 American trypanosomiasis (Chagas disease)
8.5.4 African trypanosomiasis
8.5.5 Coccidiosis
8.5.6 Toxoplasmosis
8.5.7 Malaria
8.5.8 Babesiosis
8.5.9 Theileriosis
8.6 Immunity to helminth worms
8.6.1 Intestinal nematodes
8.6.2 Filariasis
8.6.3 Schistosomiasis
8.6.4 Cestodiasis
8.7 Evasion of the immune response
8.8 Immunopathology
8.9 Immunization against parasitic infections

9 CHEMOTHERAPY, 219
W.E. Gutteridge
9.1 Introduction
9.2 Key current drugs and their limitations
9.2.1 Kinetoplastid protozoa
9.2.2 'Anaerobic' protozoa
9.2.3 Sporozoan protozoa
9.2.4 Digenean worms
9.2.5 Cestode worms
9.2.6 Nematode worms
9.3 Chemical structures of key current drugs
9.4 Biochemistry of drug action
9.4.1 Mechanisms of action
9.4.2 Mechanisms of selective toxicity
9.4.3 Mechanisms of resistance to drugs
9.5 Discovery and development of new drugs
9.5.1 Targets and their validation
9.5.2 Identification of a chemical lead
9.5.3 Overall development process
9.5.4 Drugs in the development pipeline
Appendix

10 CONTROL, 243
D.H. Molyneux
10.1 Introduction
10.2 Components of control
10.2.1 Integrated control of parasitic infections
10.2.2 Objectives of control
10.2.3 Control versus eradication
10.2.4 Diagnosis
10.2.5 The role of primary health care in parasite disease control
10.2.6 Geographical, economic and political variations in control objectives
10.3 Methods of control

10.3.1 Vaccination and chemotherapy
10.3.2 Health education
10.3.3 Control of reservoir hosts and their infections
10.4 Vector control
10.4.1 Insecticides
10.4.2 Vector ecology in relation to control
10.4.3 Insecticide application methods
10.4.4 Mosquito control
10.4.5 Tsetse control
10.4.6 Sandfly control
10.4.7 Triatomine bug control
10.4.8 Blackfly control
10.4.9 Midge control
10.4.10 Control of ticks
10.5 Snail control
10.6 Control of ectoparasites
10.7 Sanitation
Appendix: integrated approaches to control of some parasitic diseases

INDEX, 265

List of Contributors

R. M. ANDERSON FRS *Professor of Zoology and Head of the Department of Zoology, University of Oxford, UK*

C. BRYANT *Professor of Zoology, and Head of the Division of Biochemical and Molecular Biology, Australian National University, Canberra, Australia*

L. H. CHAPPELL *Reader in Zoology, University of Aberdeen, UK*

F. E. G. COX *Professor of Parasite Immunology, King's College, University of London, and Professor of Physic, Gresham College, London, UK*

W. E. GUTTERIDGE *Principal Research Scientist, The Wellcome Foundation Ltd, Beckenham, UK, and Visiting Professor of Biochemical Parasitology, University of Kent, UK*

D. T. HART *Lecturer in Molecular Parasitology, King's College, University of London, UK*

D. H. MOLYNEUX *Director, Liverpool School of Tropical Medicine, and Professor of Tropical Health Sciences, University of Liverpool, UK*

P. J. WHITFIELD *Reader in Parasitology and Head of the Division of Life Sciences, King's College, University of London, UK*

Introduction

Parasites present a continual and unacceptable threat to the well-being of millions of people in the tropics and subtropics and to domesticated animals in all parts of the world and the cost of harbouring parasites in terms of human misery and economic loss is incalculable. Parasitology is the study of parasites and their interactions with their hosts. The science of parasitology has a long history and has its roots in zoology, with its emphasis on the identification and classification of parasites and the elucidation of life cycles, and tropical and veterinary medicine with their concern for the diseases caused by parasites. However, the subject is now so intertwined with microbiology, immunology, cell biology, molecular biology and other aspects of biology and medicine that its limits have become increasingly indistinct.

It was once thought that when a parasite had been identified, implicated as a cause of disease and its life cycle elucidated, its control or eradication would follow with the development of drugs, vaccines and antivector measures. Those who thought this, seriously underestimated the complete hold a parasite has on its host and the intimacy of the relationship between them. Parasites exhibit combinations of biochemical, physiological and nutritional adaptations unique in the animal world and also display a range of mechanisms for evading the immune responses of the host unknown to other pathogens. Their ecology is also far more complex than that of free-living organisms.

Parasites, however, are reluctant to yield up their secrets and, over the last two decades, the various challenges presented have attracted the attention not only of parasitologists but also biochemists, molecular biologists, immunologists, physiologists and epidemiologists as well as those working in the more applied fields of medicine, veterinary medicine and the pharmaceutical industry. Above all, parasitology is a field in which the intellectual rewards of basic and applied research are matched by the potential benefits to be gained.

Parasitology is a very active science with over 20 major journals devoted solely to it and a similar number of books and monographs published each year. The first textbooks of parasitology were essentially zoological and were concerned with detailed descriptions of individual species of parasites with little about the diseases caused. These were soon complemented by books that concentrated on the major parasites of humans and were largely concerned with tropical diseases. Today there are several excellent textbooks that cover the important diseases of humans very well but, inevitably, many important aspects are not considered in such textbooks and areas such as biochemistry, molecular biology, physiology, immunology and epidemiology tend to be the subjects of specialized monographs. Few of these specialized monographs bridge the gap between the traditional texts and recent research developments and this gap has been partially filled by a few multiauthor works that present research findings in a more general context. Inevitably, however, such monographs, excellent as most of them are, tend to be pitched at a level too high for undergraduate courses or those just entering the field of parasitology.

It is against this background that this book has been written and the intention is to introduce the whole of modern parasitology in a succinct and comprehensive way. This book is a direct successor to *Modern Parasitology*, published over 10 years ago, during which time the subject has undergone massive changes as the techniques of

molecular biology and biochemistry, on the one hand, and the powerful tools of mathematical analysis, on the other, have taken over from more traditional approaches. This is, therefore, not really a second edition but an almost completely new version. The first two chapters cover familiar ground and describe, in a condensed form, the most important protozoan and helminth parasites that infect humans and domesticated animals and their laboratory counterparts and the third chapter deals similarly with the vectors involved and fills a major gap which was apparent in the earlier version. Taken together, these three chapters introduce the reader to the parasites and their vectors and provide a framework upon which more detailed information can be built. The fourth chapter, which has largely stood the test of time, covers parasite ecology and epidemiology in the context of modern mathematical concepts and now includes comparisons with infectious diseases caused by organisms other than parasites. The next three chapters deal with the ways in which parasites live and describe their biochemistry, molecular biology and physiology. The biochemistry chapter has been considerably revised, the molecular biology chapter is new and the physiology chapter now embraces nutrition. The eighth chapter, which has been completely rewritten, is concerned with the immunology of parasitic infections in the context of modern immunological concepts and also includes comparisons with other infectious diseases. The ninth chapter presents an up to date coverage of the basic principles of chemotherapy and has been enlarged to cover basic principles as well as the drugs used. The final chapter, which is completely new, is concerned with integrated control programmes and brings together various topics such as chemotherapy, immunization and vector control covered in earlier chapters.

This book is intended mainly for undergraduate students who are advised to read the first three chapters and then, selectively, the others in whatever order interests them or is compatible with the course they are following. Graduate students, and other postgraduate research workers who wish to put their own work into a more general context, are also advised to follow the same approach but can be more selective than undergraduates although, in reality, no area of parasitology is so distinct from any other that it cannot benefit from some comprehension of what is being done elsewhere and why it is being done.

It must be emphasized that this book is intended to be an *introduction* to modern parasitology and, as such, should be read in conjunction with other books, reviews and scientific papers. Each chapter is followed by a selected list of important and accessible references which will guide the reader towards more specific topics. The reader will also need to refer to the more general literature of the subject and some of the textbooks and monographs in the English language currently available are listed below under three headings, general texts, specialized monographs and 'bridging the gap'. Finally, reference is made to two outstanding series, *Advances in Parasitology*, published annually, and *Parasitology Today*, published monthly, both of which are essential reading for all parasitologists.

F.E.G. COX

FURTHER READING

General texts

Ash, L.R. & Orihel, T.C. (1987) *Parasites: A Guide to Laboratory Procedures and Identification*. New York, Raven Press.

Ash, L.R. & Orihel, T.C. (1990) *Atlas of Human Parasitology*, 3rd edn. Chicago, American Society of Clinical Pathologists Press.

Bell, D.R. (1990) *Lecture Notes on Tropical Medicine*, 3rd edn. Oxford, Blackwell Scientific Publications.

Commonwealth Agricultural Bureaux (1989) *Manual of Tropical Veterinary Parasitology* (translation of *Precis de Parasitologie Veterinaire Tropicale*). Wallingford, CAB International.

Cowan, G.O. & Hammond, W. (1991) *Atlas of Medical Helminthology and Protozoology*, 3rd edn. Edinburgh, Churchill Livingstone.

Despommier, D.D. & Karapelin, J.W. (1987) *Parasite Life Cycles*. Berlin, Springer-Verlag.

Katz, M., Despommier, D.D. & Gwadz, R.W. (1989) *Parasitic Diseases*, 2nd edn. New York, Springer-Verlag.

Mehlhorn, H. (ed.) (1988) *Parasitology in Focus*. Berlin, Springer-Verlag.

Muller, R. & Baker, J.R. (1990) *Medical Parasitology*. London, Gower Medical.

Peters, W. & Gilles, H.M. (1989) *A Colour Atlas of*

Tropical Medicine and Parasitology, 3rd edn. London, Wolfe Medical Publications.
Piekarski, G. (1989) *Medical Parasitology*, 3rd edn. Berlin, Springer-Verlag.
Schmidt, G.D. & Roberts, L.S. (1989) *Foundations of Parasitology*, 4th edn. New York, Williams and Wilkins.
Urquhart, G., Armour, J., Duncan, J.L., Dunn, A.M. & Jennings, F. (1987) *Veterinary Parasitology*. London, Longman.
Warren, K.S. & Mahmoud, A.A.F. (eds) (1989) *Tropical and Geographical Medicine*, 2nd edn. New York, McGraw-Hill
Zaman, V. & Keong, L.A. (1990) *Handbook of Medical Parasitology*, 2nd edn. Edinburgh, Churchill Livingstone.

Monographs

Behnke, J.M. (ed.) (1990) *Parasites: Immunity and Pathology*. London, Taylor and Francis.
Bryant, C., Behm, C. & Howell, M.J. (1989) *Biochemical Adaptation in Parasites*. London, Chapman and Hall.
Coombs, G.H. & North, M. (eds) (1991) *Biochemical Parasitology*. London, Taylor and Francis.
Esch, G.W., Bush, A.O. & Aho, J.M. (eds) *Parasite Communities: Patterns and Processes*. London, Taylor and Francis.
Hyde, J.E. (1990) *Molecular Parasitology*. Milton Keynes, Open University Press.

Bridging the gap

Englund, P.T. & Sher, A. (eds) *The Biology of Parasitism: A Molecular and Immunological Approach*. New York, Alan R. Liss.
McAdam, K.P.W.J. (ed.) (1990) *New Strategies in Parasitology*. Edinburgh, Churchill Livingstone.
Wyler, D. (ed.) (1990) *Modern Parasite Biology: Cellular, Molecular and Immunological Aspects*. New York, W.H. Freeman.

Parasitological journals

Papers on various aspects of parasitology are published in a variety of journals and for some ideas of the range used by parasitologists, reference should be made to one of the abstracting journals listed below. There are a number of journals devoted to parasitological topics and the journals in English most frequently cited are listed below:

Acta Tropica
American Journal of Tropical Medicine and Hygiene
Annals of Tropical Medicine and Parasitology
Experimental Parasitology
International Journal for Parasitology
Journal of Helminthology
Journal of Parasitology
Molecular and Biochemical Parasitology
Parasite Immunology
Parasitology
Parasitology Today
Systematic Parasitology
Transactions of the Royal Society of Tropical Medicine and Hygiene
Tropical Medicine and Parasitology
Veterinary Parasitology
Parasitology Research

Advances in Parasitology (published annually)

Abstracting journals

Protozoological Abstracts
Helminthological Abstracts
Tropical Diseases Bulletin

Between them, these three publications abstract over 1000 journals each year and provide a virtually complete data base of the available parasitological literature. They are also available on various data retrieval systems and on discs.

Chapter 1 / Parasitic Protozoa

F. E. G. COX

1.1 INTRODUCTION

There are over 45 000 named species of protozoa now living of which nearly 10 000 are parasitic in invertebrates and in almost every species of vertebrate. It is, therefore, hardly surprising that humans and their domesticated animals should act as hosts to protozoa, but the diseases thus caused are out of all proportion to the number of species involved. The protozoa that infect humans range from forms that are never pathogenic to those that cause malaria, sleeping sickness, Chagas disease and leishmaniasis, now regarded as being among the major diseases of tropical countries, and which together threaten over one-quarter of the population of the world. In domesticated animals, nagana and theileriosis take a major toll of cattle in Africa and coccidiosis, in its various forms, presents a continual threat to poultry and cattle throughout the world, particularly under conditions of intensive rearing. Even fish and invertebrates suffer from a variety of protozoan infections which create major problems for those trying to raise these animals for food.

Protozoa lie between the prokaryotic and higher eukaryotic organisms and share some of the characteristics of each. They are small, have short generation times, high rates of reproduction and a tendency to induce immunity to reinfection in those hosts that survive. These are features of infections with microparasites such as bacteria. On the other hand, protozoa are undoubtedly eukaryotic cells with organelles and metabolic pathways akin to those of the host. They have also evolved numerous adaptations that allow them to survive in their hosts and, in particular, to counteract or evade the immune response. For this reason, infections with parasitic protozoa are not short-lived as with most bacteria.

1.2 STRUCTURE AND FUNCTION OF PROTOZOA

Protozoa are unicellular eukaryotic cells measuring 1–150 μm, the parasitic forms tending towards the lower end of this range. Structurally, each protozoan is the equivalent of a single metazoan cell with its plasma membrane, nucleus, nuclear membrane, chromosomes, endoplasmic reticulum, mitochondria, Golgi apparatus, ribosomes and various specialized structures adapted to meet particular needs. Parasitic protozoa are in no way simple or degenerate forms, and their particular adaptions frequently include complex life cycles and specialized ways of entering their hosts and maintaining themselves therein. Their nutrition, physiology and biochemistry are largely geared to the parasitic habit and are specialized rather than degenerate. Sexual reproduction also occurs in some protozoa and, in the parasitic forms, is particularly important in the sporozoans in which it provides for apparently limitless variation and adaptability. These topics are discussed in more detail in Chapters 5 and 7.

1.3 CLASSIFICATION OF THE PROTOZOA

The small size of protozoa coupled with the fact that they consist of single cells with few obvious morphological features means that their classification has had to be based on a wide range of characteristics including variations in life cycles, details of fine structure and, increasingly at the species level, biochemical and molecular differences.

At one time the protozoa were regarded as a phylum within the kingdom Animalia but protozoologists now believe that the group is not a natural one but contains members that could be

classified with animals, plants or fungi. Accordingly the concept of Protozoa as a taxon has disappeared and the term is applied to the animal-like members of the kingdom Protista. There are many arguments concerning the relationships between the various taxonomic groups within the protozoa but these do not need to concern parasitologists whose main interest is in having a simple and consistent framework within which to work. The classification outlined here is essentially a simplified version of that used by Sleigh (1989) and Cox (1992) but is compatible with those used in standard parasitological textbooks such as Mehlhorn (1988) and Schmidt and Roberts (1989) (see Introduction).

Traditionally, the protozoa have been divided into four major groups distinguished by their mode of locomotion: the flagellates, which move by means of flagella; the amoebae, by pseudopodia; the ciliates, by cilia; and the sporozoans lacking any obvious means of locomotion. Following the example of Sleigh (1989) these groups will be retained here simply as convenient and traditional categories. An abbreviated outline classification of the protozoa is given in Table 1.1 in which the most important parasites are listed under their phyla and orders.

Table 1.1 An outline classification of the parasitic protozoa

KINGDOM PROTISTA (Single-celled eukaryotic organisms)

Group 1 The flagellated protozoa (Locomotion by flagella)

PHYLUM KINETOPLASTA (1–2 flagella, kinetoplast present)
Order Trypanosomatida, e.g. *Leishmania, Trypanosoma*

PHYLUM METAMONADA
Order Retortamonadida, e.g. *Chilomastix, Retortamonas*
Order Diplomonadida, e.g. *Enteromonas, Giardia*

PHYLUM PARABASALIA
Order Trichomodadida, e.g. *Dientmoeba, Histomonas, Trichomonas*

Group 2 The amoeboid protozoa (Locomotion by pseudopodia)

PHYLUM RHIZOPODA
Order Euamoebida, e.g. *Entamoeba*

Group 3 The spore forming protozoa (No obvious means of locomotion)

PHYLUM SPOROZOA (= Apicomplexa)
Order Eimeriida, e.g. *Eimeria, Isospora, Sarcocystis, Toxoplasma*
Order Haemosporidida, e.g. *Plasmodium*
Order Piroplasmida, e.g. *Babesia, Theileria*

PHYLUM MICROSPORIDIA
Order Microsporidida, e.g. *Encephalitozoon, Nosema*

Group 4 The ciliated protozoa (Locomotion by cilia)

PHYLUM CILIOPHORA
Order Trichostomatida e.g. *Balantidium*

1.4 KINETOPLASTID FLAGELLATES

The kinetoplastid flagellates are characterized by the possession of a unique organelle called the kinetoplast which contains DNA and is an integral part of the mitochondrial system. The kinetoplast is situated near the base of the flagellum and is easily seen in stained preparations. Kinetoplastid flagellates are found in invertebrates and vertebrates, the genera in mammals being *Leishmania, Trypanosoma* and *Endotrypanum* which are transmitted by insects. The typical form is an elongated organism, called a promastigote, with a kinetoplast and a flagellum at the anterior end. Variations of this form are brought about by the migration of the kinetoplast–flagellum complex within the body of the flagellate associated with changes in the mitochondrial system. The forms in the life cycle of a kinetoplastid flagellate are shown in Fig. 1.1.

1.4.1 Trypanosomes of humans in South America

Trypanosoma cruzi (Figs 1.2a, 1.3a) infects 11–12 million people in South and Central America and is infective to about 100–150 species of wild and domesticated mammals. It is not at all certain how many of these act as reservoirs of human infection but the armadillo is very important as in this host the infections are long-lived. The vectors are bugs belonging to the family Reduvi-

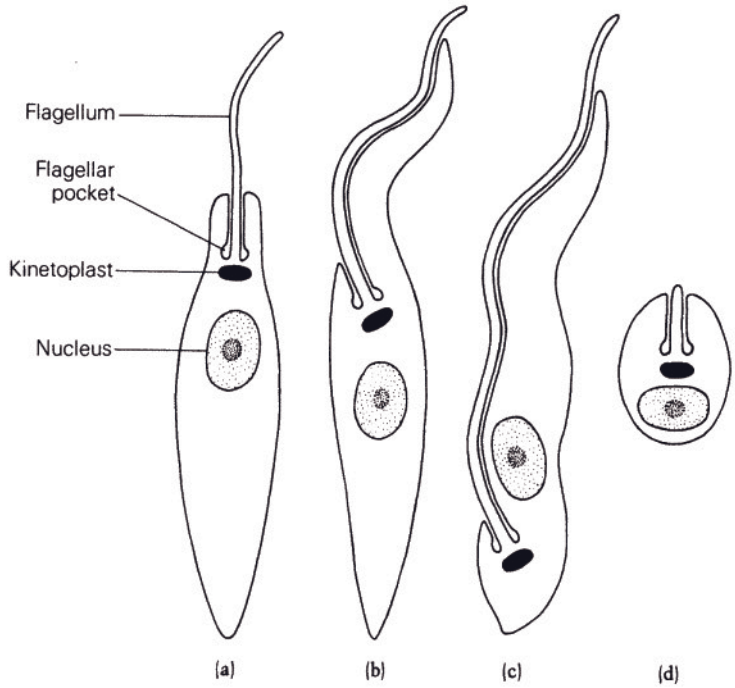


Fig. 1.1 Forms in the life cycle of a kinetoplastid flagellate.
(a) Promastigote. (b) Epimastigote.
(c) Trypomastigote.
(d) Amastigote.

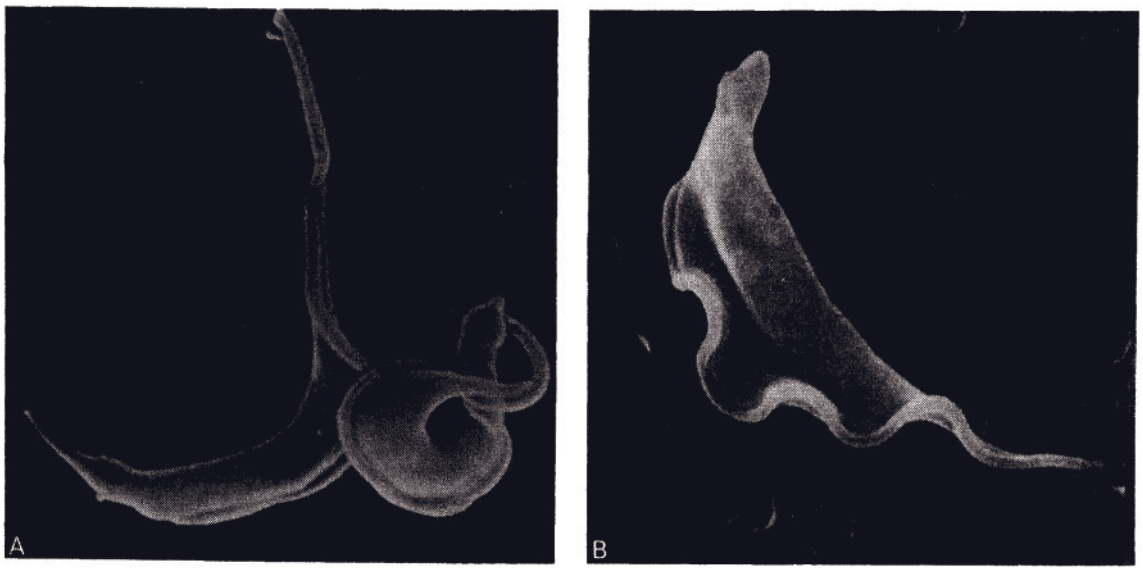


Fig. 1.2 Scanning electronmicrographs of (A): *Trypanosoma cruzi* and (B): *T. brucei*. ×2340. (Photograph (A) kindly given by Dr. D. Snary and (B) by Professor K. Vickerman.)

idae of which three genera are important in the spread of the human disease. When the bug takes up infected blood the trypanosomes multiply in the epimastigote form in the hind gut and infective or metacyclic forms are passed out with the faeces. These infect the human host if they are rubbed into the bite, another wound or the conjunctiva of the eye. Within the human host, the

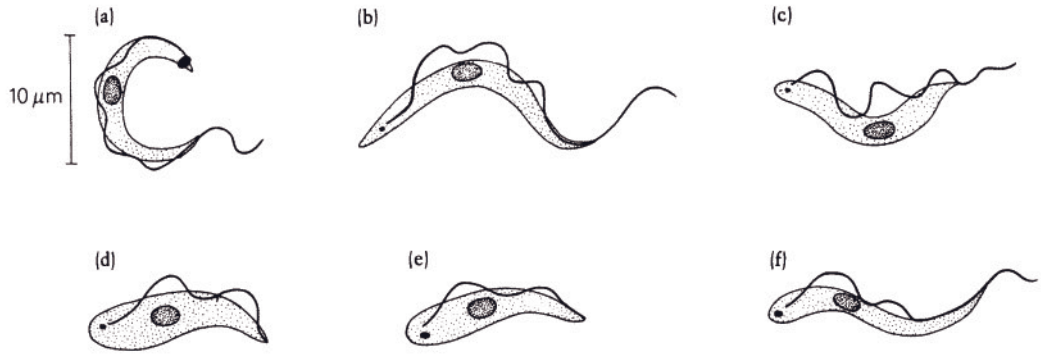


Fig. 1.3 Trypanosomes from the blood of experimentally infected mice. (a) *Trypanosoma cruzi*. (b) *T. brucei rhodesiense* slender from. (c) *T.b. rhodesiense* intermediate form. (d) *T.b. rhodesiense* stumpy form. (e) *T. congolense*. (f) *T. vivax*. All drawn from Giemsa stained slides.

trypanosomes enter various cells, particularly macrophages, muscle and nerve cells, where they round up and multiply in the amastigote form. The amastigotes develop into trypomastigotes that either enter new cells or are taken up when a vector feeds. The disease is called Chagas disease and takes various forms depending on where the amastigotes develop, the most serious consequences being cardiac failure due to parasites in the heart muscles or the loss of the nervous control of the alimentary canal due to parasites in the nervous system.

1.4.2 Trypanosomes of humans in Africa

In contrast to the American trypanosomes the African trypanosomes typically develop in the midgut of the vectors, which are tsetse flies belonging to the family Glossinidae, and are injected from the salivary glands when the fly feeds. Two subspecies infect humans, *T. brucei gambiense* and *T.b. rhodesiense* (Fig. 1.3b–d) the former in riverine conditions in West and Central Africa where it causes chronic sleeping sickness, and the latter in the savanna of East Africa where it causes acute sleeping sickness, although the distinctions between these two forms of the disease are blurred. Both *T.b. gambiense* and *T.b. rhodesiense* can infect a range of mammalian hosts and some of these are important reservoirs of *T.b. rhodesiense*. Natural reservoirs of *T.b. gambiense* seem to be less important because the infection is essentially a human–human one although pigs may be a source of human infection in some places. The vector of human sleeping sickness is the tsetse fly, *Glossina*; the wet flies of the *G. palpalis* group transmit *T.b. gambiense* and dry flies of the *G. morsitans* group transmit *T.b. rhodesiense* but, again, these distinctions are not absolute. The life cycles of these parasites are the same as that of *T.b. brucei* which is described in Fig. 1.4. The main cause of sleeping sickness as a disease is the invasion of the nervous system by the trypanosomes.

1.4.3 Trypanosomes of domesticated animals

Trypanosomiasis is endemic throughout the tsetse belt of Africa, an area of some 10 million square kilometres. The disease, which is commonly known as nagana, embraces a variety of different manifestations – but usually involves fever, anaemia, lack of appetite and wasting – and causative organisms (see Table 1.2), the three most important of which are *T. congolense*, *T. vivax* (Fig. 1.3e, f) and *T.b. brucei*. *Trypanosoma congolense* is confined to the vascular system and is a particularly important pathogen of cattle although it also affects other animals and can be transmitted by most species of *Glossina*. *Trypanosoma vivax* is also a blood parasite and, like *T. congolense*, is extremely pathogenic in cattle. *Trypanosoma vivax* can be transmitted mechanically by flies that bite and has spread

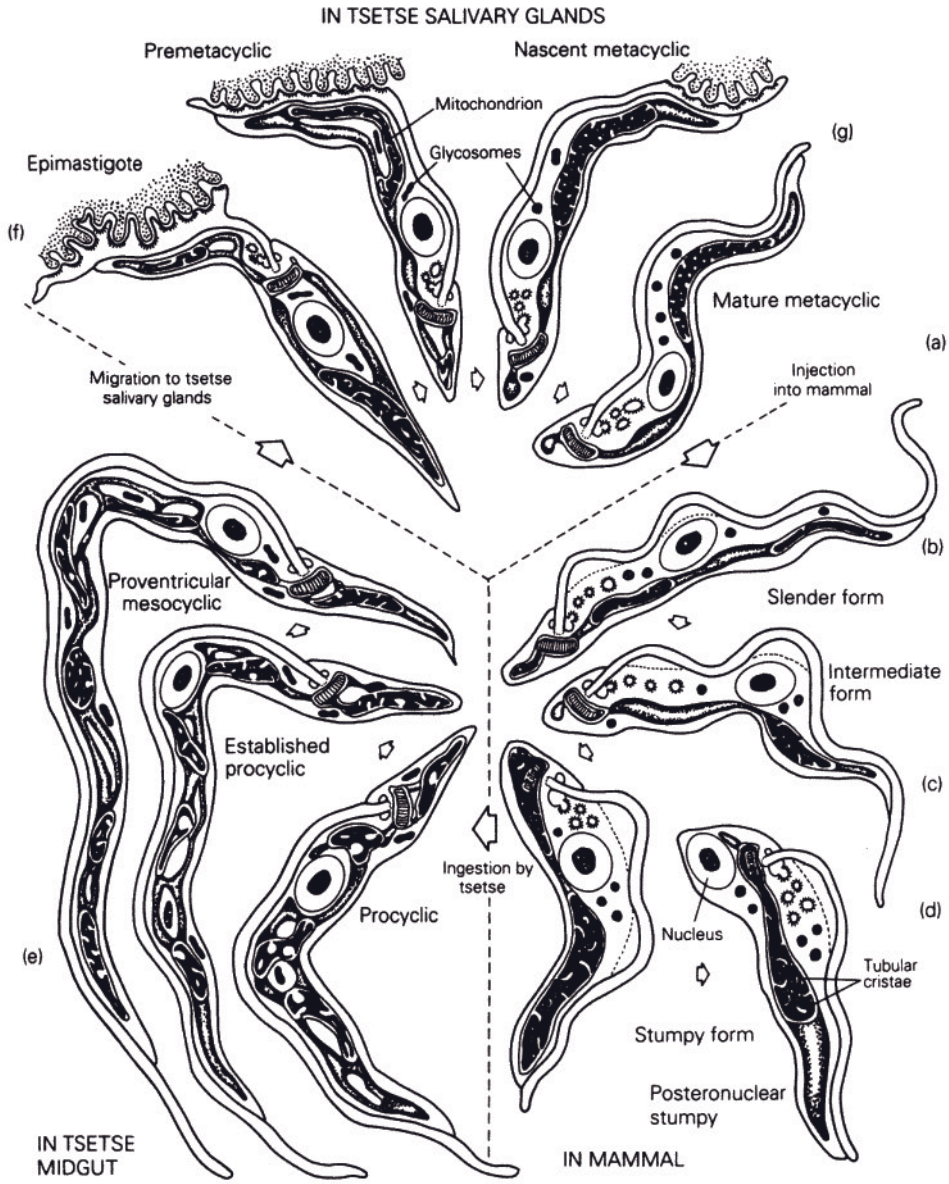


Fig. 1.4 The life cycle of *Trypanosoma brucei*. The infection begins when trypanosomes are injected into the blood of a mammal by a tsetse fly when it feeds (a). The slender forms multiply by binary fission (b) until large numbers build up in the blood and the trypanosomes transform first into intermediate (c) and then stumpy (d) forms that are infective to a tsetse fly. In the slender forms, the mitochondrion is inactive but begins to become active in the stumpy forms. In the midgut of the tsetse fly, the trypanosomes begin to undergo division (e) and then enter the proventriculus and salivary glands where they assume the epimastigote form (f) and undergo further division. The forms in the salivary glands infective to the mammal are known as metacyclic forms (g). In the tsetse fly, the mitochondrion is fully active. The blood stream forms are covered with a glycoprotein coat which is lost in the midgut of the tsetse fly and is reformed in the salivary glands. (After K. Vickerman 1985, *British Medical Bulletin*, **41**, p. 107 and reproduced by permission of the publishers, Churchill Livingstone, Edinburgh.)

Table 1.2 Trypanosomes of humans and domesticated animals

Subgenus	Species	Main hosts	Main reservoirs	Vectors	Disease	Main distribution
STERCORARIA						
Megatrypanum	*theileri*	Cattle		Tabanid flies	None	Cosmopolitan
Herpetosoma	*rangeli*	Humans, cat, dogs		Triatomid bugs	None	Central and S. America
Schizotrypanum	*cruzi*	Humans	150 species of mammals	Triatomid bugs	Chagas disease	Central and S. America
SALIVARIA						
Duttonella	*vivax*	Cattle, sheep, goats, etc.	Various wild mammals	Tsetse flies	Nagana	Africa
	vivax	Cattle		Tabanid flies	Huequera	S. America
	uniforme	Cattle	Wild ruminants	Tsetse flies	None or mild	Central and E. Africa
Nannomonas	*congolense*	Cattle, sheep, goats, etc.	Wild ruminants	Tsetse flies	Nagana	Africa
	simiae	Pigs	Warthogs	Tsetse flies	Acute in pigs	Central and E. Africa
Pycnomonas	*suis*	Pigs	Wild pigs	Tsetse flies	Acute in young	Central and E. Africa
Trypanosoma	*brucei brucei*	Equines, sheep, goats, etc.	Wild game	Tsetse flies	Nagana	Africa
	brucei rhodesiense	Humans	Wild game	Tsetse flies	Sleeping sickness	E. Africa
	brucei gambiense	Humans	Pigs	Tsetse flies	Sleeping sickness	W. Africa
	evansi	Horses, camels, etc.	Wild mammals	Tabanid flies	Surra	N. Africa, Asia, Middle East
	evansi	Equines	Wild mammals	Tabanid flies	Mal de caderas	Central and S. America
	equiperdum	Equines		Venereal contact	Dourine	Africa, Middle East

outside the tsetse belt not only in Africa but also to South America where it was imported with cattle from the Old World. The third important trypanosome is *T. brucei brucei* which has been extensively studied particularly as a model for human trypanosomiasis (see Fig. 1.4 for the life cycle). *Trypanosoma brucei brucei* is essentially a tissue parasite, living in subcutaneous and connective tissue but also appearing in the blood (Fig. 1.2b). *Trypanosoma brucei brucei* causes serious disease in horses and camels but also infects cattle. Among the other trypanosomes of domesticated animals are *T. uniforme*, which resembles *T. vivax* but generally causes mild infections, *T. simiae* which resembles *T. congolense* in pigs, and *T. suis* also in pigs but a rather rare parasite.

The *T.b. brucei* group of trypanosomes provide an interesting example of evolution in action. Not only has the basic form given rise to the human forms *T.b. gambiense* and *T.b. rhodesiense*, it has also given rise to *T. evansi* which is no longer cyclically transmitted but is passed from animal to animal on the mouthparts of biting flies and even vampire bats in South and Central America. The vampire bat can also be infected with *T. evansi* and thus acts as both host and vector. The parasite formerly called *T. equinum* in South America is now regarded as a synonym for *T. evansi*. *Trypanosoma equiperdum* has dispensed with a vector altogether and is transmitted between horses as a venereal disease. The success of this method of transmission can be seen from the fact that *T. equiperdum* has spread as a disease of horses, donkeys and mules from South and North-West Africa, Syria, Turkey and parts of Asia but has been eradicated from Europe, America, India and most of Asia.

1.4.4 Other trypanosomes of mammals

As well as the trypanosomes described above there are a number of non-pathogenic species that are commonly found in mammals. These include *T. theileri* in cattle, which is transmitted by horse flies, and *T. melophagium* in sheep and sheep keds. *Trypanosoma rangeli*, which occurs in a number of mammals including humans, primates, cats and dogs in Central and South America, is transmitted by bugs and, although the parasite is quite different from *T. cruzi*, the two are occasionally confused. *Trypanosoma rangeli* is harmless in its vetebrate host but may be harmful in the bug. Rodents are frequently infected with trypanosomes transmitted by fleas. Two species, *T. lewisi* in rats and *T. musculi* in mice, are widely used in laboratory studies.

1.4.5 *Leishmania*

The leishmanial parasites exhibit only two forms in their life cycles; amastigotes (Fig. 1.5a) in macrophages of the mammalian host and promastigotes (Fig. 1.5b) in the gut of the vector which is a sandfly (Diptera, Psychodidae). *Leishmania* species cause serious diseases in humans.

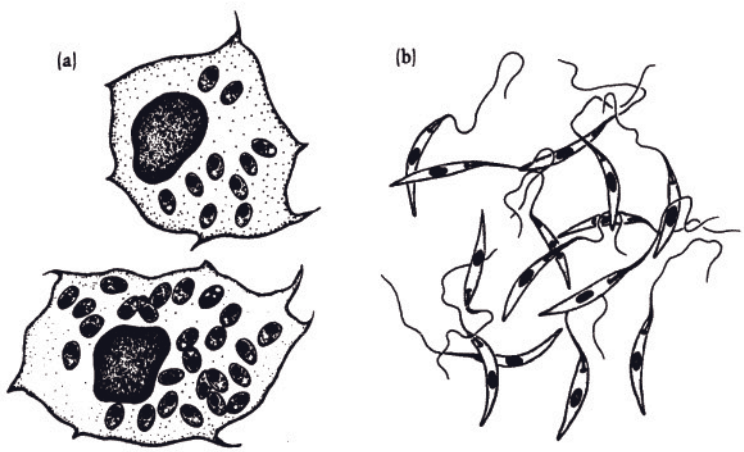


Fig. 1.5 *Leishmania major*. (a) Amastigote forms in macrophages. (b) Promastigote forms from culture, these forms are equivalent to those that occur in the sandfly. Drawn from Giemsa stained slides. (After, World Health Organization (1984) *The Leishmaniases. Technical Report Series No. 701* and reproduced by permission of the World Health Organization.)

Table 1.3 The main species of *Leishmania* that cause human disease

Species	Disease	Distribution	Reservoir	Vector
OLD WORLD				
L. tropica	Dry cutaneous; urban	Europe, Asia, N. Africa	Dogs	*Phlebotomus*
L. major	Wet cutaneous; rural	Asia, Africa	Rodents	*Phlebotomus*
L. aethiopica	Dry cutaneous; diffuse	Ethiopia, Kenya	*Hyrax*	*Phlebotomus*
L. donovani	Visceral (kala-azar)	Africa, Asia	–	*Phlebotomus*
L. infantum	Infantile visceral	Mediterranean	Dogs, foxes	*Phlebotomus*
NEW WORLD				
L. mexicana	Cutaneous	Central America	Rodents	*Lutzomyia*
L. amazonensis	Cutaneous	Brazil	Rodents, etc.	*Lutzomyia*
L. pifanoi	Cutaneous	Venezuela	Rodents	*Lutzomyia*
L. venezuelensis	Cutaneous	Venezuela	?	*Lutzomyia*
L. braziliensis	Mucocutaneous	Brazil	Rodents	*Lutzomyia*
L. guyanensis	Cutaneous	S. America	?	*Lutzomyia*
L. panamensis	Cutaneous	Panama	Sloths, etc.	*Lutzomyia*
L. peruviana	Cutaneous	S. America	Dogs	*Lutzomyia*
L. chagasi	Visceral	S. America	Foxes	*Lutzomyia*

The typical infection is cutaneous but in many species, and in particular individuals, the parasites may invade subcutaneous or deeper tissues causing hideous and permanent disfiguration. The most serious disease, kala-azar, involves the macrophages of organs such as the liver. Leishmaniasis is now known to be caused by a complex of species and subspecies. As the morphology of all these parasites is similar, the identification of species and subspecies tends to be based on isoenzyme and DNA techniques. The classification of these parasites is still in a state of flux following a change of emphasis away from morphological and disease-associated characteristics towards biochemical and molecular criteria. The most widely used scheme is summarized in Table 1.3. The approach favoured here is to accept a number of species rather than the subspecies used in earlier classifications but the various systems are compatible. There are also several other species recorded from South America, including *L. lainsoni*, *L. naiffi* and *L. shawi* that infect humans and *L. enriettii*, *L. hertigi*, *L. deanei* and *L. aristidesi* that are found only in wild animals. In the Old World, the main species causing cutaneous leishmaniasis are *L. tropica* and *L. major* and the species causing visceral leishmaniasis is *L. donovani*. In the New World *L. chagasi* causes visceral leishmaniasis but cutaneous and mucocutaneous leishmaniasis are caused by several species including *L. braziliensis*, *L. mexicana* and *L. peruviana*. A number of species of *Leishmania* have been isolated from hosts other than humans.

1.5 INTESTINAL AND RELATED FLAGELLATES

A number of flagellates occur in the alimentary canals of humans and domesticated animals and similar species are found in laboratory animals. In most cases, the life cycles are very simple and involve the ingestion of food or water contaminated with encysted forms which excyst in the intestine where multiplication by binary fission takes place. Large infestations can build up but the infections are seldom harmful although some may cause gastro-intestinal disorders. Flagellates similar to those in the intestine can occur in other parts of the body, such as the urinogenital system, and these may cause more serious infections.

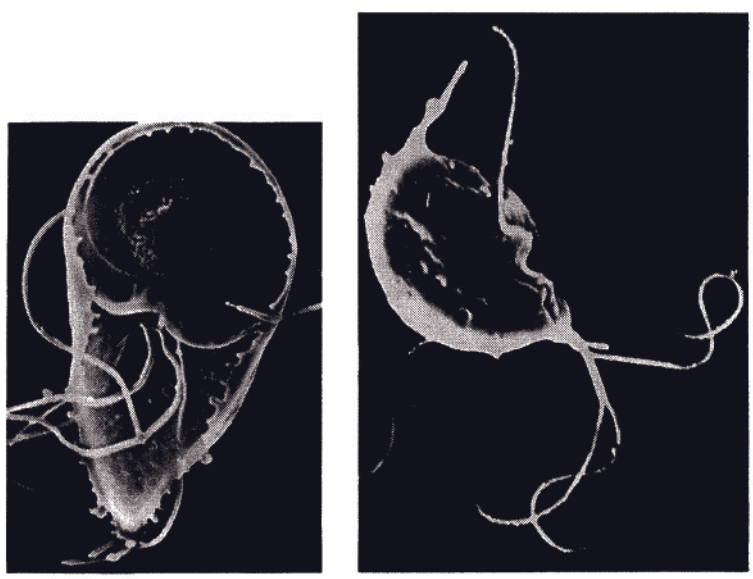
1.5.1 Intestinal and related forms in humans

Eight species of flagellate are ubiquitous and common parasites of the human gastro-intestinal

Table 1.4 Intestinal amoebae and flagellates and related forms in humans

Species	Cysts	Site	Pathology
Entamoeba histolytica	[C]	Colon/liver	Ulceration, diarrhoea
E. hartmanni	[C]	Colon	None
E. coli	[C]	Colon	None
E. gingivalis	–	Mouth	Gingivitis
Endolimax nana	[C]	Colon/caecum	None
Iodamoeba buetschlii	[C]	Colon/caecum	None
Trichomonas vaginalis	–	Vagina/urethra	Vaginitis, urethritis
T. tenax	–	Mouth	None
T. hominis	–	Colon	None
Dientamoeba fragilis	–	Colon/caecum	None
Giardia duodenalis	[C]	Duodenum	Diarrhoea
Retortamonas intestinalis	[C]	Colon/caecum	None
Enteromonas hominis	[C]	Colon/caecum	None
Chilomastix mesnili	[C]	Colon/caecum	None

tract or urinogenital system (Table 1.4). Few do any real harm but some occasionally give rise to unpleasant symptoms which can usually be easily treated. *Giardia duodenalis* (Fig. 1.6a) which is also known as *G. lamblia*, *G. intestinalis* or *Lamblia intestinalis*, is found in the upper part of the small intestine where large infestations may cause malabsorption particularly in children. The overall prevalence is usually 1–30% but can reach 70% in unsanitary institutions. It is not known for certain whether there is a reservoir host. Three species of *Trichomonas* are common in all parts of the world: *T. hominis* occurs in the caecum and large



(a) (b)

Fig. 1.6 Scanning electronmicrographs of (a) *Giardia duodenalis* and (b) *Trichomonas vaginalis*. The sucking disc of *Giardia* and the undulating membrane of *Trichomonas* are characteristic features. (a) ×2520, (b) ×1260. (Both photographs kindly given by Professor V. Zaman.)

intestine, *T. tenax* in the mouth and *T. vaginalis* (Fig. 1.6b) in the vagina and urethra of women and in the urethra, seminal vesicles and prostate of men. *Trichomonas vaginalis* may cause inflammation and discharge and is an increasingly important venereal disease afflicting some 180 million women. These trichomonads do not form cysts: *T. hominis* forms rounded resistant stages while *T. vaginalis* and *T. tenax* are transmitted by direct contact. *Retortamonas intestinalis* is a cosmopolitan species, shared with pigs and primates, in the caecum and colon of 1–10% of humans and it is occasionally associated with mild diarrhoea. *Enteromonas hominis* is cosmopolitan and harmless. *Chilomastix mesnili* is rare and harmless. *Dientamoeba fragilis* is transmitted through the eggs of the pinworm *Enterobius vermicularis* and may cause diarrhoea.

1.5.2 Intestinal and related forms in domesticated animals

The most important intestinal flagellates are found in birds and include *Histomonas meleagridis* which occurs as an amoeboid form in the cells of the small intestine and liver and as a flagellated form in the caecum of chickens and turkeys throughout the world. In turkeys it causes a serious disease, blackhead, which may kill 50–100% of young birds. Transmission is via the eggs of the caecal nematode *Heterakis gallinarum*. *Tetratrichomonas gallinarum*, also known as *Trichomonas gallinarum* or *T. pullorum*, occurs in the caecum and liver of chickens, turkeys and other gallinaceous birds throughout the world but is not a serious pathogen. *Spironucleus meleagridis*, also known as *Hexamita meleagridis*, is found in the duodenum and small intestine of turkeys and causes catarrhal enteritis in young birds. *Trichomonas gallinae* occurs in the upper digestive tract of pigeons and occasionally chickens and turkeys where it is usually harmless but may cause serious disease if the parasites invade other parts of the body, such as the brain.

In cattle, the most important, flagellate is *Trichomonas foetus*, sometimes called *Tritrichomonas foetus*. It is a parasite of the genital organs of cattle throughout the world. In the bull it is harmless but in cows may cause early abortion resulting in the loss of 50–100% of calves. Transmission is by direct contact and, as bulls never lose the infection and treatment is unreliable, control can be effected by the use of artificial insemination using uninfected donors.

1.5.3 Other flagellates

A variety of flagellates commonly occur in wild, domesticated and laboratory animals throughout the world. Mice, for example harbour species of *Giardia*, *Spironucleus (Hexamita)* and *Trichomonas* and the first two may be pathogenic in laboratory colonies.

1.6 PARASITIC AMOEBAE

Six species of amoebae are common in humans in most parts of the world but only one, *Entamoeba histolytica*, is an important pathogen.

1.6.1 *Entamoeba histolytica*

This parasite occurs throughout the world in humans, apes, monkeys, dogs, cats and rats. The trophozoite, or feeding stage (Fig. 1.7a) inhabits the lower small intestine and colon where it multiplies by binary fission and forms characteristic four-nucleated cysts (Fig. 1.7b) which are passed

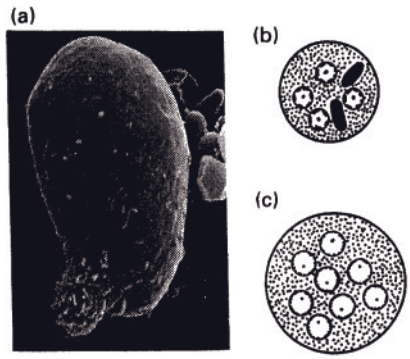


Fig. 1.7 Parasitic amoebae. (a) Trophozoite of *Entamoeba histolytica* ×1325 (scanning electronmicrogaph kindly given by Professor V. Zaman). (b) *Entamoeba histolytica* cyst and (c) *E. coli* cyst drawn from stained slides.

out and subsequently ingested in contaminated food or water. Sometimes the amoebae invade the mucosa and submucosa and may be carried via the portal vein to the liver and other parts of the body. Considerable damage may be caused in the wall of the bowel or in the liver. In most people, there is no tissue invasion and the parasite causes no harm. The symptoms following the invasion of the tissues are variable but usually include diarrhoea or dysentery with the loss of blood (amoebic dysentery). In Europe and the USA the prevalence of *E. histolytica* is less than 5% and overt symptoms are rare but in many parts of the tropics and subtropics the prevalence is more than 50% and dysentery and liver involvement may be common.

1.6.2 Other intestinal amoebae of humans

There are four other amoebae commonly found all over the world. *Entamoeba hartmanni*, once regarded as a small form of *E. histolytica*, resembles the pathogenic form but has smaller cysts. *Entamoeba coli* (Fig. 1.7c) is the most common amoeba in humans and has cysts with eight nuclei. *Endolimax nana* inhabits the upper part of the colon and has four-nucleate cysts. *Iodamoeba buetschlii* has cysts with a single nucleus. None of these four parasites is pathogenic.

1.6.3 Facultative amoebae of humans

There have been occasional reports of free-living amoebae infecting humans, sometimes with fatal results. Several species of *Acanthamoeba* can cause upper respiratory tract infections in immunocompromised individuals. *Acanthamoeba* species also act as reservoirs for *Legionella pneumophilia*, the causative agent of legionellosis. *Naegleria fowleri* and other *Naegleria* species, which are strictly speaking flagellates, have been implicated in primary meningoencephalitis in otherwise healthy individuals.

1.7 COCCIDIA

The coccidia are very common parasites mainly of the intestinal tracts of vertebrates. Some are major pathogens of domesticated animals and losses attributed to them run into millions of pounds or dollars each year. The life cycle usually involves one host and is shown in Fig. 1.8. There are a number of minor variations to this basic pattern mainly relating to the site of the infection and the number of schizogonic generations. The genera are identified on the morphology of the infective stage or oocyst. Each oocyst contains a number of sporocysts each containing sporozoites. In the two most important genera, the oocysts of *Eimeria* contain four sporocysts while those of *Isospora* contain two. Certain parasites with isosporan features have two hosts in their life cycles and these will be discussed in Section 1.7.2.

1.7.1 Coccidiosis in domesticated animals

Coccidia are extremely common in domesticated animals and some cause very serious diseases. Coccidia normally have self-limiting infections followed by the acquisition of immunity to reinfection. Under natural conditions, animals become infected with small numbers of oocysts and are only mildly affected by the infection. Under crowded conditions, such as those existing in batteries, large numbers of oocysts may be ingested causing severe or fatal infections, particularly in young animals. The actual pathological effects produced depend to a large extent on the number of oocysts ingested. It is therefore difficult to attribute pathogenicity to particular species and, as the species are extremely difficult to identify, there is considerable controversy about the number of species that exist in any given host and exactly how important one particular species may be. A list of the more important and widely accepted species of *Eimeria* is given in Table 1.5. The species in rodents, *E. nieschulzi* and *E. falciformis*, are widely used in experimental investigations. The life cycle of a typical member of the genus *Eimeria* is shown in Fig. 1.8.

1.7.2 *Toxoplasma* and related coccidia

Until 1970, all coccidians with two sporocysts in the oocyst were classified as *Isospora* species and it was assumed that all had simple life cycles in a single host like that of *Eimeria*. Since 1970, it has

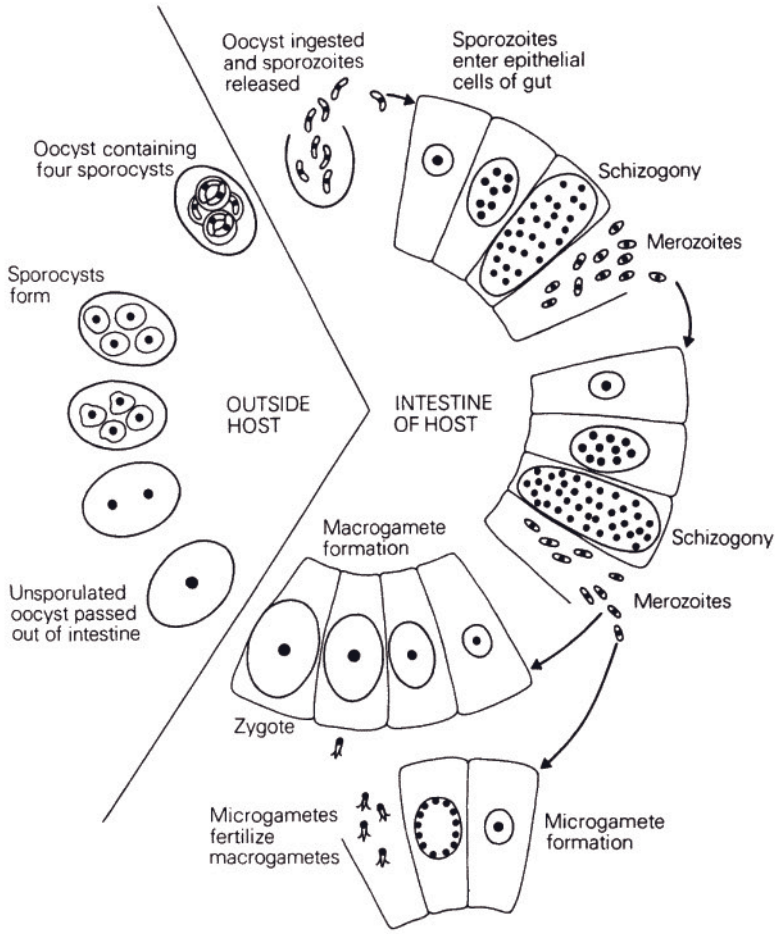


Fig. 1.8 The life cycle of *Eimeria* spp. The infection begins when oocysts are swallowed and sporozoites released in the gut. The sporozoites enter gut cells and undergo a phase of multiplication (schizogony) resulting in the formation of uninucleate merozoites. These merozoites invade other cells and the cycle is repeated two or three times. Eventually merozoites enter other cells where they develop into male and female gametocytes. The nucleus of the male or microgametocyte divides and produces flagellated microgametes which fertilize the female or macrogamete to produce a zygote. A cyst wall or oocyst forms round the zygote within which the nucleus divides twice to produce four uninucleate bodies. Another cyst wall or sporocyst forms round each of these and one further cell division occurs to produce two sporozoites in each. The oocyst containing four sporocysts each with two sporozoites is the infective stage.

There are a number of variations on this life cycle pattern, the main ones being in the number and sites of the schizogonic cycles.

become clear that many of these isosporans develop in an intermediate host which may or may not be obligatory. In such life cycles, the oocysts or sporocysts are passed out from the definitive host and are ingested by an intermediate host within which multiplication in various organs occurs and eventually cysts are formed which, when ingested by the definitive host, initiate the typical coccidian life cycle once again. The problem has been that the parasites in the intermediate hosts were all well-known and had been given valid names. The various parts of each life

Table 1.5 Important *Eimeria* species

Host	Species	Pathogenicity
Chickens	*E. acervulina*	+
	E. brunetti	++
	E. maxima	+
	E. mitis	+
	E. necatrix	+++
	E. tenella	+++
Turkeys	*E. meleagrimitis*	++
	E. adenoeides	
Geese	*E. anseris*	+
	E. nocens	++
	E. truncata	+++
Ducks	*E. danailova*	++
Cattle	*E. bovis*	++
	E. zuernii	++
Sheep	*E. crandallis*	+++
	E. ovina	++
	E. ovinoidalis	+++
	E. arloingi	++
	E. ninakohlyakimovae	++
Pigs	*E. debliecki*	++
Horses	*E. leukarti*	++
Rabbits	*E. flavescens*	++
	E. intestinalis	++
	E. stiedai	+++
Rats	*E. nieschulzi*	++
Mice	*E. falciformis*	++

+++, Very pathogenic; ++, moderately pathogenic; +, slightly pathogenic.

cycle have now been put together and it is possible to identify each parasite from the stages in either the definitive or the intermediate host. The most important species are given in Table 1.6.

This group now includes seven genera, whose characteristics are summarized below. *Isospora* is classified on the basis of stages in the definitive host while all the others are classified by stages in the intermediate host.

- *Isospora*. Direct life cycle.
- *Toxoplasma*. Intermediate host not essential. Development in the lymphoid macrophage system. Cysts thin-walled containing many organisms.
- *Hammondia*. Similar to *Toxoplasma* but intermediate host essential.
- *Cystoisospora*. Intermediate host not essential. Similar to *Toxoplasma* but thin-walled cyst contains only one infective organism.
- *Sarcocystis*. Septate cysts in muscle of intermediate host.
- *Besnoitia*. Thick-walled cysts in connective tissue of intermediate host.
- *Frenkelia*. Cysts in brain of intermediate host.

As a result of these discoveries, the species of *Isospora* in humans, cats and dogs have had to be redefined. The two species originally described from humans were *I. belli* and *I. hominis*. *Isospora belli* remains unchanged while *I. hominis* becomes *S. hominis* and *S. suihominis*. In the dog, *I. canis* becomes *C. canis*, *I. rivolta* becomes *C. rivolta* and *I. bigemina* becomes *S. tenella*, *S. cruzi* and *H. heydorni*. In the cat, *I. felis* becomes *C. felis*, *I. rivolta* becomes *S. rivolta* and *I. bigemina* could apply to so many species that it is impossible to identify the original descriptions with any certainty.

The majority of this group of parasites cause little harm to their hosts, the most important exception being *Toxoplasma gondii* (Fig. 1.9). *Toxoplasma gondii* is a parasite of felids with a very wide range of intermediate hosts, including humans. In cats, and other felids, the life cycle is

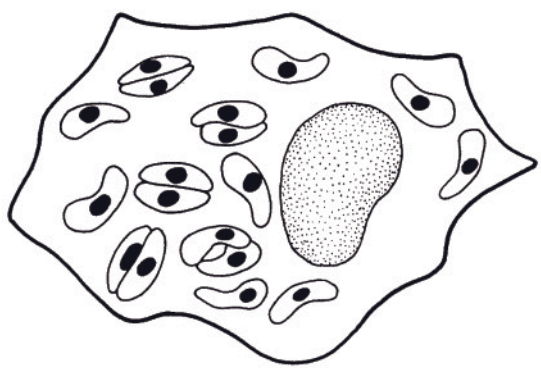


Fig. 1.9 *Toxoplasma gondii* zoites in a macrophage of an experimentally infected mouse. Drawn from a Giemsa stained slide. (The large stippled structure is the host cell nucleus.)

Table 1.6 Isosporan coccidia of humans and domesticated animals*

	Intermediate hosts						
Definitive host	None	Humans	Cattle	Sheep	Horses	Pigs	Rodents
Man	*I. belli*		*S. hominis* *S. bovihominis*			*S. suihominis*	
Cats		*T. gondii*	*S. hirsuta* (*S. bovifelis*) *B. besnoiti*	*T. gondii* *S. gigantea* (*S. ovifelis*)		*S. porcifelis*	*T. gondii* *H. hammondi* *S. muris* *B. wallacei* *C. felis* *C. rivolta*
Dogs			*S. cruzi* (*S. bovicanis*) *H. heydorni*	*S. tenella* (*S. ovicanis*)	*S. bertrami*	*S. miescheriana* (*S. suicanis*)	*C. canis* *C. ohioensis* *H. pardalis*

* This list is not complete and the nomenclature of the group is still being clarified. Some alternative names are given in parentheses.

a normal eimerian one (Fig. 1.10). If, however, the oocysts are ingested by other warm-blooded animals, multiplication occurs in various cells of the body and eventually cysts are formed. If the intermediate host is eaten by a definitive host, the parasite enters the cells of the gut and reverts to a normal eimerian life cycle. If, on the other hand, the intermediate host is eaten by another potential intermediate host disseminated infections occur as before. The infection may cause no symptoms or it may kill the intermediate host. Most humans acquire their infections from undercooked meat or from cats. Infections are normally symptomless but in the unborn fetus or immunosuppressed patients they may be very serious and occasionally in healthy individuals they may cause ocular damage. Toxoplasmosis can also cause serious infections in puppies and lambs.

1.7.3 *Cryptosporidium*

Coccidians belonging to the genus *Cryptosporidium* are relatively common parasites in the intestinal and respiratory tracts of mammals, birds and reptiles. Two species occur in mammals, *C. muris* and *C. parvum*, the latter causing gastrointestinal disorders in cattle, sheep and humans. The life cycle is typically coccidian and is confined to a single host. The oocysts, which contain four sporozoites, are long-lived and are extremely resistant to normal water purification procedures so contaminated drinking water constitutes the main source of infection. In recent years there has been an increasing number of epidemics of cryptosporidiosis. The infection is unpleasant but not normally dangerous except in immunocompromised individuals, such as AIDS sufferers, in which it can be fatal. There is no effective drug against this organism.

1.8 MALARIA PARASITES

The malaria parasites belong to the same phylum as the coccidians but to a different order, the Haemosporidida, members of which, as the name implies, are parasitic in the blood of vertebrates. All use dipteran insects as their vectors. The malaria parasites of mammals all belong to the genus *Plasmodium*, the life cycle of which is shown in Fig. 1.11, and are transmitted by female mosquitoes belonging to the genus *Anopheles*.

1.8.1 Malaria parasites of humans

Human malaria is one of the most important diseases in the world with over 500 million

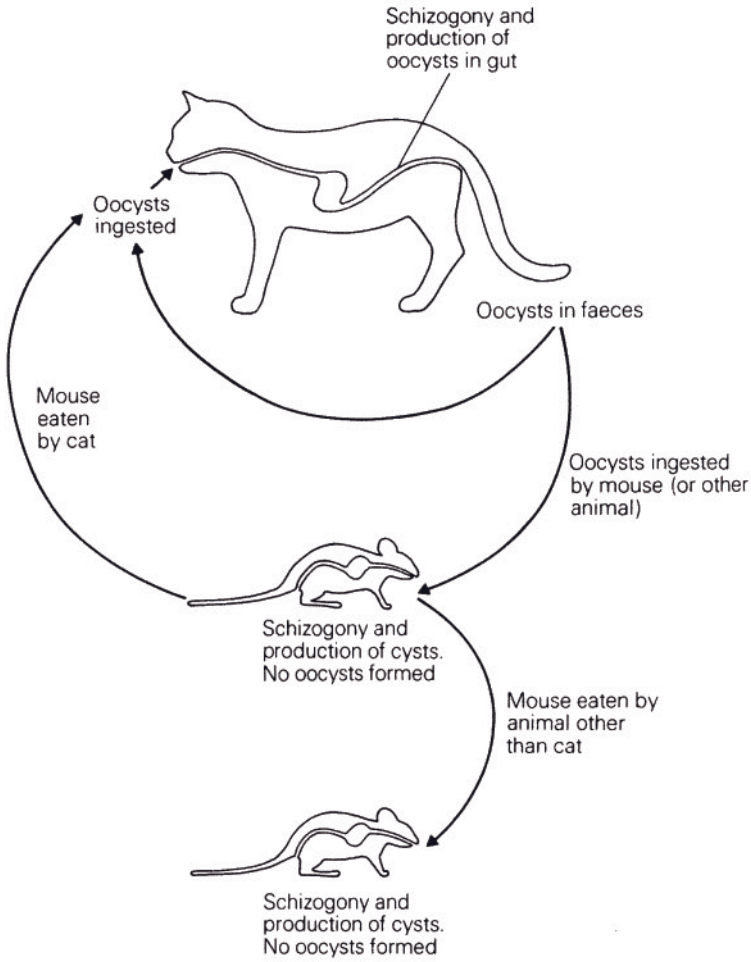


Fig. 1.10 The life cycle of *Toxoplasma*. The life cycle begins when oocysts are swallowed by a cat and the sporozoites are released in the gut. A typical eimerian life cycle with schizogony and the formation of gametocytes occurs and eventually oocysts are formed and the cycle is repeated if these are swallowed by cats. If the oocysts are swallowed by mice, schizogony occurs in various parts of the body but no oocysts are formed. Instead cysts are produced that lie dormant until the host is eaten. If eaten by a cat the normal eimerian life cycle follows. If eaten by another host an infection similar to that in mice occurs. This may occur in a variety of mammals including herbivores. Man becomes infected either by oocysts from cats or by eating infected meat. Congenital transmission in this alternative cycle also occurs.

people at risk in tropical and subtropical parts of the world especially Africa. Malaria is caused by four species of *Plasmodium*: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae* (Table 1.7). The disease is characterized by periodic fevers coinciding with the liberation of merozoites during the erythrocytic phase of the infection; these fevers occur every 72 hours in the case of *P. malariae* and every 48 hours in the other species. In all species, there is a single phase of exo-erythrocytic schizogony and in *P. falciparum* and *P. malariae* this phase lasts for 5–15 days. After this, the only parasites in the body are those in the blood and subsequent bouts of fever are caused by recrudescences of these blood forms. In *P. vivax* and *P. ovale* some of the parasites in the liver lie dormant for several years and subsequent infections due to the maturation of these forms are called relapses.

Plasmodium falciparum (Fig. 1.12a) causes malignant tertian malaria and is the most common and serious of all the forms of malaria. The infection is acute and the parasites tend to stick to endothelial cells causing blockage and cerebral damage, often resulting in death. *Plasmodium vivax* (Fig. 1.12b) causes benign tertian malaria and is the second most serious infection. *Plasmodium ovale* (Fig. 1.12c) causes ovale tertian malaria and is concentrated in West Africa. *Plasmodium malariae* (Fig. 1.12d) causes quartan

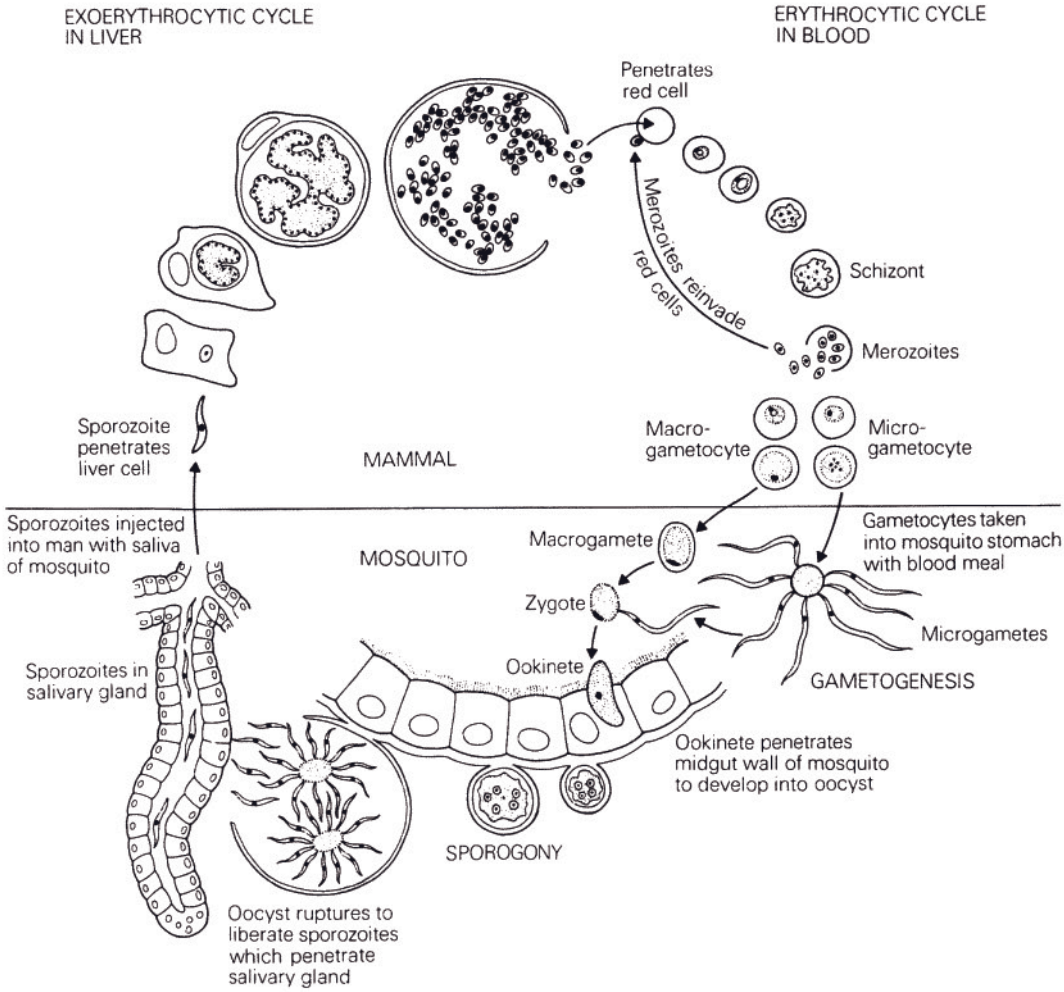


Fig. 1.11 The life cycle of *Plasmodium* spp. in mammals. The infection begins when sporozoites are injected directly into the bloodstream from the salivary glands of a mosquito. The sporozoites enter liver cells where they begin a phase of multiplication called 'exoerythrocytic schizogony', during which thousands of uninucleate merozoites are formed. These enter red blood cells in which they undergo a second phase of multiplication or erythrocytic schizogony, during which fewer than 24 merozoites are formed. These merozoites invade new red blood cells and the cycle may be repeated many times. Some of the merozoites are capable of developing into sexual stages or gametocytes. These are taken up by a mosquito. In the gut of the mosquito microgametes are produced and these fertilize the macrogametes and the resulting zygote or ookinete bores through the gut wall to come to lie on the outer surface where it forms an oocyst. Within the oocyst a third stage of multiplication occurs resulting in the formation of sporozoites that enter the salivary glands of the mosquito. (After K. Vickerman and F.E.G. Cox, 1967, *The Protozoa*, John Murray, London.)

malaria and infections may last 30 years or more. Infections with these last three parasites, although debilitating, are seldom fatal in themselves.

1.8.2 Other malaria parasites

The parasites of humans, with the exception of *P. malariae*, are not naturally transmissible to

Table 1.7 Malaria parasites affecting humans

Species	Disease	Periodicity (hours)	Distribution
P. vivax	Benign tertian	48	Cosmopolitan, between summer isotherms 16 °N and 20 °S
P. ovale	Ovale tertian	48	Mainly tropical W. Africa
P. falciparum	Malignant tertian	48	Cosmopolitan, mainly tropics and subtropics
P. malariae	Quartan	72	Cosmopolitan but patchy

other animals so the malaria parasites of primates and rodents have received considerable attention both in their own rights and as models for the human infections. There are about 20 species of *Plasmodium* in non-human primates of which *P. cynomolgi*, which resembles *P. vivax*, has been the most studied. Another species from macaques, *P. knowlesi*, is now widely used in laboratory studies despite the fact that it has a 24-hour periodicity and does not closely resemble any of the human species. *Plasmodium cynomolgi*, *P. brasilianum*, *P. inui* and *P. knowlesi* infect humans under experimental (or accidental) conditions.

The malaria parasites of rodents have been much more extensively studied than any others. These fall into two major groups, *P. berghei* and *P. yoelii* and their subspecies and *P. vinckei* and

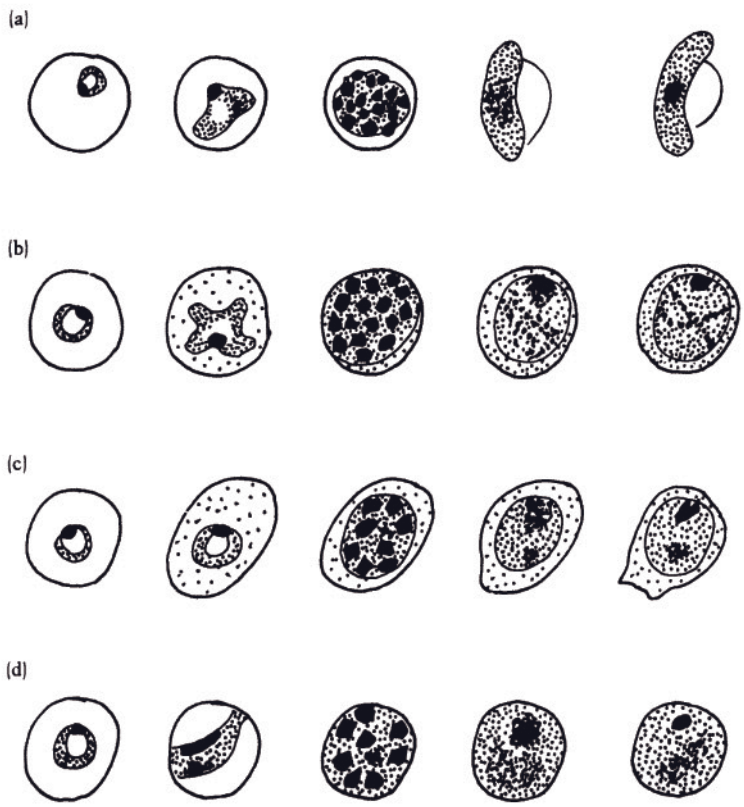


Fig. 1.12 Malaria parasites from human blood. (a) *Plasmodium falciparum*. (b) *P. vivax*. (c) *P. ovale*. (d) *P. malariae*. From left to right: ring stage, trophozoite, mature schizont, microgametocyte and macrogametocyte. In the case of *P. falciparum* only the ring stage and gametocytes appear in the peripheral blood. All drawn from Giemsa stained slides.

P. chabaudi and their subspecies. The *bergei–yoelii* group typically invade immature erythrocytes and the *vinckei–chabaudi* group invade mature cells. They all have 24-hour periodicities and only distantly resemble the human forms but, nevertheless, have provided a wealth of information on the biology of malaria parasites which would have been otherwise unobtainable.

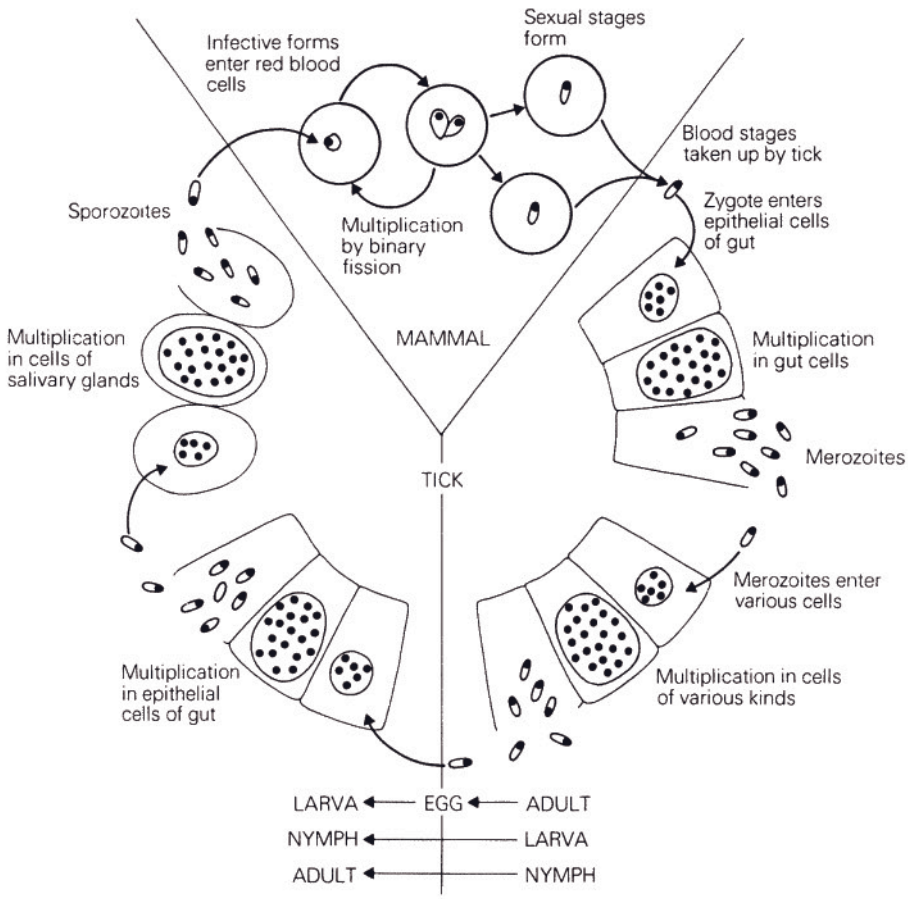


Fig. 1.13 The life cycle of *Babesia* spp. in mammals. The life cycle of *Babesia* spp. is complicated by the facts that any one of three stages in the life cycle of the tick vector may become infected and that ticks may have one, two or three hosts during their life cycles. These variations have marked effects on the life cycle of various *Babesia* species and the cycle described is a generalized one. The cycle in the mammal begins when infective forms are injected into the blood by a tick and the parasites enter red blood cells where they multiply by binary fission. Blood forms, probably gametocytes, are taken up by a tick when it feeds. These become gametes that fuse to form zygotes which enter epithelial cells of the gut where multiplication takes place. The resulting products are comparable with the merozoites in coccidian life cycles. These enter various cells in the body of the tick where further phases of multiplication occur. If the tick is a female, the merozoites may enter and multiply in the egg. When the larva hatches from the egg it is already infected and the parasites multiply once again in the epithelial cells of the gut. The uninucleate forms produced invade other tissues including the salivary glands from which small rounded infective bodies (sporozoites) are injected into the mammalian host. In some species, the nymph and not the larva harbours the infective parasites. The stage of the tick that is infected is never infective and usually the infection goes from larva to nymph, nymph to adult or adult to larva via the egg.

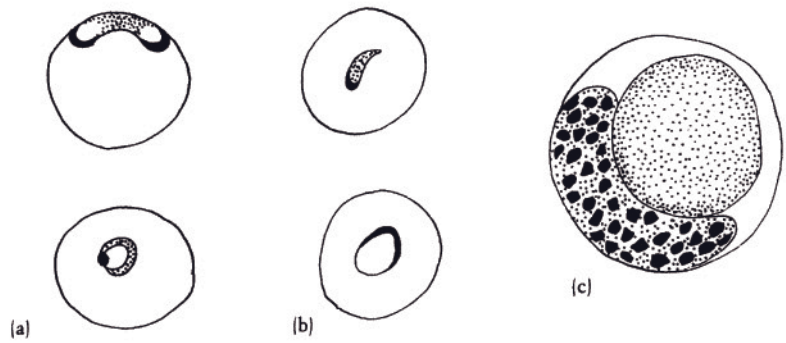


Fig. 1.14 Piroplasms from the blood of cattle. (a) *Babesia bigemina* and (b) *Theileria parva* in red blood cells. (c) *Theileria parva* schizont in a lymphocyte. All drawn from Giemsa stained slides.

1.9 PIROPLASMS

The piroplasms are parasites of the erythrocytes of vertebrates in which, if they multiply, they divide by simple binary fission. The parasites in the blood do not contain pigment and this, together with the absence of schizogony, distinguishes them from the malaria parasites. The vectors are ticks.

1.9.1 *Babesia*

Babesia species live in the blood of vertebrates and are transmitted by ticks. The life cycle is shown in Fig. 1.13. The form in the vertebrate is the trophozoite that lives in red blood cells in which it divides by binary fission to produce two merozoites, each of which invades a new cell (Fig. 1.14a). These blood stages cause serious disease in domesticated animals (see Table 1.8) and the general name given to these is babesiosis. The symptoms of babesiosis are fever, anaemia, jaundice and haemoglobinuria, and the infections are often fatal. The species are identified on the stages in the blood but as there are few morphological characters this is not altogether satisfactory. The main division is into 'large' and 'small' forms and in the past the number of genera have been created on this characteristic alone, but at present only one genus, *Babesia* is generally accepted. The distinction between 'large' and 'small' is a convenient starting point for the identification of any *Babesia* in a particular host (see Table 1.8).

There are a number of *Babesia* species in wild animals but whether or not these play any significant part in the transmission of these parasites to domesticated animals is not known. There are also two important species in rodents, *B. rodhaini* and *B. microti*, that have been widely used in laboratory studies. *Babesia microti* occasionally infects humans in America but the infections are not fatal. In Europe, splenectomized humans are sometimes infected with *B. bovis* and the infection frequently proves fatal.

1.9.2 *Theileria*

Theileria species are parasites of cattle, sheep and goats in which the majority of the life cycle occurs in the lymphoid tissues (Fig. 1.14c) and the stages infective to ticks occur in the red blood cells (Fig. 1.14b). The life cycle is shown in Fig. 1.15 and the various parasites that cause disease are listed in Table 1.9. The most serious diseases caused by *Theileria* occur in cattle in which *T. parva*, causing African theileriosis or East Coast Fever, is often lethal, and *T. annulata* is sometimes lethal but as the infected cattle remain carriers for long periods this infection is probably more important on a world scale than *T. parva*. *Theileria mutans* and *T. velifera* are not very pathogenic. *Theileria sergenti* is probably a synonym of *T. mutans*. In *T. parva* and *T. annulata* infections the damage is done during the phase of schizogony in the lymphoid tissues and the symptoms include hypertrophy of the lymphoid tissues, fever and loss of weight. In *T. mutans* (and *T. sergenti*) there may be anaemia and jaundice. In sheep and goats *T. hirci* is very pathogenic when newly introduced into an area but *T. ovis* which is morphologically indistinguishable from *T. hirci*, is hardly pathogenic at all.

Table 1.8 *Babesia* species causing disease in domesticated animals

Species	Size	Main hosts	Main vectors	Pathogenicity	Main distribution
B. bigemina	L	Cattle	*Boophilus*	+++	All continents
B. bovis	S	Cattle	*Boophilus*	++	All continents
B. divergens	S	Cattle	*Ixodes*	++	Europe
B. major	L	Cattle	*Haemaphysalis*	+	Europe, Africa
B. caballi	L	Horses	*Dermacentor, Hyalomma, Rhipicephalus*	++	All continents
B. equi	S	Horses	*Dermacentor, Hyalomma, Rhipicephalus*	+++	All continents
B. motasi	L	Sheep, goats	*Dermacentor, Haemaphysalis, Rhipicephalus*	+	Europe, Asia, Africa
B. ovis	S	Sheep, goats	*Rhipicephalus*	+	Europe, Asia, Africa
B. trautmanni	L	Pigs	*Rhipicephalus*	+	Europe, Asia, Africa
B. perroncitoi	S	Pigs	Not known		Europe, Africa
B. canis	L	Dogs	*Rhipicephalus*	+++	Europe, Asia, Africa, America
B. gibsoni	S	Dogs	*Rhipicephalus*	+++	Asia
B. herpailuri	L	Cats	?	+	Africa
B. felis	S	Cats	*Haemaphysalis*	++	Asia, Africa

+++, Most pathogenic, +, least pathogenic; L, Large; S, small.

Table 1.9 *Theileria* species causing disease in domesticated animals

Species	Main hosts	Main vectors	Pathogenicity	Main distribution
T. annulata	Cattle	*Hyalomma*	+++	Europe, Asia, Africa
T. mutans	Cattle	*Amblyomma*	+	Europe, Asia, Africa, Australia
T. parva	Cattle	*Rhipicephalus*	+++	Africa
T. sergenti	Cattle	*Haemaphysalis*	+	Asia
T. velifera	Cattle	*Amblyomma*	+	Africa
T. taurotragi	Cattle, sheep, goats	*Rhipicephalus*	+	Africa
T. hirci	Sheep, goats	*Hyalomma*	+	Africa
T. ovis	Sheep, goats	*Rhipicephalus*	+	Africa
T. separata	Sheep, goats	*Rhipicephalus*	+	Africa

+++, Most pathogenic; +, least pathogenic.

1.10 MICROSPORIDIA

There are some 700 species of microsporidians and these are found in nearly all groups of vertebrates and invertebrates, particularly fish and arthropods. Microsporidians are characterized by the possession of a thick-walled spore containing an infective body or sporoplasm surrounded by a coiled hollow tube, the polar filament, through which the sporoplasm is injected into its host. The infection begins when a spore is ingested and the sporoplasm enters a cell of the gut. The actual details of what follows vary from species to species, but multiplication by binary fission and the spread of the infection to other tissues occurs, and eventually spores are formed and released when the host dies or is eaten. *Encephalitozoon cuniculi* occurs in rodents, rabbits, carnivores and primates and there are a few records from humans. This is a parasite of peritoneal

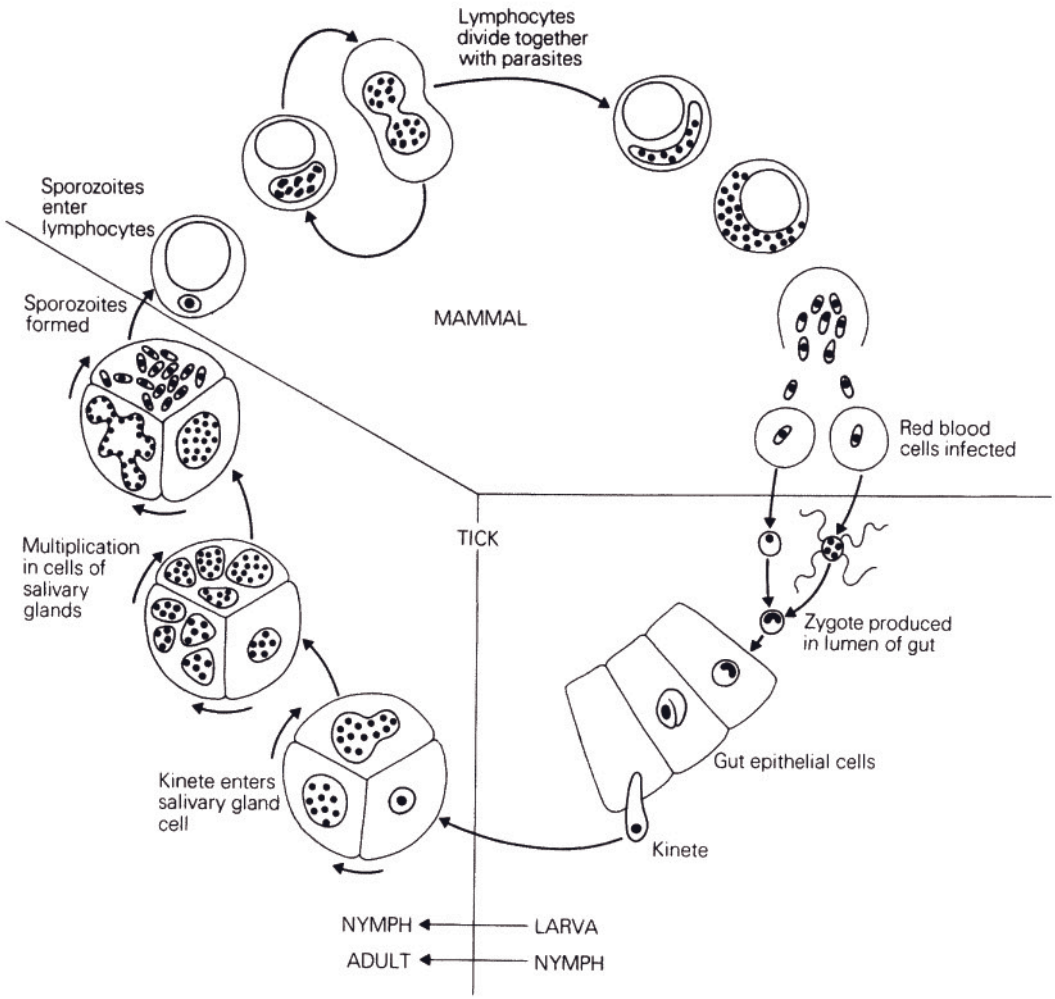


Fig. 1.15 The life cycle of *Theileria* spp. The cycle in a mammal begins when the infective stages, sporozoites, are injected by a tick. These enter lymphocytes in which they divide repeatedly causing the lymphocytes themselves to divide and the parasites to be distributed between the two daughter host cells. After a number of divisions, merozoites are formed and these invade red blood cells and are taken up by a tick when it feeds. Within the lumen of the gut of the tick, fertilization occurs and the zygote enters the epithelial cells of the gut where it develops into a motile kinete which subsequently enters the salivary glands where another phase of multiplication results in the formation of sporozoites. These are injected into the mammalian host when the tick feeds. The stage of the life cycle of the tick that is infected is never infective and there is no transovarian transmission. Thus, if the nymph is infected, multiplication and sporozoite formation occur in the salivary glands of the adult.

macrophages but may also spread to other parts of the body including the brain where spores can be found. Another microsporidian, *Enterocytozoon bieneusi*, is increasingly being reported in AIDS patients.

1.11 CILIOPHORA

The Ciliophora is a distinct phylum, considered by some to be a subkingdom, containing 4700 free-living and 2500 parasitic species. Parasitic

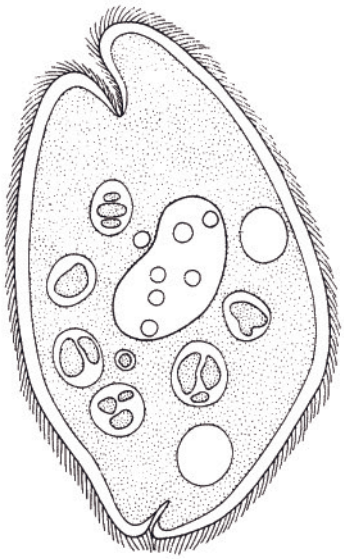


Fig. 1.16 *Balantidium coli* from *in vitro* culture. Drawn from a haematoxylin stained slide.

ciliates occur in most groups of vertebrates and invertebrates and those in amphibians and earthworms are frequently encountered in elementary biology classes. Few of the parasitic ciliates are of any economic importance.

1.11.1 *Balantidium coli*

Balantidium coli (Fig. 1.16) is a common parasite of pigs in all parts of the world and has also been recorded in rats, dogs, monkeys, apes and humans. It is difficult to know how many human cases there have been but about 1000 have been recorded, mainly in the tropics. The ciliate lives in the lumen of the large intestine and may invade the gut wall where it produces ulcers resembling those caused by *Entamoeba histolytica* although the majority of cases are asymptomatic. Transmission is by cysts and epidemiological evidence suggests that most human infections are acquired from pigs.

1.12 *PNEUMOCYSTIS*

The taxonomic position of *Pneumocystis* is uncertain but it is almost certainly a fungus. However, as it has been long regarded as a protozoan, it is included here. *Pneumocystis carinii* is a natural parasite occurring in the lungs of about 80% of humans in which it exists as a harmless amoeba forming cysts which are the transmission stages. In immunocompromised individuals parasite numbers increase until they fill the alveolar spaces, causing pneumonia which may be fatal. Pneumocystosis is a common complication in people suffering from AIDS.

REFERENCES AND FURTHER READING

Bruce-Chwatt, L.J. (1985) *Essential Malariology*, 2nd edn. London, Heinemann.

Canning, E.U. & Lom, J. (1986) *The Microsporidia of Vertebrates*. London, Academic Press.

Chang, K-P. & Bray, R.S. (eds) (1985) *Leishmaniasis*. Amsterdam, Elsevier.

Coombs, G.H. & North, M. (eds) (1991) *Biochemical Protozoology*. London, Taylor and Francis.

Cox, F.E.G. (1992) Systematics of parasitic protozoa. In J.P. Kreier & J.R. Baker (eds) *Parasitic Protozoa*, 2nd edn., Vol. 1, pp. 55–80. San Diego, Academic Press.

Dubey, J.P. & Beattie, C.P. (1988) *Toxoplasmosis of Animals and Man*. Boca Raton, CRC Press.

Dubey, J.P., Speer, C.A. & Fayer, R. (1989) *Sarcocystosis of Animals and Man*. Boca Raton, CRC Press.

Gardiner, C.H., Fayer, R. & Dubey, J.P. (1988) *An Atlas of Protozoan Parasites in Animal Tissues*. U.S. Department of Agriculture Handbook No. 651.

Garnham, P.C.C. (1966) *Malaria Parasites and Other Haemosporidia*. Oxford, Blackwell Scientific Publications.

Hoare, C.A. (1972) *The Trypanosomes of Mammals*. London, Tindall & Cox.

Honigberg, B.M. (1989) *Trichomonads Parasitic in Humans*. New York, Springer-Verlag.

Hopkin, J. (1991) *Pneumocystic carinii*. Oxford, Oxford University Press.

Knell, A.J. (ed.) (1991) *Malaria*. Oxford, Oxford University Press.

Kreier, J.P. & Baker, J.R. (1987) *Parasitic Protozoa*. Boston, Allen & Unwin.

Kreier, J.P. & Baker, J.R. (eds) (1992–3) *Parasitic Protozoa*, Vols 1–7. New York, Academic Press.

Lee, J.J., Hutner, S.H. & Bovee, E.C. (1985) *An Illustrated Guide to the Protozoa*. Lawrence, Kansas, Society of Protozoologists.

Levine, N.D. (1973) *Protozoan Parasites of Domesticated Animals and of Man*, 2nd edn. Minneapolis, Burgess Publishing Co.

Levine, N.D. (1988) *The Protozoan Phylum Apicomplexa*, Vols 1 and 2. Boca Raton, CRC Press.

Long, P. (ed.) (1982) *The Biology of the Coccidia*. London, Edward Arnold.

McGregor, I.A. & Wernsdorfer, W. (eds) (1988) *Malaria. Principles and Practice of Malariology*. Vols 1 and 2. Edinburgh, Churchill Livingstone.

Martinez-Palomo, A. (1986) *Amoebiasis*. Amsterdam, Elsevier.

Matsumoto, Y. & Yoshida, Y. (1986) Advances in *Pneumocystis* biology. *Parasitology Today*, **2**, 137–142.

Mehlhorn, H. (ed.) (1988) *Parasitology in Focus: Facts and Trends*. Berlin, Springer-Verlag.

Meyer, E.A. (ed.) (1990) *Giardiasis*. Amsterdam, Elsevier.

Molyneux, D.H. & Ashford, R.W. (1983) *The Biology of Trypanosoma and Leishmania, Parasites of Man and Domestic Animals*. London, Taylor and Francis.

Norval, R.A.I., Perry, B.D. & Young, A.S. (eds) (1992) *The Epidemiology of Theileriosis in Africa*. London, Academic Press.

Peters, W. & Killick-Kendrick, R. (eds) (1987) *The Leishmaniases in Biology and Medicine*, Vol. 1. *Biology and Epidemiology*, Vol. 2. *Clinical Aspects and Control*. London, Academic Press.

Ristic, M. (ed.) (1988) *Babesiosis of Domestic Animals and Man*. Boca Raton, CRC Press.

Rondanelli, E.G. (ed.) (1987) *Amphizoic Amoebae*. Human Pathology, Infectious Diseases Color Atlas Monographs 1. Padua, Piccin Nuova Libraria.

Sleigh, M.A. (1989) *Protozoa and Other Protists*. London, Edward Arnold.

Smith, H.V. & Rose, J.B. (1990) Waterborne crytosporidiosis. *Parasitology Today*, **6**, 8–12.

Stephen, L.E. (1986) *Trypanosomiasis. A Veterinary Perspective*. Oxford, Pergamon Press.

Tzipori, S. (1988) Cryptosporidiosis in perspective. *Advances in Parasitology*, **27**, 63–129.

World Health Organization (1984) *The Leishmaniases*. WHO Technical Report Series No. 701. Geneva, WHO.

World Health Organization (1986) *Epidemiology and Control of African Trypanosomiasis*. WHO Technical Report Series No. 739. Geneva, WHO.

World Health Organization (1987) *The Biology of Malaria Parasites*. WHO Technical Report Series No. 743. Geneva, WHO.

Young, A.S. & Morzaria, S.P. (1986) Biology of *Babesia*. *Parasitology Today*, **2**, 211–219.

Chapter 2 / Parasitic Helminths

P. J. WHITFIELD

2.1 INTRODUCTION

The vast majority of metazoan parasites of vertebrates are representatives of two phyla – the acoelomate Platyhelminthes and the pseudocoelomate Nematoda. 'Helminth' is a practically useful, but imprecisely defined, term which includes all the cestodes and digeneans in the former group and all the parasitic members of the latter. It is as the causative agents of a terrible list of debilitating, deforming and killing diseases of humans and their agricultural animals that helminths are principally studied.

Some helminth infections are numbered among the major human infectious diseases. Schistosomiasis (bilharzia), caused by digeneans of the genus *Schistosoma* which inhabit blood vessels, is a most important cause of morbidity with over 200 million infected persons in Africa, South America and the Far East. Even more sufferers exist in tropical and subtropical zones with the major nematode diseases. It is quite conceivable that one billion are infected with both ascariasis caused by *Ascaris lumbricoides* and trichuriasis whose causative agent is *Trichuris trichiura*. Insect vector-transmitted filarial nematodes like *Wuchereria bancrofti*, *Brugia malayi* and *Onchocerca volvulus* cause highly pathogenic forms of filariasis that harm hundreds of millions of patients. Human cestode disease is a relatively nonpathogenic affliction although two types of larval cestodiasis – hydatid disease and cysticercosis – can both be highly injurious.

2.2 STRUCTURE AND FUNCTION OF HELMINTHS

Helminths are very diverse in their structure, physiology and behaviour. This diversity results partly from their varying taxonomic origins, and partly from their multiple adaptations for their particular one-, two- or three-host life cycles.

Digenean and cestode platyhelminths share a solid triploblastic acoelomate body plan, with complex reproductive organs embedded in mesenchymal tissue, and a gut where present, possessing only a single, oral opening. The reproductive system is almost always hermaphroditic. All these worms possess a living syncytial body wall whose outer surface and secretory activity is differently modified in the two groups.

Nematodes possess a pseudocoelomate body cavity which plays an important hydrostatic skeletal role in locomotion. Most nematodes are dioecious, with the male and female reproductive tracts located in the body cavities of the separate sexes. These worms have a body wall consisting of a syncytial hypodermis surmounted by an apparently non-living, mainly collagenous cuticle and underlain by groups of longitudinal muscles. In almost all species there is a functional gut with a mouth and anus.

Helminths use many different life cycle modes, and some like the nematode *Strongyloides stercoralis* and the cestode *Hymenolepis nana*, can use more than one mode. Direct life-cycle strategies, with only a single host species involved, are used by many gut-dwelling nematodes and also by *H. nana* in one of its life-cycle modes. Indirect life cycles are those in which more than one host species is used in order to complete one circuit of the parasite's life history. In such cycles, the final or definitive host, that is the host in which parasitic sexual reproduction takes place, is almost always a vertebrate. The intermediate hosts, those in which development, growth, encystment or asexual multiplication occurs, can be vertebrates or invertebrates. Indirect life cycles

with two or three hosts are the rule among digeneans and the vast majority of cestodes. Among the nematodes, filarial worms and *Dracunculus medinensis* (the guinea worm) utilize two-host indirect cycles. In the dioecious schistosomes and nematodes, sperm transfer between the sexes is obligatory. In the hermaphroditic digeneans and cestodes self-fertilization is sometimes possible but unidirectional or reciprocal cross-fertilization is nearly always favoured. Parthenogenesis is rare, but is used by both the nematode *Strongyloides stercoralis* and the lung-inhabiting digenean *Paragonimus*.

Transmission of helminth infections from host to host is achieved by eggs or larvae. Eggs are usually directly ingested by a host. Larvae may be similarly ingested, consumed while attached to a plant or eaten while located in an intermediate host which acts as a prey item for the next host in the life cycle. Free-living mobile larval forms such as digenean miracidia and cercariae and L_3 larval nematodes are often able to find, recognize and invade new hosts. They possess impressive sensory and locomotory abilities which enable them to carry out these functions. Transmission is discussed in more detail in Chapter 7, Section 7.2.

Table 2.1 An outline classification of helminths parasitic in vertebrates

PHYLUM: PLATYHELMINTHES
Class 1 Monogenea
Class 2 Cestoda (*Diphyllobothrium, Taenia, Echinococcus*)*
Class 3 Aspidogastrea
Class 4 Digenea (*Schistosoma, Fasciolopsis, Fasciola, Paragonimus*)
PHYLUM: NEMATODA
Order 1 Rhabditida (*Strongyloides*)
Order 2 Strongylida (*Necator, Ancylostoma*, etc.)
Order 3 Ascaridida (*Ascaris, Toxocara*, etc.)
Order 4 Oxyurida (*Enterobius*)
Order 5 Spirurida (*Dracunculus, Wuchereria, Brugia, Loa, Onchocerca*)
Order 6 Enoplida (*Trichinella, Trichuris*)

* Important genera which infect man are listed after the appropriate taxa.

2.3 CLASSIFICATION OF PARASITIC HELMINTHS

Table 2.1 provides a working outline classification for the helminth groups considered in any detail in this book. More detailed classification systems will be provided for each of the major helminth groups as they are considered in turn. In using these classifications it must be remembered that there are still major disagreements about the relationships between the higher taxonomic levels. It is also true that most helminth species descriptions are still centred upon morphological and host specificity criteria. Increasingly though, molecular criteria which involve genomic and isoenzyme polymorphisms are also being utilized in species discriminations. It is to be hoped that these will open the way for the development of effective natural taxonomies.

2.4 PLATYHELMINTH PARASITES OF VERTEBRATES

Of the four classes of entirely parasitic platyhelminths, only two, the Cestoda and Digenea, cause important diseases in humans or agricultural animals, although monogeneans of fish can cause serious losses in stocks kept under high-density fish farming conditions.

2.4.1 Cestodes

Cestodes are a unique and, in many ways, aberrant group of platyhelminth parasites, representing the most extreme specializations of the basic flatworm body plan for endoparasitism. With very few exceptions they all share two remarkable attributes: (1) they possess no gut; and (2) they have a very elongated body, often hundreds of times longer than broad. One small subclass, the Cestodaria, have compact non-segmented bodies, but members of the principal subclass, the Eucestoda, have a characteristically segmented adult body made up of a string of proglottids each of which contains in time a complete set of reproductive organs (Fig. 2.1). A mature adult eucestode may consist of several thousand proglottids behind an anterior attachment organ – the scolex – which is

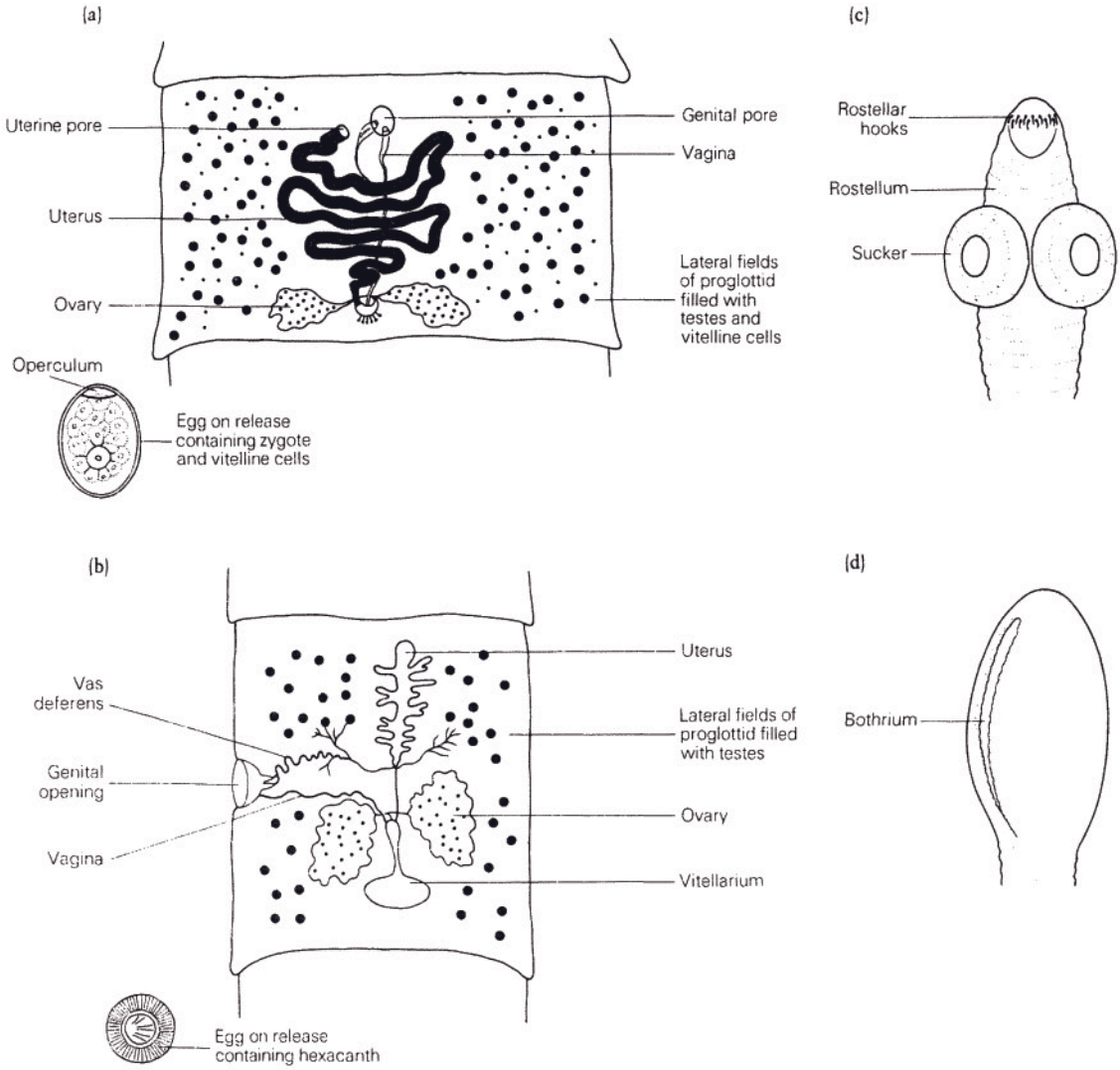


Fig. 2.1 Proglottids, eggs and scoleces of pseudophyllidean and cyclophyllidean cestodes. (a) Proglottid of *Diphyllobothrium latum*, a pseudophyllidean, demonstrating extensive areas of vitelline cells, genital openings on the ventral proglottid surface, and a uterine pore through which the gravid uterus can communicate with the outside world. The egg of *D. latum* when released is unembryonated. (b) Mature proglottid of *Taenia saginata* or *T. solium*, demonstrating a lateral genital opening and a uterus which does not directly communicate with the outside world. The egg of *T. saginata* or *T. solium* when released in human faeces contains a fully formed hexacanth larva. (c) The scolex of the cyclophyllidean *Echinococcus granulosus* from the dog gut, with four suckers and a hooked rostellum. (d) The unhooked scolex of the pseudophyllidean *D. latum* with two muscular grooves or bothria.

equipped with muscular grooves or suckers and sometimes also with hooks (Fig. 2.1). The serial multiplication of hermaphroditic reproductive organ sets which the segmented body represents, is an extraordinary modification for enhanced reproductive capacity. It avoids the production constraints of a single reproductive system and enables individual cestodes to sustain daily egg

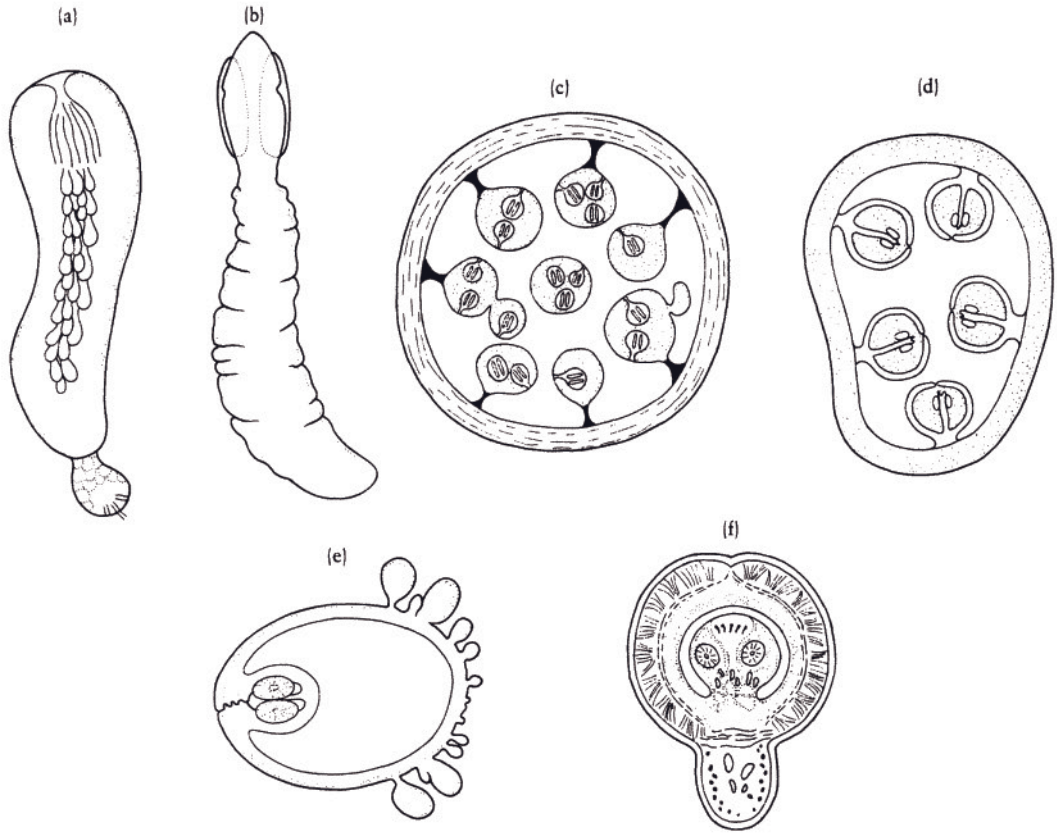


Fig. 2.2 Cestode larval stages. (a) Procercoid larva of *Diphyllobothrium latum* with a central core of gland cells and retained hooks from the hexacanth stage. (b) Plerocercoid larva of *D. latum* with anterior bothria present. (c) Hydatid cyst of *Echinococcus granulosus* with an outer laminated layer and proliferative brood capsules within it containing infective protoscoleces. (d) Coenurus larva of *Multiceps multiceps* with infective protoscoleces budding directly from a germinal membrane. (e) Cysticercus larva of *Taenia crassiceps* with scolex invaginated into wall of bladder. The posterior portions of the external bladder wall produce new cysticerci by exogenous budding. Such budding does not occur from the otherwise similar cysticerci of *T. saginata* and *T. solium*. (f) Cysticercoid larva of *Hymenolepis nana* with the invaginated scolex housed within an anterior vesicle.

outputs of hundreds of thousands or even millions of eggs.

The body wall of a cestode is a living syncytial tegument, the outer plasma membrane of which is thrown into a regular array of specialized microvilli termed microtriches, each surmounted by an electron-dense spine. The tegumentary plasma membrane is covered with a polyanionic glycocalyx. Microtriches produce a large amplification of surface area, operating in a digestive/absorptive manner in these gutless helminths to acquire external nutrients. Organic molecules of low molecular weight are absorbed by diffusion and active transport mechanisms across the plasma membrane. The latter also bears intrinsic phosphohydrolases which probably play a role in nutrient uptake. There is evidence that the tegument can also absorb macromolecules such as proteins by endocytosis. This repertoire of nutrient uptake techniques seems to restrict adult eucestodes to nutrient-rich internal locations within their vertebrate final hosts. The vast majority are found in the lumen of the small intestine attached to its mucosa by their scoleces. Except

for *Hymenolepis nana*, all eucestodes exhibit only an indirect life cycle with larval (metacestode) development and/or asexual multiplication occurring in one or two intermediate hosts. Figure 2.2 illustrates a selection of cestode larvae.

2.4.2 Human cestodiasis

Within the Eucestoda there is considerable uncertainty about the appropriate subdivision of the taxon into orders. Conveniently however, the species that cause human disease all fall within two well-recognized and reasonably homogeneous orders the Pseudophyllidea and the Cyclophyllidea. Table 2.2 outlines the major differences between these two groups.

Tapeworm-generated disease or cestodiasis in humans can be considered under two headings, namely larval cestodiasis in which larval cestodes in a variety of organ sites are the origin of disease symptoms and adult cestodiasis where the pathology is due to adult worms in the human gut. Table 2.3 lists the main examples of human cestodiasis and Fig. 2.3 describes the life cycles of a typical pseudophyllidean and cyclophyllidean – *Diphyllobothrium latum* and *Taenia saginata*.

Table 2.2 An outline classification of pseudophyllidean and cyclophyllidean cestodes

Class: Cestoda

Subclass: Eucestoda

Order 1: Pseudophyllidea. Scolex with two long superficial bothria. Mainly gut-dwelling parasites of non-elasmobranch fish, fish-eating mammals including man and birds. Proglottids dorso – ventrally flattened, usually bearing the uterine pore and genital apertures medially on the ventral surface. Each egg hatches in water to release a ciliated coracidium larva containing a hexacanth. Indirect life cycles including procercoid and plerocercoid larvae, e.g. *Spirometra, Diphyllobothrium*

Order 2: Cyclophyllidea. Scolex typically with four large suckers surmounted with a muscular rostellum normally armed with hooks. Gut-dwelling parasites of amphibians, reptiles, birds and mammals including man. Eggs contain non-ciliated hexacanth larvae. Genital apertures marginal on proglottids. Posterior gravid proglottids often shed containing eggs. Indirect life cycles include a variety of nonproliferative and proliferative larval forms in vertebrate and invertebrate intermediate hosts, e.g. *Taenia, Echinococcus*

Larval cestodiasis

There are three main types of human larval cestodiasis: sparganosis caused by plerocercoids (= spargana) of diphyllobothriid tapeworms in the

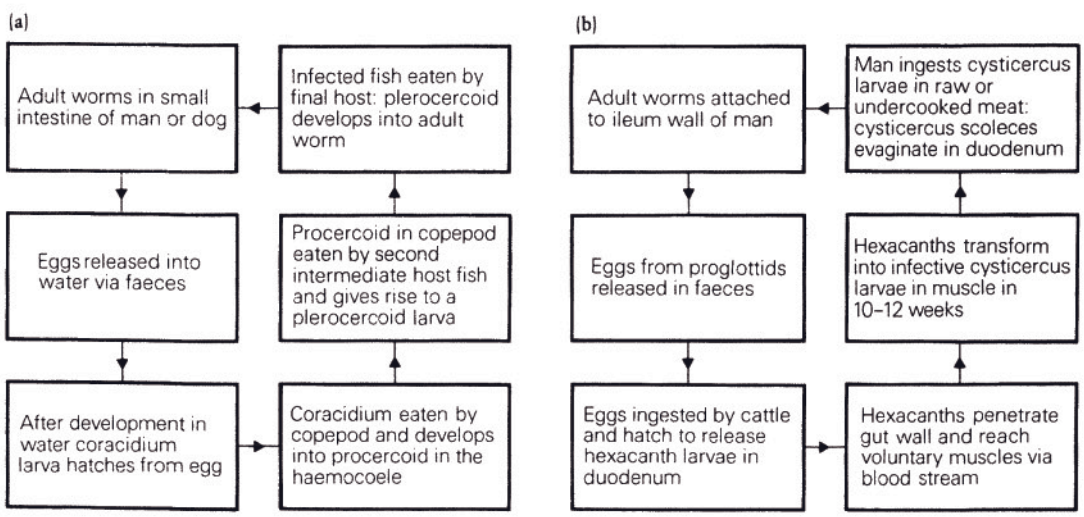


Fig. 2.3 Outline life cycles of cestodes. (a) A pseudophyllidean, *Diphyllobothrium latum*. (b) A cyclophyllidean, *Taenia saginata*.

Table 2.3 Human cestodiasis

Parasite*	Disease	Adult (A) or larval (L)	Location of worms in man	Geographical distribution	Typical pathology
PSEUDOPHYLLIDEANS					
Diphyllobothrium latum	Diphyllobothriasis	A	Lumen of small intestine	Finland, Central Europe, Italy, France, Ireland, Japan, Siberia, Argentina, Great Lakes area of USA and Canada	Very rarely pernicious megaloblastic anaemia
Spirometra spp.	Sparganosis	L	A variety of deep tissues	Tropical and subtropical regions of Africa, N. and S. America, Europe, Far East and Australasia	Mild, various
CYCLOPHYLLIDEANS					
Taenia saginata	Beef tapeworm infection	A	Lumen of small intestine	Cosmopolitan	Very infrequently gut obstruction or perforation
T. solium	Pork tapeworm infection	A	Lumen of small intestine	Cosmopolitan	Very infrequently gut obstruction or perforation; risk of cysticercosis
T. solium	Cysticercosis	L	A variety of deep tissues including the brain	Cosmopolitan, but particularly in S. and Central America, USSR, India and S. and E. Africa	A range of brain pathologies are produced by larvae in the CNS, including epilepsiform attacks
Hymenolepis nana	Dwarf tapeworm infection	A	Lumen of small intestine	Cosmopolitan especially in children	Usually none; diarrhoea and abdominal pain in heavy infections
Echinococcus granulosus	Echinococcosis: hydatid disease	L	A variety of deep tissue sites with liver and lungs predominating	Most sheep and cattle farming areas of the world	Various; depending on the site of the hydatid cysts

*A number of other cestodes occasionally infect man, namely *Bertiella studeri*, *Dipylidium caninum* and *Hymenolepis diminuta* (adult cestodiasis); *Echinococcus multilocularis*, *Mesocestoides* spp. and *Multiceps* spp. (larval cestodiasis).

genera *Diphyllobothrium* and *Spirometra*; cysticercosis caused by cysticercus stage larvae of *T. solium*; and hydatid disease resulting from the proliferative hydatid cyst larvae of *Echinococcus granulosus*. In none of these cases are humans obligate hosts for the parasites – they contribute very little to parasitic reproductive success being so rarely consumed by the relevant final hosts. (Some authorities refer to most non-adult cestode development stages as metacestodes.)

A variety of carnivores are the normal final hosts for sparganosis-producing *Diphyllobothrium* and *Spirometra* species. Eggs in their faeces hatch to produce coracidia which develop into procercoids in copepods of freshwater habitats. The crustaceans are eaten by a wide range of amphibians, reptiles and mammals, in which plerocercoids develop. Spargana are wandering plerocercoids in human tissues. Persons become infected in a number of ways. They may ingest copepods containing procercoids when drinking untreated water from streams and lakes. They may also acquire infections by eating raw poultry, frogs and snakes or by poulticing inflamed eyes or abscesses with fresh frog or snake skin. Such poultices enable the plerocercoids to migrate directly into human tissues. Spargana may wander slowly within the body causing short-lived lumps to appear. Ultimately the spargana die, are calcified and surrounded with a thin fibrous capsule. Most infections occur in Japan, Korea, China and Vietnam.

Adult worms of the pork tapeworm *T. solium* inhabit the human intestine while the larval stages normally develop in pig muscles. Human cysticercosis occurs when people eat *T. solium* eggs, and cysticercus larvae, each about 10 mm long, subsequently become lodged in a variety of tissues. Symptoms are particularly severe if the parasites occur and then die in the human central nervous system. The commonest mode of human infection is probably human faecal contamination of food, but it is possible that direct autoinfection occurs in patients harbouring adult worms, if segments containing eggs are regurgitated from the small intestine into the stomach so that egg activation begins.

Hydatid disease or echinococcosis is one of the most harmful cestodiases. It is a complex disease from the point of view of parasite taxonomy. Most human infections are with the endogenously budding hydatid larvae of several strains of *E. granulosus* which has discrete spherical cysts. Humans can act as accidental intermediate hosts for *E. granulosus* in its domestic cycle (where it is transmitted between dogs as final hosts and sheep or cattle as intermediate hosts) or in one of its feral cycles utilizing wild carnivores and herbivores. Less frequently, humans become infected by strains of *E. multilocularis* whose irregularly expanding cysts are intensely pathogenic. The latter disease is always feral, with foxes acting as final hosts and rodents as intermediate hosts. In all instances, human infection occurs because of contact with faecally contaminated material from infected canine hosts. The highest community prevalences of hydatid disease around the world are always in cattle or sheep herding populations with high levels of human–dog contact.

Adult cestodiasis

The common adult cestodiases of human hosts are generally less pathogenic than cysticercosis or hydatid disease. Adult cestodes at low densities in the human gut often cause no symptoms. Only rarely, when parasite densities are high, do problems due to gut-wall damage or intestinal obstruction occur. The only other serious consequences of adult cestodiasis are the increased risk of cysticercosis in carriers of adult *T. solium*, and the geographically restricted risk of pernicious anaemia in those infected with *D. latum*.

In global terms only four adult cestodiases are at all common, namely those caused by *D. latum*, *T. saginata*, *T. solium* and *Hymenolepis nana*.

Diphyllobothrium latum (Figs 2.1, 2.2 & 2.3) is a pseudophyllidean tapeworm whose transmission is due to consumption of raw, undercooked or lightly smoked fish containing viable plerocercoids. Dogs can also act as final hosts. The pernicious megaloblastic anaemia caused by *D. latum* infections appears to be confined to a proportion of patients in Finland or of Finnish ancestry. It is caused by the competitive uptake of vitamin

B_{12} by the worms which restricts the amount of dietary B_{12} available for the human host.

Taenia saginata (Figs 2.1, 2.2 & 2.3), the beef tapeworm can sometimes reach 20 m in length but 5 m is more usual. It has a cosmopolitan distribution due to the practice of eating raw or undercooked beef. In this way infective cysticercus larvae (about 8 mm in length) in the muscles of a cow are ingested. Larvae evert their unhooked scoleces in the duodenum and attachment and subsequent growth occurs in the duodenum. It is possible that over 60 million cases exist worldwide.

Taenia solium is very similar in morphology and life-cycle characteristics to *T. saginata*. It differs mainly in having a hooked rather than an

Table 2.4 Other cestodes

Name	Final hosts	Intermediate hosts	Comments
CYCLOPHYLLIDEA			
(a) **Taeniidae**			
Taenia crassiceps	Fox	Small mammals	Exogenously budding metacestode larvae in the peritoneal cavity and other tissue spaces of intermediate hosts. Can be maintained by syringe passage of larvae in mice and rats in the laboratory
T. ovis	Dog	Sheep	Larvae develop in sheep muscles. Economic importance in the meat industry
Multiceps multiceps	Dog, coyote, fox, jackel	Sheep, goats, cattle, horses, (occasionally humans)	Larvae form a budding coenurus developing in brain and spinal cord of sheep causing a disease called gid or staggers. Very dangerous larval cestodiasis in man
(b) **Hymenolepidae**			
Hymenolepis diminuta	Rats, mice, hamsters (occasionally humans)	Many insects including fleas and beetles (*Tenebrio* and *Tribolium* in laboratory)	The most commonly used laboratory model cestode. Life cycle easily maintained experimentally
(c) **Dilepidiidae**			
Dipylidium caninum	Dogs, cats (occasionally humans)	Fleas	Causes an uncommon and nonpathogenic human adult cestodiasis especially in children. Infections caused by ingesting infected fleas from pets
(d) **Anoplocephalidae**			
Moniezia expansa and *M. benedini*	Sheep, cattle	Soil inhabiting mites	Causes a common adult cestodiasis of low pathogenicity in sheep
(e) **Davaineidae**			
Raillietina cesticillus	Chickens	Many arthropod species, especially beetles	Causes a common adult cestodiasis in chickens

unarmed adult scolex and fewer lateral branches in the gravid proglottid uterus. Human consumption of undercooked or raw pork is the route of infection. Thorough cooking or prolonged deep freeze storage at −10°C or below kills the cysticercus larvae in the meat.

Hymenolepis nana is only 15–40 mm in length. It can occur at high densities in an infected person's small intestine. Children and young adults are particularly at risk especially those in institutions. Low density infections produce few or no symptoms, but at higher infection levels of more than 2000 worms, vomiting, diarrhoea, loss of appetite and abdominal pain have been recorded. Transmission of the parasite is mainly by a method which is extremely unusual among cestodes, that is the ingestion of eggs which complete larval then adult development in the same human host.

2.4.3 Other cestodes

A number of other eucestode species can be considered of importance despite the fact that they are not normally human parasites. Their significance stems either from their use as laboratory models for studies on tapeworm physiology, development, biochemistry or chemotherapy, or from the parasites' utilization of agricultural animals as hosts. The main characteristics of some of these species are outlined in Table 2.4.

2.4.4 Digeneans

Adult digeneans are flattened or cylindrical platyhelminths that in humans and agricultural animals always inhabit endoparasitic locations. The vast majority of species live in the gut or its developmental offshoots such as the bile duct and lungs. Externally, adult digenean worms are char-

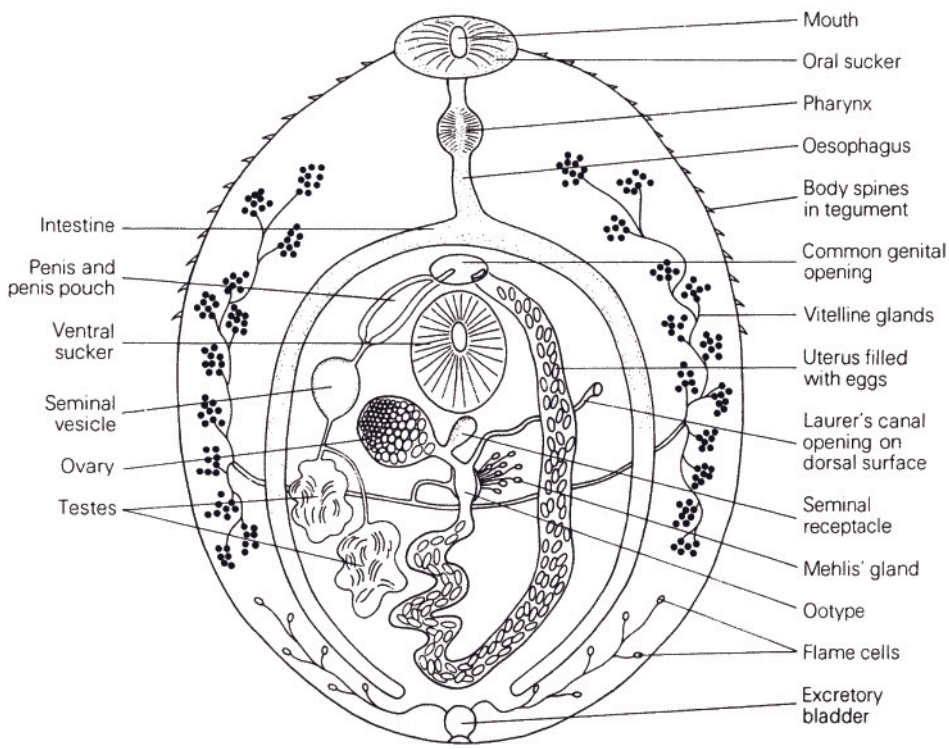


Fig. 2.4 A hypothetical adult digenean demonstrating the main morphological features.

acterized by an oral sucker around the anterior mouth and often an additional ventral sucker or acetabulum. The oral sucker is an important feeding organ while both sucker types are involved in attachment to internal host surfaces and locomotion. The outer surface of the body is a living syncytial tegument, the distal cytoplasm of which often contains spines. The internal organization of a typical hermaphroditic digenean (only schistosomes are dioecious) is described in Fig. 2.4. A basic taxonomy of digeneans is outlined in Table 2.5, with special emphasis on those groups that contain species that infect humans.

The life cycles of the great majority of digeneans display a remarkable and highly characteristic alternation of asexual and sexual reproductive phases, in molluscan and vertebrate hosts respectively. The basic life-cycle patterns employed by digeneans and examples of their larval stages are shown in Fig. 2.5. Hermaphroditic adults which normally cross-inseminate, utilize sexual reproduction in the final host, and tanned eggs are produced. These leave the host in faeces, urine or sputum and the zygote within the egg develops or has already developed by this stage into a ciliated larva – the miracidium. The miracidium then infects a gastropod mollusc either by direct penetration by a free-swimming, hatched miracidium

Table 2.5 An outline classification of digeneans (several families excluded)

CLASS: DIGENEA

Superorder 1: Anepitheliocystida. In the cercaria the bladder wall of the excretory system is the retained wall of the primitive bladder formed from the fusion of the two main lateral excretory canals

Order 1: Strigeatida. Cercariae fork-tailed
- **Family (i) Bucephalidae** (e.g. *Bucephalus*)
- **Family (ii) Strigeidae** (e.g. *Alaria, Cotylurus*)
- **Family (iii) Schistosomatidae.** The schistosomes: adults parasitic in the blood vessels of birds and mammals. Dioecious with males and females occurring in *in-copulo* pairs with the female held in the gynaecophoric canal of the male (e.g. *Schistosoma*)

Order 2: Echinostomida. Cercariae with cyst-producing gland cells. Encystation of cercariae occurs on vegetation or in molluscs
- **Family (i) Echinostomatidae.** The echinostomes: adults parasitic in the intestine, bile ducts or ureters of reptiles, birds and mammals. Elongate forms with a raised collar behind the oral sucker carrying large backwards pointing spines. (e.g. *Echinostoma*)
- **Family (ii) Fasciolidae.** Large, flattened, spinose leaf-shaped worms of mammals. (commonly herbivores) (e.g. *Fasciola, Fasciolopsis*)
- **Family (iii) Paramphistomatidae.** The amphistomes: gut parasites of mammals (commonly herbivores). Large, thick-bodied digeneans with an anterior oral sucker and a ventral sucker at the extreme posterior end of the worms (e.g. *Paramphistomum, Gastrodiscoides*)

continued

Table 2.5 *Continued*

Superorder 2: Epitheliocystida. In the cercaria the bladder wall of the excretory system has a thick epithelial organization with mesodermal origins which replaces the original primitive bladder

Order 1: Plagiorchiida. Operculate eggs. Oral stylet usually present in oral sucker of cercaria
- **Family (i) Plagiorchiidae.** Small flukes, mainly parasites of amphibians and birds, occasionally of fish, reptiles and mammals. Genital opening between well spaced oral and ventral suckers, tandem testes behind ovary. Y-shaped excretory bladder. Cercariae encyst in arthropods and possess oral stylet (e.g. *Plagiorchis*)
- **Family (ii) Dicrocoeliidae.** Small flukes found in the intestine, liver, gall bladder and pancreas of most vertebrate groups. Oral sucker subterminal, vitelline glands do not extend in front of ventral sucker. Cercariae encyst in arthropods and possess oral stylet (e.g. *Dicrocoelium*)
- **Family (iii) Troglotrematidae.** Flukes of birds and mammals, often in lungs or intestine but also in nasal cavities, frontal sinuses and subcutaneous tissues. Vitelline glands compact. Cercariae encyst in arthropods and possess oral stylet (e.g. *Paragonimus*)

Order 2: Opisthorchiida. Operculate eggs. Cercariae have no oral stylet
- **Family (i) Opisthorchiidae.** Medium-sized flukes of the gall bladder and bile duct in mammals, birds and reptiles. Weakly developed suckers (e.g. *Opisthorchis*)
- **Family (ii) Heterophyidae.** Small or minute flukes found in a variety of sites in mammals and birds. Genital sucker, closely associated with the ventral sucker (gonotyl) often present (e.g. *Heterophyes, Metagonimus*)

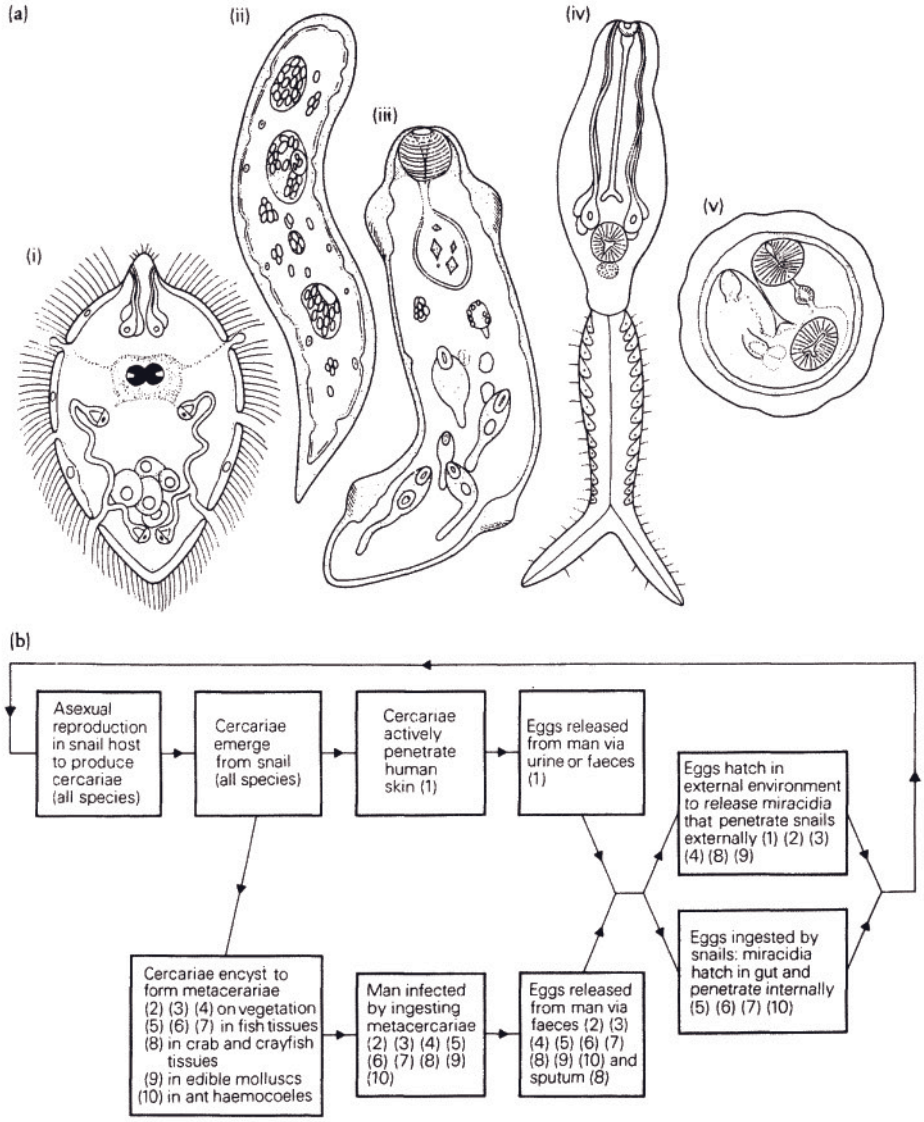


Fig. 2.5 (a) Diagrammatic representation of digenean larval stages. The larvae illustrated are completely schematic and do not represent an actual developmental sequence. (i) Miracidium: with tiers of epithelial ciliated cells, anterior gland cells, central 'eye spot' consisting of two pigment cup ocelli overlying a nervous cerebral ganglion, flame cells and posteriorly positioned germinal cells. (ii) Sporocyst: a sac shaped larval stage with no gut and a central cavity containing clusters of dividing germinal cells. (iii) Redia: with a large oral sucker and a simple gut, muscular processes in the body wall and a central cavity containing developing larval stages. (iv) Cercaria: a larva with a muscular propulsive tail and a head with gut, oral and ventral suckers and often penetration glands and cystogeneous glands. (v) Metacercaria: a transformed cercarial head surrounded by a secreted cyst wall. The cercarial head usually shows some development of somatic and reproductive characteristics towards the adult state. (b) Diagrammatic flow-chart of the basic organization of the life cycles of medically important digeneans that infect man. Species identities: 1: *Schistosoma*; 2: *Fasciolopsis*; 3: *Fasciola*; 4: *Gastrodiscoides*; 5: *Opisthorchis*; 6: *Heterophyes*; 7: *Metagonimus*; 8: *Paragonimus*; 9: *Echinostoma*; 10: *Dicrocoelium*.

or by the ingestion of the unhatched egg by a snail. Within the molluscan host the miracidium transforms into a sporocyst which is a tegument-covered, gutless germinal sac, containing germinal cells. These develop (in different species) into either a second generation of sporocysts or into a new larval type with a gut – the redia. Rediae can often produce further generations of rediae but eventually rediae or daughter sporocysts begin, again asexually, to produce cercariae, which are the larval stages that leave the molluscan host. A cercaria is a tailed, actively swimming larval form, the head of which will develop into an adult worm and often already possesses partially developed reproductive organs. Cercariae leave the snail, the first intermediate host, often with a marked circadian periodicity, and they or the metacercariae which develop from them, infect the final host.

The sequence of asexually reproducing larval stages in the mollusc is often able to sustain very high overall reproductive rates for this part of the life cycle. Ultimately many thousands of cercariae may develop from a single miracidial infection of a snail. Digeneans typically demonstrate greater host specificity with respect to their first intermediate hosts than they do to any subsequent hosts in the life cycle.

The majority of digenean life cycles involve metacercariae. These are cercariae that have shed their propulsive tails and have encysted either on external objects like snail shells or vegetation, or within second intermediate host species – vertebrate or invertebrate. Within these cysts, produced by cystogenous glands in the cercarial head, the cercaria carries out a partial development towards somatic and reproductive maturity. The remainder of this development is completed when the cyst is consumed by a final host. Only in a few digeneans is the free-swimming cercaria directly infective to the final host by an active penetration process that eliminates the need for a metacercarial phase. Although uncommon, this process has great epidemiological significance as it is the infection mode employed by schistosome cercariae.

Of the 6000 or so known digenean species only about a dozen are regular and important human parasites. Many more species, though, are spasmodically diagnosed as accidental human infections. The main non-schistosome digeneans which infect humans are listed in Table 2.6 along with some of their basic biological characteristics. Schistosomes, however, must be regarded as the most important human digeneans with a global total of over 200 million infected persons, a significant proportion of whom will experience moderate-to-severe levels of morbidity.

2.4.5 Human schistosomiasis

Four species of the digenean genus *Schistosoma* are important human parasites. Of these *S. mansoni*, *S. haematobium* and *S. japonicum* have widespread distributions, while *S. intercalatum* is restricted to specific foci in parts of Africa. *Schistosoma haematobium* causes urinary schistosomiasis whereas the other three species are the causative agents of the intestinal form of the disease.

Schistosomes are bizarre digeneans. Many aspects of their morphology, physiology and life-cycle tactics are unorthodox or unique when compared with the other members of the taxon. Adult worms live in the lumina of blood vessels and feed directly on the cellular and plasma fractions of blood. The species causing intestinal schistosomiasis live in the mesenteric veins of the gut while *S. haematobium* occupies the vesical veins of the bladder wall. As an adaptation for these unusual microhabitats, the worms are threadlike in shape, 10–30 mm in length but only 0.2–1.0 mm in width. They are also dioecious and the male and female worms show considerable sexual dimorphism (Fig. 2.6). Cylindrical elongate females live permanently in an extensive ventral groove, the gynaecophoric canal, of the shorter, stouter males. In most schistosomes, female sexual maturity only follows successful pairing with a male worm.

Living as they do in a host location in which immunological defences might be expected to be both rapidly engendered and effective, adult schistosomes possess a range of adaptations in the molecular organization of their outer surface which enable them to partially counter these defences (see Chapter 8, Section 8.6.3). In this way adult worms are able to live and reproduce

Table 2.6 Some features of non-schistosome digenean diseases of humans

Name	Site of adult worms in man	Route of egg emergence	Snail (first intermediate) host and mode of snail infection	Mode of human infection	Geographical distribution
Fasciolopsis buski	Small intestinal mucosa, rarely in stomach or colon	Faeces	*Segmentina* (external miracidial invasion)	Metacercarial cysts on water plants, such as water caltrop and water chestnut: eaten	China, Taiwan, India, Thailand, Laos, Kampuchea and Bangladesh
Heterophyes heterophyes	In crypts of jejunum and upper ileum	Faeces	*Pironella* and *Cerithidia* (egg ingestion)	Metacercarial cysts in fish, such as mullet and *Tilapia*: eaten	Egypt, Israel, Romania, Greece, Japan, China, Taiwan, Philippines
Metagonimus yokogawai	Muscosal folds of jejunum	Faeces	*Semisulcospira* (egg ingestion)	Metacercarial cysts in fish, such as carp and trout: eaten	Japan, Korea, China, Taiwan, Siberia
Gastrodiscoides hominis	Mucosal lining of caecum and ascending colon	Faeces	*Helicorbis* (external miracidial invasion)	Probably by ingestion of metacercarial cysts on water plants such as water caltrop	India, Bangladesh, Vietnam, Philippines
Opisthorchis sinensis	Bile duct	Faeces	*Bulinus, Parafossarulus, Alocima* (egg ingestion)	Metacercarial cysts in freshwater fish: eaten. Juvenile flukes migrate directly up bile duct from gut	China, Taiwan, Korea, Japan, Vietnam
Fasciola hepatica	Bile duct	Faeces	*Lymnaea* (external miracidial invasion)	Metacercarial cysts on watercress or lettuce: eaten. Juvenile flukes penetrate gut wall then liver from the perivisceral cavity	Central and S. America, Cuba, France, UK, N. Africa
Paragonimus westermani	In cysts in lungs, rarely in a variety of extra-pulmonary sites	Sputum and faeces	*Semisulcospira, Thiara* and *Oncomelania* (external miracidial invasion)	Metacercarial cysts in freshwater crabs and crayfish: eaten	China, Taiwan, Korea, Japan, Philippines, India, Malaysia, Indonesia

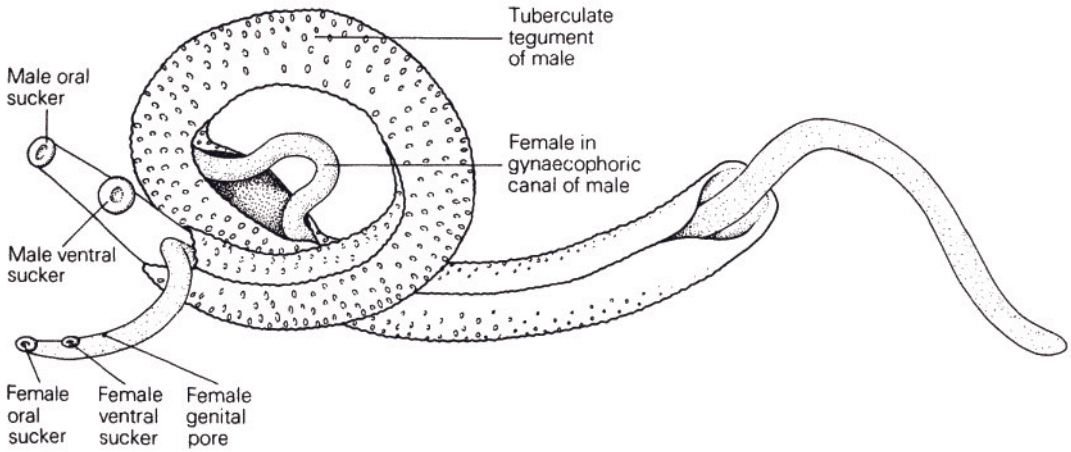


Fig. 2.6 *In copulo* pair of adult schistosomes (based on *S. mansoni*).

for many years in a host who is relatively resistant to new infections.

Pairs of adult worms produce eggs which are laid into the lumina of the venules in which they live. There is no direct, non-pathological route by which these eggs can reach the outside world from this location. In fact, most schistosome eggs possess a sharp shell spine which helps to provide a means of escape. Spines lodge in the intima of the venule and impede the movement of eggs by blood flow. Small blood vessels packed with eggs may rupture, enabling them to move into surrounding connective tissue. A proportion of these eggs eventually reach the outside world via the lumen of the gut or bladder in faeces or urine. This necessarily unusual exit route for schistosome eggs is at the heart of their considerable pathogenicity. Many eggs become lodged in the tissues all over the body. In these locations, living and then moribund or dead eggs become immobilized in spherical granulomatous lesions. It is these progressively accumulating lesions in many different organs which give rise to most chronic schistosome-induced pathology.

The eggs which do leave an infected person in urine or faeces hatch on contact with freshwater and the emergent miracidia infect a range of aquatic and amphibious snails in which infective cercariae are produced. All human digenean infections other than schistosomiasis are initiated when people eat metacercarial cysts. Schistosome transmission is quite different. Furcocercariae emerging from the snails survive on average for about a day at 20°C, swimming tail-first through the water. During this brief, free-swimming and non-feeding existence fuelled by endogenous glycogen reserves, they are directly infective to people entering the water in which they are swimming. Aided by small backward-pointing tegumental spines and cytolytic secretions a cercaria rapidly penetrates bare human skin, often down the side of a hair shaft and sheds its tail in the process. The penetrant cercarial head can now be considered as an immature adult schistosome or schistosomulum. Schistosomula enter the peripheral blood system and are carried eventually to the lungs, usually within a week of skin penetration. From the lungs the worms migrate to the liver where they pair up and mature. Pairs of worms then move to their final egg-producing sites. Figure 2.7 illustrates the general organization of human schistosome life cycles while Table 2.7 outlines specific information on the four major species.

Schistosomiasis is very largely a rural disease of the tropics. Contact with mud or water carrying infective cercariae comes about by children playing in water, water gathering or washing and very importantly in the course of work. Agricultural practices which involve direct human contact with irrigation water are especially hazardous. One reason for the increasing prevalence of all rural schistosomiases is the expanding programme of construction of dams for hydroelectric

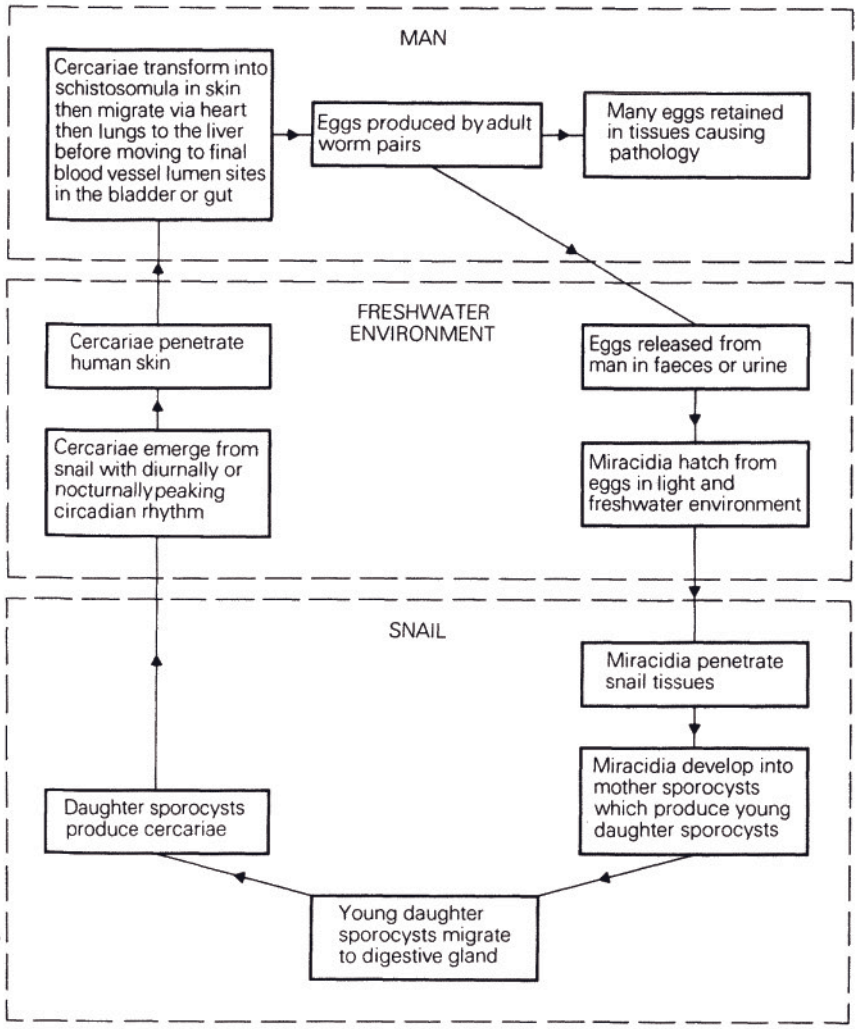


Fig. 2.7 Diagrammatic flow-chart of the main features of the life cycles of human schistosomes.

or irrigation purposes in developing countries. Such schemes inevitably produce new water-bodies for snail colonization.

The pathological effects of intestinal and urinary schistosomiasis are somewhat different. Those, for instance, of *S. mansoni* intestinal schistosomiasis are slowly progressive and complex. During the initial invasion stage there may be a transient dermatitis or 'swimmer's itch'. Thereafter most pathology is the direct or indirect result of the host's immunological responses to parasite eggs (see Chapter 8, Section 8.8). In heavy infections eggs in the lining of the gut cause granulomatous reactions there which can extend into the gut lumen as pseudopapillomas, with or without egg calcification. Extensive change of this sort may cause colonic obstruction and blood loss. The hepatic portal system carries many eggs to the liver and eggs trapped there are the foci of new granulomatous lesions. General damage to the liver induced in this way produces liver enlargement (hepatomegaly) and following portal hypertension, splenomegaly also occurs. Damage to the portal circulation causes collateral

Table 2.7 Some features of human schistosomes

Name	Site in man	Route of egg emergence	Intermediate hosts	Geographical distribution	Reservoir hosts
Schistosoma mansoni	Mesenteric veins	Faeces	*Biomphalaria* spp.	Egypt, Middle East, W. Central and S.E. Africa, Malagasy, Brazil, Venezuela and some Caribbean islands	Probably not important except in S. America where some rodents are infected
Schistosoma haematobium	Vesical veins of the bladder	Urine	*Bulinus* spp.	Africa, Malagasy and Middle East	No important reservoir hosts
Schistosoma japonicum	Mesenteric veins	Faeces	*Oncomelania* spp.	China, Philippines, Japan, Vietnam, Thailand, Laos and Kampuchea	Important throughout range dogs, rats, pigs, cattle, etc
Schistosoma intercalatum	Mesenteric veins	Faeces	*Bulinus* spp.	Limited distribution in Zaire, Central African Republic, Cameroon and Gabon	No important reservoir hosts

circulatory shunts to be set up and these enable eggs in the bloodstream to bypass the filtering action of the liver. Consequently, eggs begin to reach the lungs and heart causing pathology there.

The pathology caused by *S. intercalatum* is similar to that of *S. mansoni* but less severe. *Schistosoma japonicum* infections are often characterized by colonic pathology associated with the presence of large numbers of calcified eggs.

The symptoms of urinary schistosomiasis caused by *S. haematobium* are closely linked with the bladder location of the adult worms and their eggs. Eggs are deposited in the walls of the bladder itself and the ureters. Granulomatous reactions, and later fibrosis and calcification, induce a wide range of pathological manifestations including haematuria and dysuria, hyperplasia of the bladder lining which can progress to bladder cancer, partial blockage of the ureters and secondary damage to the kidneys.

2.4.6 Other digeneans

Fasciola hepatica, the liver fluke, is primarily a parasite of sheep and cattle but it also infects humans. There is also a wide range of other digenean infections of agricultural stock that only very rarely cause human disease. Among the liver and bile-duct-inhabiting species are *F. gigantica*, living in a variety of agricultural and feral ruminants in Africa and the Far East; *F. magna* that infects deer, horses, cattle and sheep in North America; and *Dicrocoelium dendriticum* infecting sheep and other herbivores particularly in Europe and Asia. Other important parasites of ruminants include the paramphistomes, usually in the genus *Paramphistomum*, which are especially damaging to cattle.

Other schistosomes also warrant some attention. *Schistosomatium douthitti*, a parasite of rodents, has been used as an easily maintained laboratory analogue of human schistosomes. In many of the warmer parts of the world cattle and sheep are severely affected by a large number of *Schistosoma* species. *Schistosoma bovis* in Southern Europe, Africa and Asia, *S. mattheei* in Southern Africa and *S. spindale* in Africa and India all cause serious losses.

2.5 NEMATODE PARASITES OF VERTEBRATES

The nematodes are the most successful group among the pseudocoelomic, eutelic Aschelminthes. The relative lack of interspecific morphological variation among nematodes belies their ecological diversity. They are almost all unsegmented, spindle-shaped roundworms with bilateral symmetry (Fig. 2.8). Both free-living and parasitic species take this form and the vast majority have a highly conservative life-cycle developmental sequence (Fig. 2.9). This starts when dioecious adults sexually produce eggs that hatch to release L_1 larvae, which with intervening cuticular moults and size increases, develop through three more larval phases (L_2, L_3 and L_4) before attaining full sexual maturity after the final post-L_4 moult.

The cuticle which is repeatedly moulted, secreted anew and rearranged during development is a central element in the structural organization of all nematodes. It is a multi-layered covering of the nematode body consisting of collagen and other components. A number of surface invaginations of the body wall (buccal cavity, pharynx, excretory pore, vulva, chemosenosory pits called amphids and phasmids, rectum, cloaca and spicule pouches) are also cuticle-lined. Stylets, teeth and cutting blades in the buccal cavity and the copulatory spicules are essentially cuticular structures.

The body plan and behavioural repertoire of nematodes appear to have provided a degree of preadaptation for endoparasitic lifestyles within this group. The chemically and physically resistant cuticle presumably enabled originally free-living species to exist in the damaging conditions in vertebrate guts into which they could be accidentally transferred by host feeding. Similarly the substrate burrowing abilities of many nematodes must have made the penetration of host integuments and internal tissues a distinct possibility.

Table 2.8 outlines a classification of nematodes that are parasitic in vertebrates itemizing species that infect humans. The horrifyingly long inventory of human parasitic diseases can be split

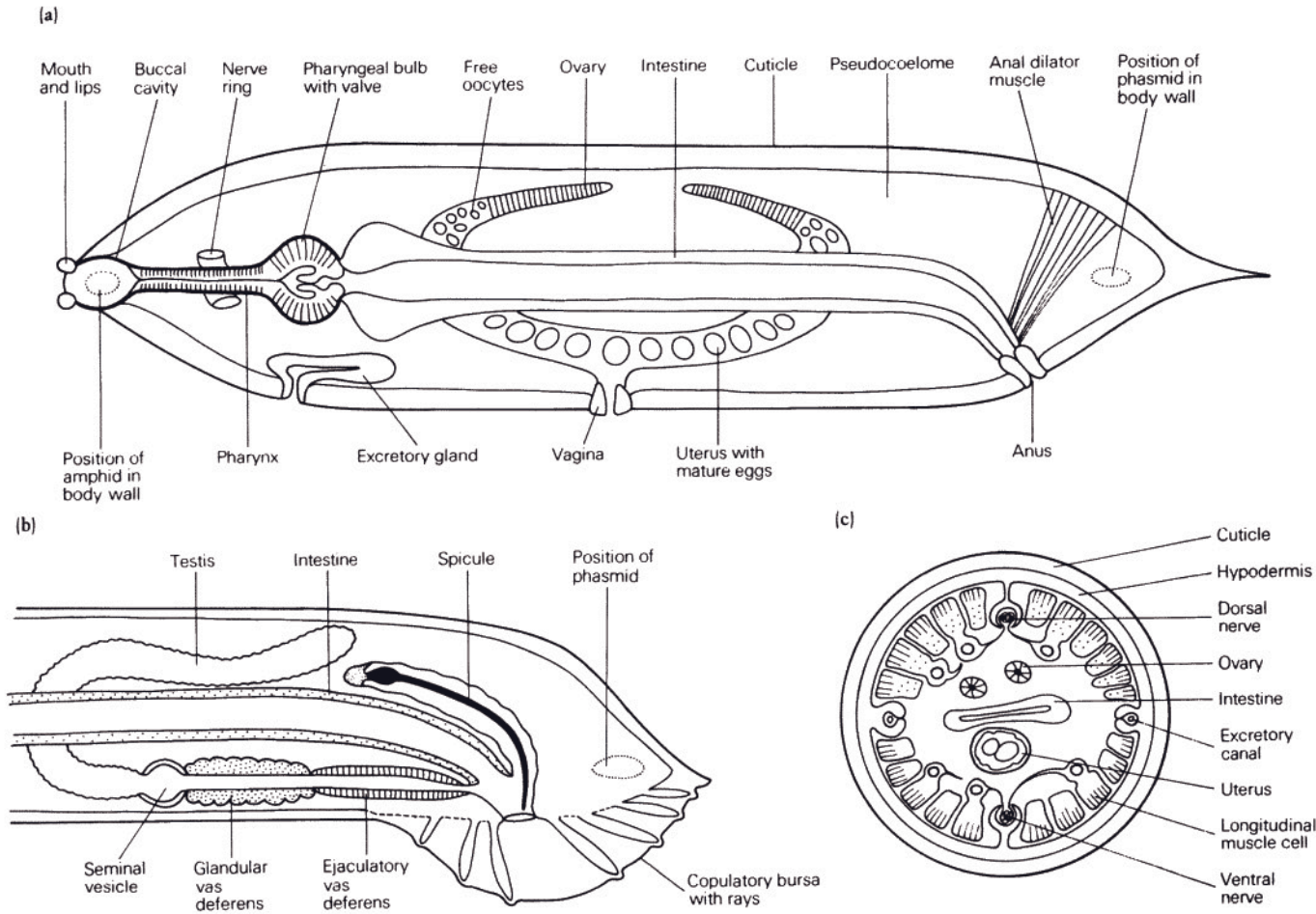


Fig. 2.8 Highly schematic representations of nematode morphology. (a) A sexually mature female worm. (b) The posterior end of a sexually mature male worm. (c) A tranverse section through a female worm.

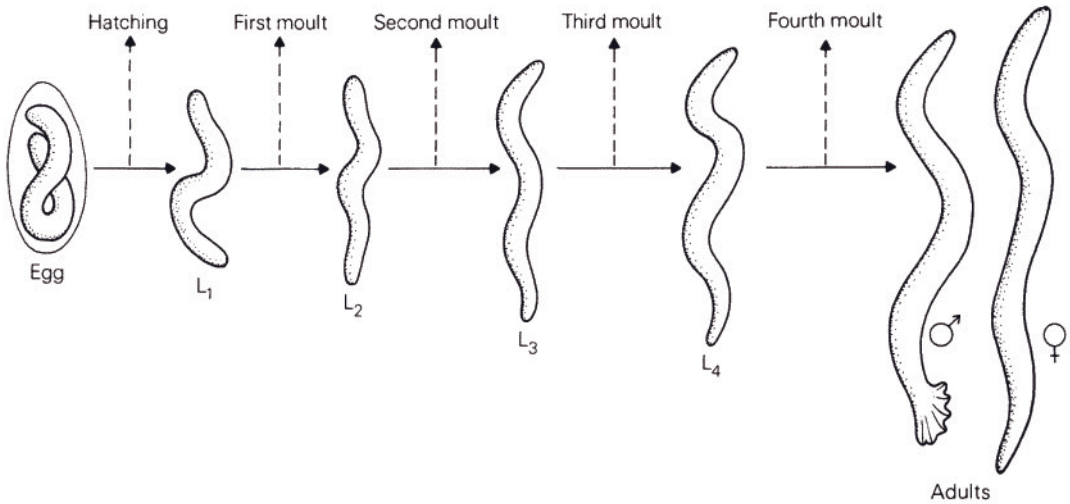


Fig. 2.9 A typical nematode developmental sequence.

Table 2.8 Outline classification of the nematode parasites of vertebrates with particular emphasis on orders and superfamilies containing important human parasites

PHYLUM: NEMATODA

Subclass 1: Secernentea (Posterior phasmid chemoreceptive organs present)

Order 1: Rhabditida. Parasitic female adults parthenogenetic, pharynx often possesses prominent posterior muscular bulb (e.g. *Strongyloides*)

Order 2: Strongylida. Adult males possess copulatory bursa with supporting rays. L_1 and L_2 larvae often free living

Superfamily 1: Ancylostomatoidea. Prominent buccal capsule often with cuticular teeth or cutting plates – 'hookworms' (e.g. *Ancylostoma, Necator*)

Superfamily 2: Strongyloidea

Superfamily 3: Trichostrongyloidea

Superfamily 4: Metastrongyloidea

Order 3: Ascaridida. Large intestinal nematodes; three-lipped mouth; simple pharynx (e.g. *Ascaris, Toxocara*)

Order 4: Oxyurida. Pharynx possesses posterior bulb with valves. Adult female has long pointed post-anal tail (e.g. *Enterobius*)

Order 5: Spirurida. Pharynx divided into two sections, a shorter anterior muscular portion and a longer glandular posterior one

Superfamily 1: Filarioidea. Very elongate adults; usually viviparous; intermediate hosts blood sucking arthropods – 'filarial worms' (e.g. *Wuchereria, Brugia, Loa, Onchocerca, Dipetalonema, Mansonella*)

Superfamily 2: Dracunculoidea. Very elongate adults with extreme sexual dimorphism – females much longer than males. Mature female vulva nonfunctional; viviparous; intermediate hosts copepods (e.g. *Dracunculus*)

Superfamily 3: Gnathostomatoidea

Superfamily 4: Thelazoidea

Superfamily 5: Habronematoidea

Superfamily 6: Physalopteroidea

Subclass 2: Adenophorea (Phasmids absent; pharynx usually forms a stichosome)

Order 1: Enoplida

Superfamily 1: Trichuroidea. Adult body divided into slim anterior region and broader posterior section. Female possesses only a single ovary and uterus; males have single or absent spicule (e.g. *Trichinella, Trichuris*).

Superfamily 2: Dioctophymatoidea

epidemiologically into three subsets (Table 2.9). Direct life cycle intestinal forms and insect vector-transmitted filarial species are two homogeneous groupings. The remaining species are a heterogeneous mixture of larval and adult infections that are neither insect transmitted nor have

Table 2.9 Nematode species causing important disease in humans

Name	Geographical distribution
INTESTINAL PARASITES	
Strongyloides stercoralis	Worldwide in tropical zone
Ancylostoma duodenale	Worldwide in tropics and subtropics plus Mediterranean fringes
Necator americanus	Worldwide in tropics and subtropics including S.E. states of USA
Enterobius vermicularis	Cosmopolitan
Ascaris lumbricoides	Cosmopolitan
Trichuris trichiura	Cosmopolitan
FILARIAL PARASITES	
Wuchereria bancrofti	Asia, Africa, S. America, Pacific Islands
Brugia malayi	S.E. Asia
Onchocerca volvulus	Yemen, Africa, S. and Central America
Loa loa	W. and Central Africa
Dipetalonema perstans	Africa, S. America
Dipetalonema streptocerca	W. and Central Africa
Mansonella ozzardi	S. America, Caribbean
OTHER NEMATODES	
Toxocara spp. (only larvae in humans)	Cosmopolitan
Dracunculus medinensis	Africa, Middle East, Pakistan, India
Trichinella spiralis (adults intestinal)	Cosmopolitan

simple direct life cycles with free-living eggs or larvae as infective stages.

2.5.1 Human intestinal nematodes

These are the most important human intestinal helminth parasites in terms of both their overall prevalences and their potential for causing serious clinical harm. All the six important species (Table 2.9) have direct life cycles and, apart from *Enterobius vermicularis*, they are all soil-transmitted in the sense that the eggs or larvae responsible for transmission normally become infective during a period of development in the soil. They are sometimes termed geohelminths because of this characteristic. Similar modes of transmission and the extensive and overlapping geographical distributions of these helminths, together ensure that many individuals suffer from concurrent infections with two or more species of these intestinal parasites. Such multiple infections are often particularly harmful.

Ascaris lumbricoides (Fig. 2.10), is the largest human intestinal nematode and probably one of the most prevalent with between 800 million and a billion persons infected globally. Although most cases occur in the Far East and tropical Africa it is a truly cosmopolitan parasite. Transmission potential is determined largely by human

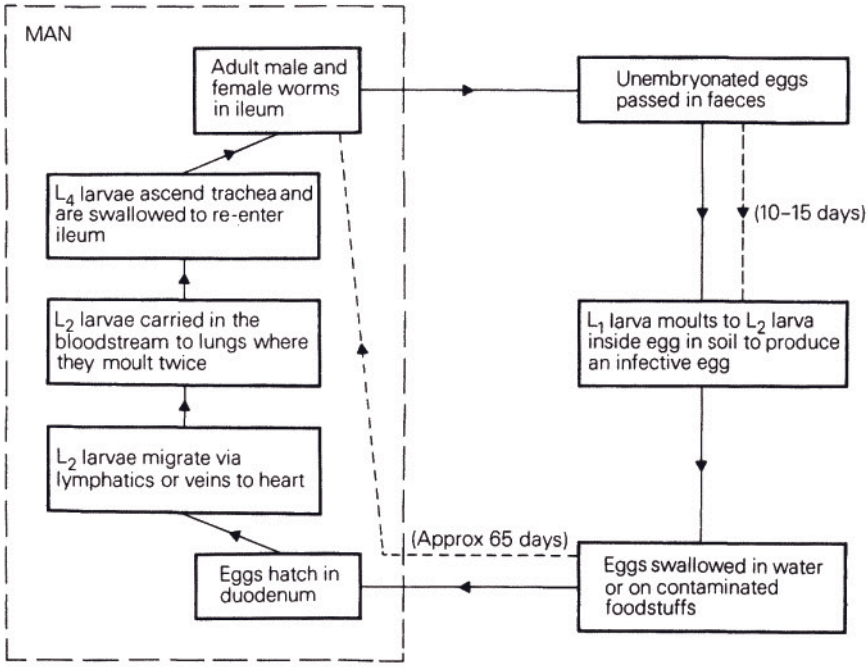


Fig. 2.10 The life cycle of *Ascaris lumbricoides*.

faecal disposal practices and is highest where soil around dwellings is heavily contaminated with faeces or where faecal slurry (night soil) is used as an agricultural fertilizer. The very long-lived eggs (maximum survival around 7 years) are typically ingested via uncooked, unwashed vegetables or in contaminated water.

Migrating *Ascaris* larvae cause allergic bronchopneumonia in previously infected and sensitized patients along with bronchitis, bronchospasm and urticaria. Adult worms in the small intestine in high density can cause obstruction and worms can migrate out of the gut into the bile duct, pancreatic duct, oesophagus, mouth and occasionally the liver. Worms may also perforate the intestine inducing peritonitis.

Trichuris trichiura (Fig. 2.11), the causative agent of trichuriasis or whipworm infection, is an unusually shaped worm about 4 cm long with an extremely long, thin pharyngeal region and a wider posterior section containing the rest of the gut and the reproductive organs. The buccal cavity has a small stylet with which the worms disrupt the caecal mucosa. The thin anterior region lies embedded shallowly in the surface of the mucosa with the rear portion free in the gut lumen. Infections are most common in humid tropical countries with global infections probably totalling well over 500 million cases. Low density *Trichuris* infections can be without symptoms but higher density infections, especially in undernourished children can be highly pathogenic and result in chronic bloody diarrhoea, colic, anaemia and rectal prolapse.

Ancylostoma duodenale and Necator americanus (Fig. 2.12), two morphologically and developmentally similar blood-feeding nematodes, cause human hookworm disease (ancylostomiasis). Both forms are extensively distributed in the tropical and subtropical zones of the world with a probable total prevalence of 700–900 million cases. Hookworms are transmitted to humans by skin-penetrating L_3 larvae that develop in faecally contaminated soil. Adult worms attach themselves to gut villi and use cutting blades or teeth in their buccal capsules to abrade the mucosal surface.

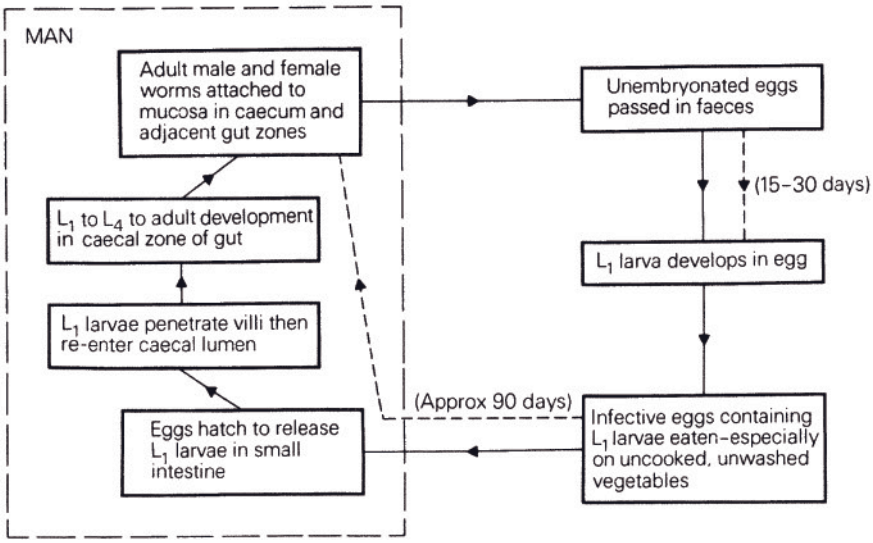


Fig. 2.11 The life cycle of *Trichuris trichiura*.

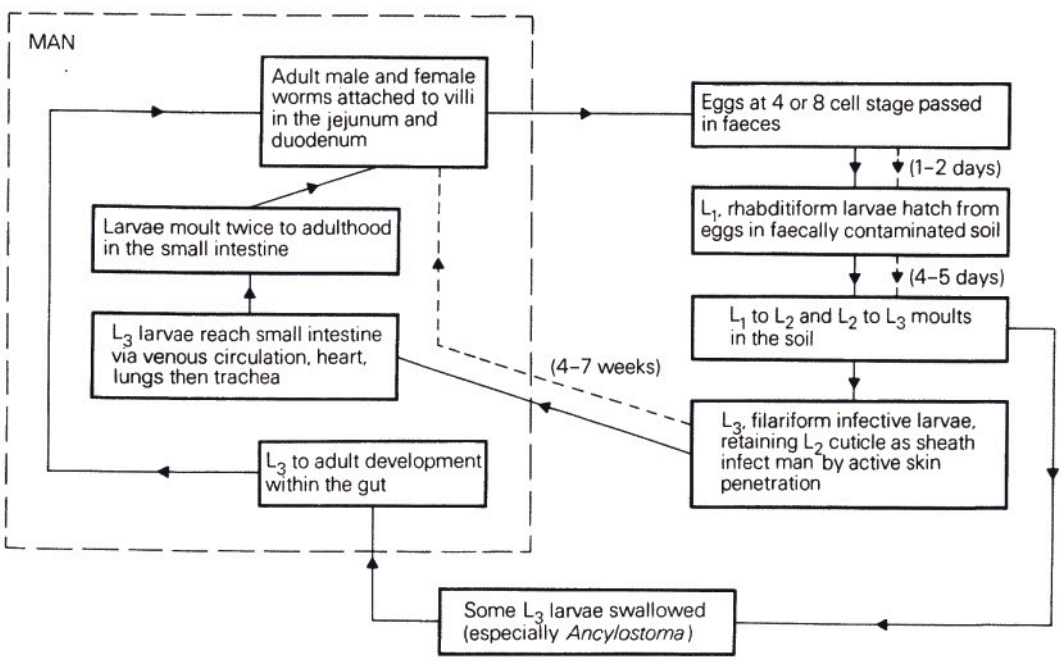


Fig. 2.12 The life cycle of human hookworms.

They then feed on blood so that anaemia is a prominent symptom in many cases of hookworm disease.

The disease induces three quite distinct types of pathology. Invading L_3 larvae cause an allergic dermatitis with a papular and sometimes vesicular rash that is termed ground itch. Lung pathology – focal haemorrhages and allergic

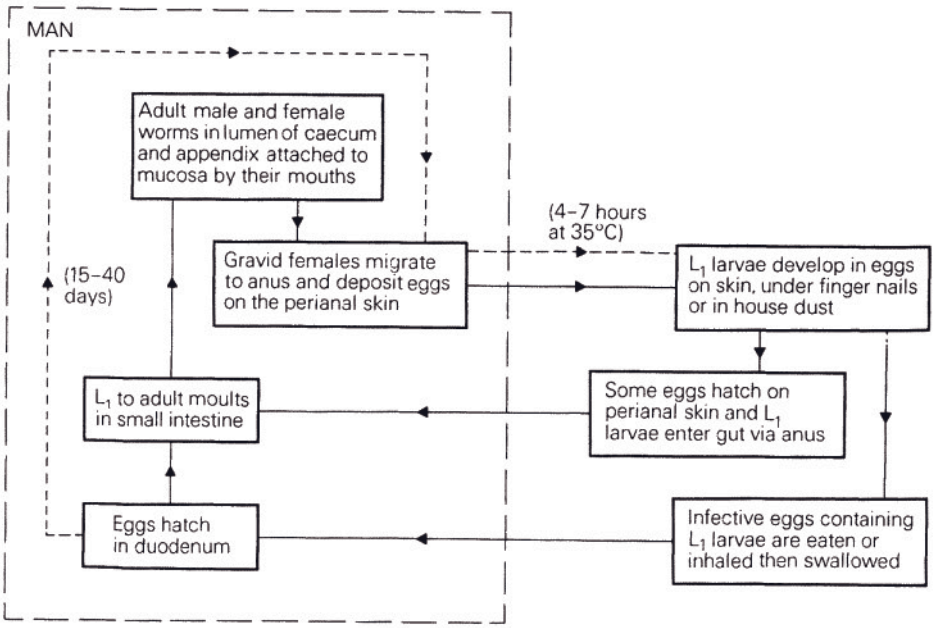


Fig. 2.13 The life cycle of *Enterobius vermicularis*.

pneumonia – can be provoked by migrating larvae. The most important damage, though, is caused by the blood-feeding adults. Up to 200 ml of blood per day may be lost due to this cause by a patient with a heavy infection although some of the iron in this deficit is reabsorbed. The final degree of anaemia and associated protein loss in a particular patient is a complex resultant of hookworm species, worm load and host nutritional status.

L_3 larvae of a number of non-human hookworm species can penetrate human skin and cause irritating 'cutaneous larval migrans' as they move laterally in the skin. Such larvae never develop to adulthood so the infections are self-limiting.

Enterobius vermicularis (Fig. 2.13), the causative agent of enterobiasis or pinworm disease affects some 500 million individuals, mainly children, globally and is more common in temperate than tropical countries. It is of only minor pathogenic significance and the mode of infection can be considered contaminative as the eggs are infective almost immediately after release onto the perianal skin. Infective eggs are found in clothing and bedding and children can reinfect themselves by transferring eggs from anus to mouth with the fingers. This is facilitated by the pruritus ani which is the commonest symptom of infections to become apparent. Probably most infections are symptomless and self-limiting. Ectopic worms may be found in some girls in the vagina and uterus.

Strongyloides stercoralis (Fig. 2.14) infections (strongyloidiasis) occur either when L_3 larvae penetrate the skin or develop directly within the gut. The life-cycle organization of this parasite is further complicated by the existence in some circumstances of an entirely free-living cycle of sexually reproducing adults and their larvae in the soil. This alternative route can produce L_3 larvae that are infective. The pathology associated with this disease can be divided into larval and adult-generated phases. The larvae give rise to dermatitis at their sites of invasion. They then migrate to the lungs where they cause allergic pneumonia. High densities of egg-laying adult females in the gut cause mucosal inflammation and malabsorption. Some larvae can re-enter the gut mucosa or penetrate the perianal skin to

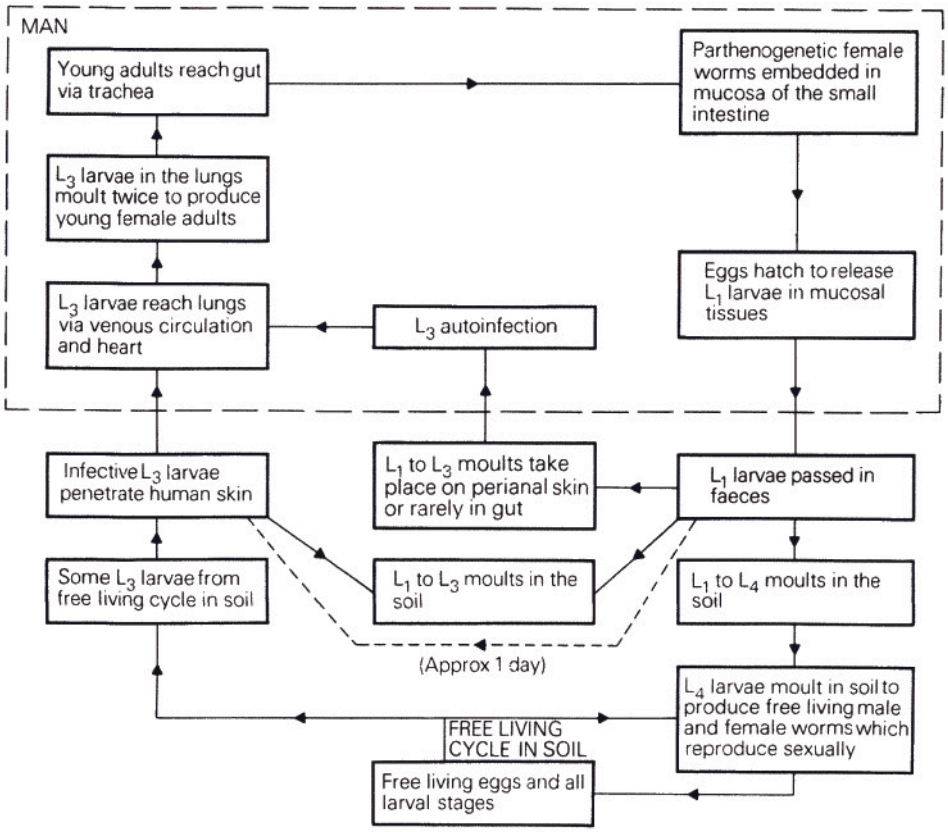


Fig. 2.14 The life cycle of *Strongyloides stercoralis*.

maintain a chronic infection status. In immunosuppressed hosts this autoinfection route can be amplified to produce a considerable and sometimes life-threatening larval invasion of many organ systems.

2.5.2 Human filariasis

Filarial worms are long-lived nematodes that all require a period of larval development (L_1 to L_3) in a blood-sucking insect host. These biting vectors initiate new human infections. Table 2.9 lists the seven major filarial species and Fig. 2.15 outlines the basic features of their essentially similar life cycles. Of the seven, *Wuchereria bancrofti* which causes lymphatic filariasis and *Onchocerca volvulus* which induces river blindness and onchodermatitis are widespread and extremely damaging infections. *Brugia malayi* and *Loa loa*, although pathogenic, are much more restricted in distribution while *Dipetalonema perstans*, *D. streptocerca* and *Mansonella ozzardi* cause relatively few serious infections.

Adult filarial worms are rarely seen diagnostically. Diagnosis depends on collection and microscopical identification of L_1 larvae, termed microfilariae, in either the peripheral blood or skin. Most, if not all, filarial species are divided into geographical subspecies or strains which may utilize different vector species, display differing circadian periodicity of microfilarial density in the blood and be associated with distinctive human pathological syndromes (see Chapter 7, Section 7.2.6).

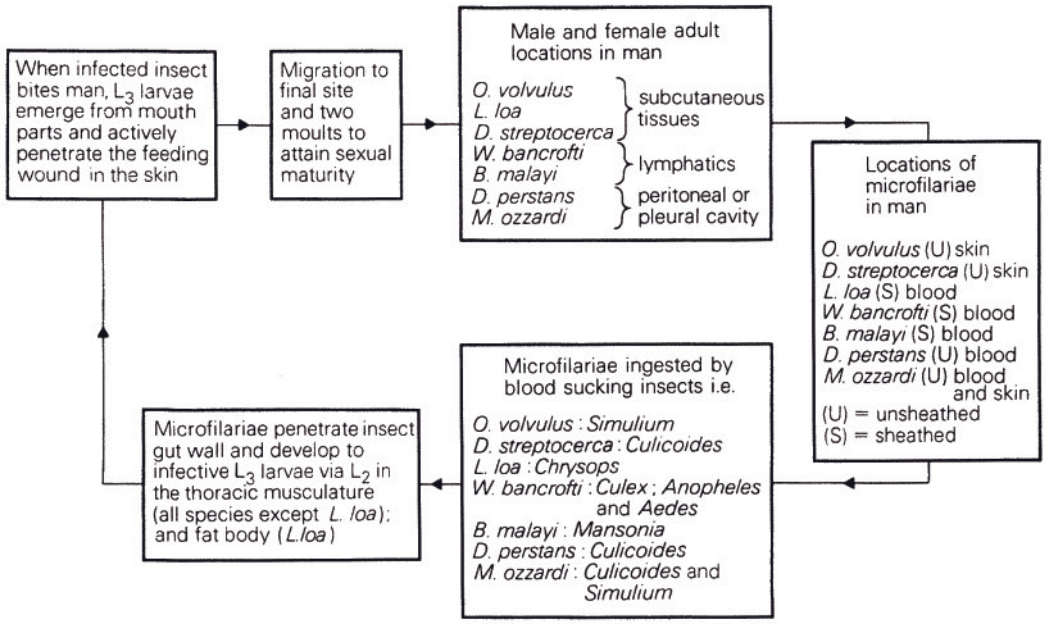


Fig. 2.15 The life-cycle organization of the seven most important human filarial parasites.

Lymphatic filariasis

Two filarial species *Wuchereria bancrofti* and *Brugia malayi*, which are very similar morphologically, live as adults in the afferent lymphatic vessels of the human host and produce blood-dwelling sheathed microfilariae. Diagnosis of lymphatic filariasis depends largely on finding and identifying these larvae in the peripheral blood. The characteristic pathologies associated with these infections, however, are hardly ever related to the larvae but instead to the adult worms in the lymphatics. The clinical course of pathogenesis is strongly linked with inflammatory and immunological host responses to the adults and commonly passes through three phases. The first or incubation phase – the time between infection and the first appearance of blood microfilariae – is rarely associated with symptoms although there may be some lymphatic inflammation and fever. The second phase of indeterminate duration is associated with adult worms producing microfilariae and is termed the acute inflammatory phase. It is marked by intermittent bouts of lymphatic inflammation and pain along with fever. In *Wuchereria* infections there may also be episodes of inflamed lymph nodes in the inguinal region and scrotal changes including orchitis, hydrocoele and epididymitis. When it occurs, the final or obstructive phase displays irreversible lymphatic-centred damage with both filarial species. The most disfiguring aspect of these changes is the condition termed elephantiasis. This can occur to the legs, arms, scrotum, vulva and breasts. It is a chronic lymphoedema associated with very extensive fibrous infiltration and thickening of the skin.

Taken together, Bancroftian filariasis and *Brugia* infections occur in some 250 million people at any one time. *Wuchereria* cases, transmitted by *Culex*, *Anopheles* and *Aedes* mosquitoes, are predominantly found in India, the Far East, Polynesia and East Africa. The urban cycle of this disease which typically occurs in shanty town conditions is gradually assuming an increasing importance. *Brugia* infection, transmitted by *Mansonia* vectors, is an almost entirely rural disease restricted to South-East Asia. Some forms of *Brugia*-induced lymphatic filariasis possess forest-dwelling animal reservoir hosts such

as monkeys and forest cats. Bancroftian filariasis has no such zoonotic complication.

Onchocerciasis

Onchocerca vovulus causes human infections and considerable morbidity across Africa and in minor pockets in South and Central America and in Yemen. Within this geographical range about seven distinct parasite strains exist, each transmitted with its own species of blackfly in the genus *Simulium*, and each associated with its own particular pathological pattern. Most blackfly species have to breed in well-oxygenated, fast-flowing freshwaters and the detailed spatial distribution of onchocerciasis infections largely reflects this riverine pattern.

The disease causes two types of severe pathology – ocular changes including blindness (river blindness) and onchodermatitis. Both are the result of immune responses to microfilariae, in contrast to the damage caused in lymphatic filariasis where adult worms are responsible. The unsheathed microfilariae of *Onchocerca* are found in the skin rather than the blood system and arise from groups of copulating adult worms located in fibrous nodules in subcutaneous tissues. These nodules, which may be several centimetres in diameter, can often be seen externally as rounded elevations of the skin. Other, deeper nodules are, however, invisible externally. Diagnosis of infections is based on microfilarial identification in skin snips, each 2–3 mm in diameter.

Microfilariae induce a wide range of skin changes in infected patients. Early, light infections may produce an itchy rash. In more chronic infections patchy depigmentation or increased pigmentation can occur and the skin becomes thickened and coarse while losing its elasticity. These changes in the integument predispose to hernias, 'hanging groins' or pendulous pouches under the eyes. Microfilariae moving through the skin reach the eyes and here they produce the most striking pathology linked with *Onchocerca*. The final stage of this is blindness, the 'river blindness' which is especially common in the savannah areas of West and Central Africa. In heavily infected villages close to rivers with high *Simulium* densities, as many as 30% of the population may become blind. Total blindness, though, is only the distressing endpoint of a progressive and accumulative series of changes that over a number of years involve all portions of the eyes.

Other human filarial infections

Loa loa causes loiasis in the rain-forest zones of West and Central Africa and is transmitted by large day-feeding tabanid flies in the genus *Chrysops*. Adult worms live subcutaneously but do not form permanent nodules. They move around inducing transient 'calabar swellings' and sometimes visibly cross the front of the eye under the conjunctiva.

Other filarial species, *Dipetalonema streptocerca* from Africa, *D. perstans* in Africa, Central and South America and *Mansonella ozzardi* from the Caribbean and South America are not of great pathological significance.

2.5.3 Other human nematode diseases

Dracunculiasis

This disease which is also called guinea worm disease, is caused by *Dracunculus medinensis*, the mature females of which may reach almost a metre in length. Dracunculiasis is widespread in much of India as well as parts of West and Central Africa, with more restricted foci in Pakistan, Iraq, Iran and Saudi Arabia. The parasites have an indirect life cycle and human infections occur when people drink water contaminated with copepods containing infective L_3 larvae of the nematode. Ingested larvae penetrate the human gut wall and spend about 12 weeks growing, moulting to adulthood and mating in the subcutaneous tissues. After copulating, female worms move down through the body reaching a lower extremity like the ankle or foot about 8–10 months after the original infection. Here the mature female, with its uterus filled with about one million L_1 larvae, induces a blister in the host's skin which subsequently bursts. This enables large numbers of actively swimming L_1 larvae to leave the lesion each time it is immersed in water, over a period of 3–4 weeks. Copepods then ingest larvae which develop into L_3 larvae in these intermediate hosts.

This indirect life cycle means that the disease is usually focally transmitted. Sites of infection are often small discrete water sources such as pools with gently shelving sides in Africa, or constructed step wells in India. In both such circumstances persons washing, drinking or collecting water are required to stand in the water. This contact enables L_1 larvae from infected persons to enter the water and infect copepods. Blister formation can be an extremely painful process and the open wound of the blister often becomes secondarily infected. Adult female worm infections closely associated with bony joints can lead to arthritis.

Trichinosis

Trichinosis, caused by *Trichinella spiralis*, is a cosmopolitan disease which demonstrates a very low vertebrate host specificity. Short-lived adult infections in the guts of a wide range of carnivorous and omnivorous mammals give rise to large numbers of invasive L_1 larvae which migrate to voluntary muscles throughout the bodies of these same hosts. Here they encyst. The cysts are the infective stages which can be transmitted to any new host when infected flesh is eaten. In domestic cycles throughout the world, human hosts become infected by eating cyst-containing

Table 2.10 Nematodes of domesticated animals (including species utilized as laboratory models)

Name	Final hosts	Comments
ORDER STRONGYLIDA		
Dictyocaulus viviparus	Cattle	Adult worms parasitic in lungs
Haemonchus contortus	Sheep	'Stomach worm'; blood-feeding injurious parasite, particularly pathogenic in young hosts
Nippostrongylus brasiliensis	Rats	Adults parasitic in rat intestine; much used laboratory nematode in immunological, developmental and physiological studies
Ostertagia ostertagi	Sheep	Stomach-inhabiting trichostrongylid
Stephanurus dentatus	Pigs	Adults in kidney of pigs; eggs passed out in urine
ORDER ASCARIDIDA		
Ascaridia galli	Chickens	Adults parasitic in small intestine
Ascaris suum	Pigs	Adults parasitic in the intestine of pigs; closely related to *Ascaris lumbricoides*
Heterakis gallinarum	Chickens and turkeys	Large numbers found in the intestinal caecae of turkeys; important as the carrier of the infective agent of the protozoan disease 'black spot', *Histomonas meleagridis*
ORDER OXYURIDA		
Syphacia obvelata	Rodents	Adults parasitic in the gut of rats and mice; used in laboratory studies
ORDER SPIRURIDA		
Dirofilaria spp.	Dogs	Adult filarial worms in the heart and pulmonary artery of dogs; immature worms occasionally found in lungs or pulmonary artery of humans
Onchocerca gutturosa	Cattle	Adult filarial worms in connective tissue on the surface of the nuchal ligament

pork from pigs. In feral cycles meat from wild boar, bears, bushpigs or warthogs can give rise to infections.

Although adult worms in the small intestine do give rise to some gut damage, the main pathogenic phase of the infection in humans is the population of migrating and encysting larvae. Usually no symptoms occur until the larvae reach the muscles and then, in heavy infections, a confusingly diverse range of serious symptoms can arise. Usually, a marked eosinophilia is apparent, with vomiting and diarrhoea followed by a high fever, muscle pain and in severe cases, evidence of cardiac and central nervous system pathological damage.

Toxocariasis

In humans this is a zoonotic infection brought about by the inadvertent ingestion, usually by children, of infective eggs of the ascarid species *Toxocara canis* and *T. cati*. These are normally found as adults in dogs and cats. The L_2 larvae which hatch from the eggs in children migrate round the body causing widespread small granulomas in the sites where they eventually die. The disease is a form of visceral larval migrans. Lesions are commonest in the liver and lungs but also occur in muscles, brain, skin and eyes; ocular pathological damage being the most serious consequence of human toxocariasis. Such changes occur in only a small proportion of infected children in which the larvae cause granulomatous endophthalmitis with retinal degeneration occurring.

2.5.4 Other nematodes

In addition to those species which are the causative agents of medically important human diseases, a number of other nematodes are of significance either because they infect agricultural animals or because they have been utilized extensively as laboratory models. Table 2.10 lists such species.

REFERENCES AND FURTHER READING

Anderson, R.C., Chabaud, A.G. & Willmot, S. (1976–1985) *C.I.H. Keys to the Nematode Parasites of Vertebrates*. Farnham Royal, Commonwealth Agricultural Bureaux.

Arai, H.P. (ed.) (1980) *Biology of the Tapeworm Hymenolepis diminuta*. London, Academic Press.

Arme, C. & Pappas, P.W. (eds) (1983) *The Biology of the Eucestoda*, Vols 1 and 2. London, Academic Press.

Basch, P.F. (1991) *Schistosome Biology*. Oxford, Oxford University Press.

Bird, A.F. & Bird, J. (1991) *The Structure of Nematodes*, 2nd edn. New York, Academic Press.

Bundy, D.A.P. & Cooper, E.S. (1989) *Trichuris* and trichuriasis in humans. *Advances in Parasitology*, **28**, 107–173.

Campbell, W.C. (ed.) (1983) *Trichinella and Trichinosis*. New York, Plenum Press.

CIBA Foundation (1987) *Symposium 127 – Filariasis*. Chichester, John Wiley.

Coombs, I. & Crompton, D.W.T. (1991) *A Guide to Human Helminths*. London, Taylor and Francis.

Craig, P.S. & Macpherson, C. (eds) (1990) *Parasitic Helminths and Zoonoses in Africa*. London, Unwin Hyman.

Crompton, D.W.T., Nesheim, M.C. & Pawlowski, Z.S. (eds) (1989) *Ascariasis and its Prevention and Control*. London, Taylor and Francis.

Farley, J. (1991) *Bilharzia. A History of Imperial Tropical Medicine*. Cambridge, Cambridge University Press.

Frenkel, J.K., Taraschewski, H. & Voigt, W.P. (1988) Important pathological effects of parasitic infections of man. In H. Mehlhorn (ed.) *Parasitology in Focus*, pp. 538–590. Berlin, Springer-Verlag.

Gilles, H.M. & Ball, P.A.J. (eds) (1991) *Hookworm Infections*. Amsterdam, Elsevier.

Grove, D.I. (1989) *Strongyloidiasis: A Major Roundworm Infection of Man*. London, Taylor and Francis.

Grove, D.I. (1990) *A History of Human Helminthology*. Wallingford, C.A.B. International.

Kim, C.W. (ed.) (1985) *Trichinellosis*. Albany N.Y., State University of New York Press.

Lee, D.L. & Atkinson, H.J. (1977) *Physiology of Nematodes*, 2nd edn. New York, Columbia University Press.

Mahmoud, A. (1987) *Schistosomiasis*. New York, Ballière Tindall/Saunders.

Mehlhorn, H. & Walldorf, V. (1988) Life Cycles: Metazoa. In H. Mehlhorn (ed.) *Parasitology in Focus*, pp. 1–148. Berlin, Springer-Verlag.

Miyazaki, I. (1991) *An Illustrated Book of Helminthic Zoonoses*. International Medical Foundation of Japan.

Muller, R. & Baker, J.R. (1990) *Medical Parasitology*. London, Gower Medical Publishing.

Peters, W. & Gilles, H.M. (1989) *A Colour Atlas of Tropical Medicine and Parasitology*, 3rd edn. London, Wolfe.

Rollinson, D. & Simpson, A.J. (eds) (1987) *The Biology*

of Schistosomes – From Genes to Latrines. London, Academic Press.

Schad, G.A. & Warren, K.S. (eds) (1990) *Hookworm Disease: Current Status and New Directives*. London, Taylor and Francis.

Schmidt, G.D. & Roberts, L.S. (1989) *Foundations of Parasitology*, 4th edn. St. Louis, Times Mirror Mosby.

Smyth, J.D. & Halton, D.W. (1983) *The Physiology of Trematodes*, 2nd edn. Cambridge, Cambridge University Press.

Smyth, J.D. & McManus, D.P. (1989) *The Physiology and Biochemistry of Cestodes*. Cambridge, Cambridge University Press.

Thompson, R.C.A. (ed.) (1986) *The Biology of Echinococcus and Hydatid Disease*. London, George Allen and Unwin.

Thompson, R.C.A. & Allsopp, C.E. (1988) *Hydatosis: Veterinary Perspectives and Annotated Bibliography*. Wallingford, C.A.B. International.

Warren, K.S. (1989) Selective primary health care and parasitic diseases. In K.P.W.J. McAdam (ed.) *New Strategies in Parasitology*, pp. 217–231 Edinburgh, Churchill Livingstone.

World Health Organization (1987) *Onchocerciasis*. WHO Technical Report Series No. 752. Geneva, WHO.

Index

Page numbers in *italic* type refer to figures. Page numbers in **bold** type refer to tables

Acanthamoeba 11
Acanthocephala
  hatching and excystation 166
  nervous system 177
  reproduction 175
  surface morphology 183, *184*, 185
  transmission stages 158
acaricides 256–7
acetate 122–3, **126**, 126
acetylcholine 178, 226
aconitate hydratase 125
acyl CoA transferase *128*, 129
acyltransferase, membrane-bound 189
ADCC *see* antibody-dependent cell mediated cytotoxicity
Adenophorea **42**
adenosine triphosphate synthesis *see* ATP synthesis
adenylate cyclase 134–5
adenylate energy charge 118–19
adrenalin (epinephrine) 178, 180
Aedes 48, 53, *55*, **60**, 252
Aedes aegypti 53, **54**, 56, 251
Aedes simpsoni 56
Aedes trivittatus *95*, 112
aerial spraying 255–6, 258
agarose gel electrophoresis 139
age, host
  degree of parasite aggregation and 105
  at infection, reproductive rate and 97–8
  schistosomiasis prevalence and 108, *109*, 209
age–intensity curves 77, 105
age–prevalence curves 77, 105
aggregated parasite distribution 78–9, *80*, **81**
  density-dependent processes and 96
  reproductive rate and 103–5
  transmission breakpoints and 110
  transmission by infective agent and 87
AIDS (HIV infection)
  cryptosporidiosis 14
  epidemiology 99, 100
  Pneumocystis carinii pneumonia 22, 221
  toxoplasmosis 205, 234
alanine **126**
albendazole 222, 223, 226, 229, 236
alimentary systems 182–3
allopurinol 236
alocima **36**
amastigotes *3*, 4, 7
Amblyomma **20**, 70, 71
amino acids
  metabolism 130–2
  sequencing 141
  transport *186*, 187, 188
amodiaquine 221, 236
  mechanism of action 225, 226, 228
  resistance 230
amoebae 2, **9**, 10–11
  facultative 11
amoebapore 173
amoebiasis
  chemotherapy 220
  immune response 201–2
  see also Entamoeba histolytica
amoebic dysentery 11
amphotericin B 219, 220, 226, 229, 236
ampicillin resistance gene *140*, 141
amprolium 221, 225, 229, 236
anabiosis 168–9
Ancylostoma
  control 260, 262
  hatching of eggs 166
Ancylostoma braziliense 169
Ancylostoma caninum *94*, 208, 212, 215
Ancylostoma duodenale **43**, 44–6
  epidemiology 94, 112
  immune response 208
Anepitheliocystida **33**
animal models 200–1
Anisakis simplex **177**
annual biting rate (ABR) 58
annual transmission potential (ATP) 58
Anopheles 14, 48, **60**
  appearance *54*, *55*
  control 252, 253, 254, 255
Anopheles albimanus **59**
Anopheles balabacensis **59**
Anopheles cruzi 56
Anopheles culicifacies **59**
Anopheles darlingi **59**
Anopheles dirus **59**
Anopheles farauti **59**
Anopheles funestus **59**
Anopheles gambiae 56, **59**, *102*, 246
  biology **54**
  species complex **72**, 73, 253
Anopheles koliniensis **59**
Anopheles maculipennis complex **72**
Anopheles minimus **59**
Anopheles punctulatus **59**
Anopheles saccharovi **59**, **72**
Anopheles stephensi **59**
anthelmintics 221–3
  mechanisms of action **224**, 227
  mechanisms of selectivity **228**, 229
  resistance 229–31
antibodies 195–6, 200
  cleaving *211*, 212
  inhibition of binding *211*, 212
  monoclonal 149, 153
antibody-dependent cell mediated cytotoxicity (ADCC) 196, 197–8, 199
  helminths 207, 208, 209–10
antigenic variation *211*, 212
  Plasmodium 206
  trypanosomes 143–4, 203–4
antigen presenting cells (APC) 194, *195*
antigens
  incorporation of host 209, 211
  isolation and identification 148–9
  shedding *211*, 212
  vaccine design 153–4
anti-idiotypic vaccines 215
antimonials 223, 226, 229
antioxidants *211*, 212
antiprotozoal drugs 220–1
  mechanisms of action **224**, 225–7
  mechanisms of selectivity 227–9
  resistance 229, 230–1
  under development 235
antisense oligonucleotides 144–5
anti-TNF monoclonal antibodies 214
Argasidae 69
arginine
  metabolism 131–2
  transport 187
arrested larval development (ALD) 168
arsenicals 223, 226, 229

Rhombomys opimus 251, 257
ribosomal RNA (rRNA) 156
Rickettsia 69
Rickettsia mooseri 68–9
Rickettsia prowazeki 67
Rickettsia rickettsia 71
river blindness 49, 209
control 251, 258
RNA
antisense 144–5
editing 145–6
extraction/purification 138–9
sequencing 139
synthesis 134
RNA technology 138–41
robenidine 221, 226, 229, 240
Rocky Mountain spotted fever 71
Romanomermis culicovorax 85

salinomycin 219, 221, 226, 240
Salmonella typhimurium 201
sandflies 7, 58–62
control 256–7
life cycle 58–62
Sandflies, *continued*
sanitation 260, 262
Sarcocystis 13
Sarcocystis bertrami **14**
Sarcocystis bovicanis **14**
Sarcocystis bovifelis **14**
Sarcocystis bovihominis **14**
Sarcocystis cruzi 13, **14**
Sarcocystis gigantea **14**
Sarcocystis hirsuta **14**
Sarcocystis hominis 13, **14**
Sarcocystis miescheriana **14**
Sarcocystis muris **14**
Sarcocystis ovicanis **14**
Sarcocystis ovifelis **14**
Sarcocystis porcifelis **14**
Sarcocystis (Cystoisospora) rivolta 13, **14**
Sarcocystis suicanis **14**
Sarcocystis suihominis 13, **14**
Sarcocystis tenella 13, **14**
Sarcoptes scabei 66, 259
satranidazole 220, 225, 228, 240
scabies mite 66, 260
Schistosoma 34, 35–40
Schistosoma bovis 40, 162, 210, 215
Schistosoma haematobium 35, **39**, 40
chemotherapy 222
control 260, 262
epidemiology 78, 107, 108
immune response 210
immunopathological effects 214
intermediate hosts **71**
migrations 170
transmission 162
Schistosoma intercalatum 35, **39**, 40
Schistosoma japonicum 35, **39**, 40
chemotherapy 222
control 259, 262
epidemiology 107
intermediate hosts **71**
transmission 162
Schistosoma mansoni 35, 37, 38–40
adenylate cyclase 134
chemical communication 176
chemotherapy 222
control 263
ecdysteroid hormones **177**
epidemiology 85, 88, **94**, 107–8, 109, 111
immune response **194**, 200, 209, 210, 212
immunopathological effects 214
intermediate hosts **71**
membrane 129
migrations 170
nutrition 188
transmission 159–60, 162
Schistosoma margrebowiei 162
Schistosoma mattheei 40, 215
Schistosoma rodhaini 162
Schistosoma spindale 40
Schistosomatium douthitti 40
schistosome derived inhibitory factor (SDIF) 212
schistosomes 25
cercarial transformation 160, 162–4, **165**
chemical communication 176
digestive enzymes 188, 189
eggs 37, 38–40, 158–9, 209
energy metabolism 125
entry into host 160
hatching of eggs 166
heat shock proteins 161
nitrogen metabolism 132
nutrition 183
timing of cercarial shedding 162
vaccines 154
schistosomiasis 24, 35–40, 53
chemotherapy 222, 251
control 259, 262
epidemiology 95, 107–8, 111–12
immune response 209–10, 212
immunopathology 214
intestinal 35, 38–40
urinary 35, 40
vaccine 216
schistosomin 179
schistosomulum 37, 164, **165**
immune response 209, 212
schizogony 12, 15, 174
erythrocytic 16
exo-erythrocytic 15, 16
periodicity 161
schizont 17
scolex 25–6
seasonal variations 111–13
arrested larval development 168
transmission rate 82–4
Secernentea **42**
Segmentina **36**
Segmentina hemisphaerula **71**
'self-cure' reactions 208
self-fertilization 25, 174, 175
Semisulcospira **36, 71**
Semisulcospira libertina **71**
sense organs 177–8
sensory biology 169, 177–8
serological tests 154, 245
epidemiological studies 76, 77, 97, 113–14
serotonin (5-hydroxytryptamine) 134, 178, 179, 180
sexual behaviour 99, 100–1
sexually transmitted infections 7, 10, 68
epidemiology 98–9, 100–1
sexual maturity
Schistosoma mansoni 176
time to reach **94**, 103
sexual reproduction 174–5
sibling species 73
Simulium blackflies 48, 49, 56–8
control 252, **254**, 257–8
life cycle 56–8
prevalence of infection 89
Simulium damnosum complex 56, 58, **60**
control 252, 253, 258
species complex **72**, 73
Simulium metallicum **60**
Simulium naevei complex 57–8, **60**, 246, 252, 258
Simulium ochraceum 58, **60**, 258
Simulium roraimense **60**
Simulium soubrense complex **72**
Siphonaptera 66, 68–9
skin penetration 160
sleeping sickness 4, 53
chemotherapy 220
control 246, **247**, 252
immunology 203–4, 216
snails (molluscs) **36**, 37, 38, 71–3
control 259, 262
dynamics of parasite populations and 107, 108, 109
entry mechanisms 160
location by miracidia 159
parasite-induced hormones 179
sole (*Solea solea*) 159
southern blotting 139
spargana 30
sparganosis 28–30
species complexes, vector **72**, 73
spermidine 135, 151
Spirometra **29**, 30
Spirometra mansonoides 179, **180**
Spironucleus (Hexamita) 10
Spironucleus (Hexamita) meleagridis 10
Spirurida **42, 50**
sporocysts 11, 12, 34, 35
sporozoa 2
chemotherapy 221
sporozoites 11, 12, 16, 18, 21
Stephanurus dentatus **50**
sterile male-release programmes 256
sterols 130
stibogluconate, sodium 220, 223, 226, 229, 240
Stieda body 165
Strigeatida **33**
Strongylida **42, 50**
Strongyloides ratti 130
Strongyloides stercoralis 24, 25, **43**, 46–7
structure activity relationships (SAR) 234
subpopulation 75, 94
succinate **126**, 126, 127, 128
sulphadiazine 221, 225, 229, 240
sulphadoxine 221, 225, 229, 240
sulphamethoxazole 221, 225, 229, 240

sulphaquinoxaline 221, 225, 229, 240
superoxide dismutase 212
suramin 220, 223, 240
  mechanism of action 150–1, 226, 229
surface, parasite 183–8
  morphological adaptations 183–5
  nutrient transport mechanisms 185–8
swimmer's itch 38
synchrony, reproductive 175
syncytial layer 185
Syngamus trachea 158, 215
Syphacia muris 161
Syphacia obvelata **50**
systematic relationships 155–6

tabanid flies 49, 62, 64–5
Tabanus 64, 65
Taenia crassiceps *27*, **31**
Taenia hydatigena 216
Taenia multiceps 216
Taenia ovis **31**, 210
  vaccine 154, 216
Taenia pisiformis 166, 167
Taenia saginata *26*, **29**, 30, 31
  hatching of eggs 166
  immune response 210
  life cycle *28*
  vaccine 216
Taenia solium *26*, **29**, 30, 31–2
  chemotherapy 222
  cysticercosis **29**, 30
  immune response 210
  vaccine 216
tampans 69
tanning 158, 159
tapeworms *see* cestodes
taxonomy, molecular techniques 155–6
TCA cycle *see* tricarboxylic acid (TCA) cycle
tegument 184
telomeric gene expression 144
temephos **254**, 258
temperature
  changes, host entry and 160–1
  parasite development and 112
  responses, larvae 178
  transmission and 111–12
terpenes 130
tetracycline 219, 221, 226, 228, 240
tetrahydrofolate 225, 229
Tetratrichomonas gallinarum 10
Theileria 19, **20**
  immune response 207, 211–12
  life cycle *21*
  vaccines 216
  vectors 69–71
Theileria annulata 19, **20**, 207, 216, 261
Theileria hirci 19, **20**
Theileria mutans 19, **20**
Theileria ovis 19, **20**
Theileria parva 19, **20**, 71, 207
  control 261
  vaccine 216
Theileria separata **20**
Theileria sergenti 19, **20**
Theileria taurotragi **20**
Theileria velifera 19, **20**
theileriosis 1, 19, 207
  chemotherapy 221
  control 259, 261–2
T helper cells 194, 199
  induction of inappropriate signals 212
  type 1 (T_H1) 194, *195*, 199, 212
  type 2 (T_H2) 194, *195*, 212
thiabendazole 220, 223, 240
Thiara **36**, **71**
threonine dehydrogenase 129
thymidylate synthetase 133–4, 153
tick paralysis 71
ticks 18, 19, 69–71
  control 258–9, 261
  hard 69–71
  resistant cattle 258
  soft 69
tinidazole 220, 225, 228, 240
tissue invasion 169–73
T lymphocytes 208
  see also cytotoxic T cells; T helper cells
Toxocara **43**, 51, 166
Toxocara canis 51, *80*, 169, 214
Toxocara cati 51
Toxoplasma gondii 11–14
  cell invasion 173
  cysts 157
  immune response 205, 211, 212
  life cycle *15*
toxoplasmosis 13–14, 205
  chemotherapy 221, 235
  immunopathology 214
transfer RNA (tRNA) 139
transmission 79–90, 157–62
  by biting arthropod (vector) 88–90
  breakpoints 108–10
  circadian rhythms and 161–2
  climatic factors 111–12
  direct 79, 80, 81–4
    macroparasites 102–6
    microparasites 96–101
  heat shock proteins and 160–1
  helminth infections 25, 85
  horizontal 80
  indirect 79–80
    macroparasites 106–8
    microparasites 101–2
  by infective agent 84–7
  by ingestion 88, *89*
  stages *see* infective stages
  thresholds 96, 102, 109
  vertical 80
transmission potential, annual (ATP) 58
transport
  competitive inhibition *185*
  mediated (active) *185*, 186
  membrane 185–8
  non-competitive inhibition *185*
trans-splicing 144
Transversotrema patialense *85*
traps
  mosquito 255
  tsetse 253, 256
trehalose 118
Triatoma *65*, 66
Triatoma dimidiata **59**
Triatoma infestans **59**, 257
triatomine bugs 2–3, 65–6
  control 253, 257
Tribolium confusum 87, *88*, *89*
tricarboxylic acid (TCA) cycle 119, 130
  helminths 125, 126
  trypanosomes 120, 121
Trichinella spiralis **43**, 50–1, 118, 158
  cell invasion 173
  immune response 201, 212
  migrations *170*
Trichobilharzia ocellata 179
trichomonads
  energy metabolism 119, 121
  energy stores 118
Trichomonas 9–10
Trichomonas (Tritrichomonas) foetus 10, 134
Trichomonas gallinae 10
Trichomonas gallinarum 10
Trichomonas hominis 9–10
Trichomonas pullorum 10
Trichomonas tenax **9**, 10
Trichomonas vaginalis **9**, *9*, 10, 134, 182
trichomoniasis, chemotherapy 220
trichostrongyles
  arrested larval development 168
  larval exsheathment 167
Trichostrongylus 166
Trichostrongylus axei 168
trichuriasis 44
Trichuris muris 212
Trichuris trichiura 24, **43**, 44
  control 259
  epidemiology *82*, *113*
  life cycle *45*
triclabendazole 222, 226, 229, 240
trimethoprim 221, 223, 225, 229, 240
Tritrichomonas (Trichomonas) foetus 10, 134
trophozoites 10, *17*, 18
Trypanosoma brucei (brucei) *3*, *5*, **6**, 7
  calmodulin 135
  chemotherapy 151
  discontinuous mRNA transcription *145*
  genetic exchange 147
  immune response 203, *204*
  integrated control 261
  lipids 129
  vectors **59**, 63
Trypanosoma brucei gambiense 4, **6**, 7, 155
  amino acid transport 187
  chemotherapy 220
  control 247, 261
  immune response 203
  vectors **59**
Trypanosoma brucei rhodesiense 4, **6**, 7
  chemotherapy 220
  control 246, 261
  immune response 203
  vectors **59**
Trypanosoma congolense **4**, **6**, **59**

control 261
immune response 203, 204
Trypanosoma cruzi 2–4, **6**, 155, 182
cell invasion 173
control 257, 262
energy metabolism 119
immune response **194**, 203, 211, 212
immunopathological effects 214
nutrient acquisition 187
vectors **59**, 65–6
Trypanosoma equinum see Trypanosoma evansi
Trypanosoma equiperdum **6**, 7, 187
Trypanosoma evansi **6**, 7, 64, 65
Trypanosoma lewisi 7, 187
Trypanosoma musculi 7, *94*
Trypanosoma rangeli **6**, 7, 257
Trypanosoma simiae **6**, 7
Trypanosoma suis **6**, 7
Trypanosoma theileri **6**, 7, 65
Trypanosoma uniforme **6**, 7
Trypanosoma vivax 4–7
epidemiology *78*
immune response 203, 204
integrated control 261
vectors **59**, 64, 65
trypanosomes 2–7
antigenic variation 143–4, 203–4
cAMP 135
chemotherapy 150–1, 220
chromosomes 148
control 252, 261, 262
discontinuous mRNA transcription 144–5
drug resistance 220, 229, 230
energy metabolism 118, 119–21, 123
genetic exchange 147
heat shock proteins 161
homologous gene recombination 147
immune response 203–4, 212
immunopathological effects 214
isoenzymes 155
lipids 129, 130
migrations *170*
nitrogen metabolism 130, 133
nutrient acquisition 187, 189
reproduction 174
RNA editing 145–6
taxonomic relationships 156
telomeric gene expression 144
vectors **59**, 62–3, 65–6
trypanosomiasis
African *see* nagana; sleeping sickness
South and Central American *see* Chagas disease
domesticated animals 4–7, 246, 261
trypanothione metabolism 151, *152*, 226
trypomastigote *3*, 4, 203
tsetse fly *see Glossina*
tularaemia 65, 71
tumour necrosis factor (TNF) 198, 200, 213, 214
Tunga 68
Tunga penetrans 67, 68
typhus 67, 68–9

ubiquinone 127, 130
underdispersion 78, **81**
urea 131
urocystidium larva 174
urocystis larva 174

vaccines 214–17
babesiosis 207, 216
development 153–4
disease control 251, 261
population dynamics and 98
recombinant 137, 153–4, 216
types 215
vacuoles
contractile 189
parasitophorous 172, 173, 183–4, *186*
vampire bat 7
variant surface glycoprotein (VSG) 144, 203, *204*
vector-borne diseases
circadian larval migrations 162
epidemiology 101–2
vectors (arthropod) 53–73, 79–80
climate effects on infectivity 112
control 101–2, **244**, *248*, 252–9, 261, 262
ecology 253
identification 73
species complexes **72**, 73
transmission by 88–90
vectors (molecular biology)
cloning *140*, 141
DNA transfection 146
vaccine 153–4
venereal diseases *see* sexually transmitted infections
viral infections
immunity 193, 199–200
measures of infection 76, 77
perpetuation in host population 90–3
population dynamics 97
transmission 81–4, 89, 90
vitamin B_{12} 30–1, 181–2
vitelline proteins 158–9

water supply 260
water velocity, host location and 159–60
western blotting 149
whipworms *see Trichuris trichiura*
World Health Organization (WHO) 247
WR 6026 235, 241
WR 238, 605 235, 241
Wuchereria bancrofti 24, **43**, 47, 48–9
immune response **194**
larval migrations 162, **163**, *163*
transmission 89–90
vectors 53, **60**

xanthine phosphoribosyl transferase 132
Xenopsylla 68
Xenopsylla cheopis 68
X-ray crystallography 233

yellow fever 53, 246
epidemiology 76, 77, 89, 90, 101
Yersinia pestis 68

zooprophylaxis 255
zymodenes 154, 155

Printed in the United Kingdom
by Lightning Source UK Ltd.
136266UK00001B/203-216/A