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Medical Parasitology

A Textbook

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Foreword

My heartfelt congratulations to the authors, Professor Dr. Rohela Mahmud, Professor Dr. Yvonne Ai-Lian Lim and Dr. Amirah Amir, for bringing out this textbook on medical parasitology. Why you may ask another textbook on medical parasitology when so many already exist? The answer is simple. Most of the textbooks until recently have been written by western authors on an academic slant without considering the actual reality and needs of students and researchers in endemic countries of Asia-Pacific or other regions. As the authors rightly point out, the study of medical parasitology is indeed daunting to the uninitiated, and this book aims to promote an easy yet comprehensive way of learning the subject.

Like the authors, I have been teaching medical parasitology to medical and non-medical students in Malaysia as well as in Southeast Asia for the past four decades, and there was no "one" reference book that I could recommend to students on issues related to parasitic infections in the Asia-Pacific and in particular the south-east region. This book—well written and comprehensive—fills that gap. It will be a useful book not just to medical students but to medical scientists, clinicians, veterinary scientists, biologists, researchers and public health workers in tropical medicine.

This book integrates available information on parasitic diseases in the Asia-Pacific region through reader-friendly illustrations, case reports, diagnostic methodologies, treatment and preventive methods. With the emphasis given on the global elimination of neglected tropical diseases (NTD) by the World Health Organization (WHO) which affects millions of people, especially the poor in the developing world, I hope this book will help to contribute knowledge towards prevention, control, treatment and elimination of parasitic diseases in this region as well as globally.

Once again, my congratulations to the authors in bringing out this book at this timely moment.

Emeritus Dato Dr. C.P. Ramachandran
Academician Professor
Retired Chief of Filariasis Research and Control
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Preface

*Medical Parasitology: A Textboo*k is the fruit of many years of experience in teaching medical students in the field of parasitology. We are teachers in one of the very few existing departments of parasitology around the world. This book intends to provide a systematic comprehension of the various medically important human parasites; their distribution, morphology, life cycle, pathogenesis and clinical features; and laboratory diagnosis, treatment, prevention and control. The main emphasis is on the protozoan and helminthic parasites including a brief mention of vectors relevant to infections caused by these parasites. Ectoparasites of medical importance are also included.

The study of parasitology is daunting to the uninitiated. This book aims to promote an easy yet comprehensive way of learning this subject. It attempts to simplify the complexity of medical parasitology into parts that are easy to understand, integrating the essential information of parasitic infections. This integration of knowledge will be achieved through reader-friendly illustrations, inclusion of a collection of case reports, samples of test questions and the images of human parasites. Essentially, the book provides a "one-stop learning package" for medical parasitology.

This book will be useful for medical students, medical lecturers, clinicians, researchers and also those interested in the fields of biology, zoology, microbiology, pathology, entomology, medicine, veterinary medicine, allied sciences, tropical medicine and public health.

We hope this book will be beneficial to a wide range of readers by giving them a better understanding and appreciation of medically important parasites and their infections.

Kuala Lumpur, Malaysia

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Amirah Amir

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Introduction

1

Medical Parasitology is the study of organisms that parasitize humans. According to the definition, parasites include the viruses, bacteria, fungi, protozoa and metazoan (helminths and arthropods). Since viruses, bacteria and fungi are not categorized as animals, they have been incorporated into the discipline of Microbiology.

The discipline of Parasitology includes protozoa, helminths, and arthropods whose existence depends on the availability of hosts and these are obligate parasites. Those which can survive and reproduce without a host are facultative parasites. Very few of these facultative parasites infect humans (e.g. the free-living amoebae). Ectoparasites are referred to as parasites living on the host body surface while endoparasites live inside the body of host. Entomology is the study of insects. In Parasitology, insects play a role as vectors of several infections although several are true parasites in their own right. On the other hand, acarology is the study of ticks and mites. These are mainly ectoparasites.

Parasitic diseases have caused some of the most serious health problems in the world today, particularly in the tropics and subtropics regions. One of the most significant parasitic diseases, malaria, kills approximately half a million people each year. Most of them are children under the age of 5 years in Sub-Saharan Africa.

The neglected tropical diseases (NTDs) include parasitic diseases such as Chagas' disease, cysticercosis, echinococcosis, human African trypanosomiasis, schistosomiasis, leishmaniasis, soil-transmitted helminthiasis, lymphatic filariasis, and onchocerciasis. These NTDs affect more than one billion people, mostly in rural areas of low socio-economic countries, trapping one sixth of the world's population in a vicious cycle of poverty and neglect.

Though not in all cases, parasitic diseases are mostly confined to developing countries. However, geographic distributions of parasitic diseases are evolving and changing due to ease of international travel and influx of refugees and migrants to developed countries for leisure, education, and economic reasons. Gastrointestinal diseases, liver diseases, vector-borne diseases, scabies, and tuberculosis are common among migrants. Inbound migrants may harbour long-eliminated diseases in the host country which may still be endemic in their country of origin and the

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importation of infection may cause problems in diagnosis, transmission, prevention, and control.

Another important contributing factor to the high incidence of parasitic infections is the prevalence of opportunistic infections such as toxoplasmosis, strongyloidiasis, microsporidiosis, and cryptosporidiosis in the immunocompromised especially HIV/AIDS patients. HIV/AIDS remains one of the world's most significant public health challenges, particularly in low- and middle-income countries. More than 36 million people were living with HIV at the end of 2015. The group of people was at high risk of acquiring opportunistic parasitic infections.

Occurrence of zoonotic parasitic infections is also a challenge. In 2004, a large focus of zoonotic *P. knowlesi* (simian malaria) infection was reported in humans in Sarawak, Malaysia. Since then, many human cases have been reported in various Southeast Asian countries. This malaria parasite is capable of producing severe disease and can be fatal. Due to the similar morphological features of its early stage to *P. falciparum* and late stage to *P. malariae*, microscopic diagnosis is a challenge. In many instances, molecular technique is used to confirm the species.

In addition, there are other parasites that have been reported to cause zoonosis in humans which include cysticercosis, cryptosporidiosis, microsporidiosis, hydatid disease, trichinellosis, babesiosis, toxoplasmosis, and cynomolgi malaria. Clinicians have to be aware of these zoonotic infections to make early diagnosis and prompt treatment. Public health personnels have to be more alert and vigilant regarding these zoonotic infections to ensure that they do not cause any outbreak.

In diagnosis of parasitic infections, microscopic identification of the organisms based on their morphological characteristics remains the gold standard. In Parasitology, *in vitro* culture was for a long time virtually impossible for most parasites. Nevertheless, in recent years, technical advances have allowed the *in vitro* cultivation of protozoan parasites (e.g. *Plasmodium, Giardia, Toxoplasma, Cryptosporidium, Blastocystis*) including helminths. The culture techniques for helminths are still in their infancy and are carried out mostly for research, rather than for routine laboratory diagnosis.

In recent years, diagnostic tools for parasitic infections have been improved with the introduction of molecular techniques such as polymerase chain reaction (PCR). PCR is an upcoming diagnostic tool that can be used to confirm parasitic infections. Molecular techniques are also increasingly being used for species identification or strain-typing. Immunological technique using monoclonal antibodies to detect specific antigens has also been found useful for rapid diagnostic test of malaria and filariasis.

This textbook presents essential information on parasites of medical importance. It is meant for medical students, medical educators and clinicians as a reference for parasitic infections. Case reports are also included in the handbook to provide real-life clinical scenarios for reference.

It is hoped that readers will find this book helpful and of practical use.

Protozoa and Helminths

2

Protozoa: General Characteristics

Protozoa are single-celled eukaryotic microorganisms belonging to kingdom Protista. The body wall is covered by cell membrane. Its cytoplasm is made up of ectoplasm and endoplasm. The nucleus is usually single but may be double or multiple. Reproduction can be asexual (e.g. binary fission, schizogony, endodyogeny) or sexual (e.g. gametogony).

Protozoa can be divided into the following groups:

1. *Amoebae* (Has pseudopodia as a mean of locomotion)
   Amoebae of medical importance:
   - Amoeba in the large intestine: *Entamoeba histolytica*
   - Free-living amoebae in CNS and eye: *Naegleria*, *Acanthamoeba*
2. *Flagellates* (Has flagella as organ of locomotion)
   Flagellates of medical importance:
   - Hemoflagellates: *Trypanosoma*, *Leishmania*
   - Gastrointestinal: *Giardia lamblia*
   - Urogenital: *Trichomonas vaginalis*
3. *Apicomplexa* (Has a structure called apical complex which serves as the organ of attachment to host cells. They have an alternating sexual and asexual life cycle)
   Apicomplexa of medical importance:
   - Blood: *Plasmodium*, *Babesia*
   - Tissue: *Toxoplasma gondii*, *Sarcocystis*
   - Gastrointestinal: *Cryptosporidium*, *Cystoisospora*, *Cyclospora*
4. *Ciliate* (Has cilia for locomotion)
   Ciliate of medical importance:
   - Gastrointestinal: *Balantidium coli*
5. Microsporidia
   Microsporidia of medical importance:
   - Gastrointestinal: *Enterocytozoon bieneusi*

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Table 2.1 Protozoa of medical importance to human

Species	Habitat in human	Disease/clinical features
Entamoeba histolytica	Large intestine	Amoebic dysentery, amoebic liver abscess (ALA)
Naegleria fowleri (free-living amoeba, FLA)	Central nervous system (CNS)	Primary amoebic meningoencephalitis (PAM)
Acanthamoeba (FLA)	CNS, eye	Granulomatous amoebic encephalitis (GAE), amoebic keratitis
Giardia lamblia	Small intestine	Malabsorption, diarrhoea
Trichomonas vaginalis	Vagina, urethra	Vaginitis, urethritis
Trypanosoma brucei	Blood, lymph node, CNS	Sleeping sickness
Trypanosoma cruzi	Heart, colon	Chagas' disease
Leishmania donovani	Reticuloendothelial system (liver, spleen, bone marrow)	Kala azar, Post-kala azar dermal leishmaniasis
Leishmania tropica	Skin	Cutaneous leishmaniasis (oriental sore)
Leishmania braziliensis	Naso-oral mucosa	Mucocutaneous leishmaniasis
Toxoplasma gondii	CNS, eye, musculoskeletal	Toxoplasmosis
Microsporidia	Gastrointestinal tract (GIT)	Diarrhoea
Plasmodium	Erythrocytes	Malaria
Babesia	Erythrocytes	Babesiosis
Cystoisospora belli	Small intestine	Diarrhoea
Cryptosporidium parvum	Small intestine	Diarrhoea
Balantidium coli	Large intestine	Dysentery

The important protozoan pathogens of human are as shown in Table 2.1.

Helminths: General Characteristics

Helminths are metazoa which are multicellular worms. They are bilaterally symmetrical. Helminths are classified into 2 phyla: Platyhelminthes and Nemathelminthes. Trematodes (flukes) and cestodes (tapeworms) belong to phylum Platyhelminthes and nematodes (roundworms) belong to phylum Nemathelminthes.

Body of helminths has a cuticle or integument which is the outer covering. Nemathelminthes possess a cylindrical body with a body cavity. Alimentary canal is complete with absence of suckers and they are sexually differentiated.

Platyhelminthes possess a body which is flattened dorsoventrally with absence of body cavity. Alimentary canal is absent or rudimentary. Suckers are present and most of the worms are hermaphrodite.

Most helminths require more than 1 intermediate host for completion of their life cycle. Helminths unlike protozoa do not multiply in the human body apart from few exceptions (those helminths showing autoinfection). Heavy worm load follow multiple infections.

Amoebae

3

Entamoeba histolytica

Distribution

Entamoeba histolytica has a worldwide prevalence, especially where sanitation is poor and is more common in developing countries of the tropics. Majority of cases are asymptomatic.

Habitat

Entamoeba histolytica is found in the human colon.

Morphology

Entamoeba histolytica occurs in 3 forms.

1. Trophozoite
2. Precyst
3. Cyst

Trophozoite is the vegetative form of the parasite and the only form present in tissues. It is irregular in shape and varies in size from 12 to 60 μm; average being 20 μm (Fig. 3.1a). It has a cytoplasm which consists of ectoplasm and endoplasm. Ectoplasm is clear and transparent. Endoplasm is finely granular and contains nucleus, food vacuoles and phagocytosed erythrocytes. Pseudopodia are finger-like projections formed by movements of ectoplasm in one direction.

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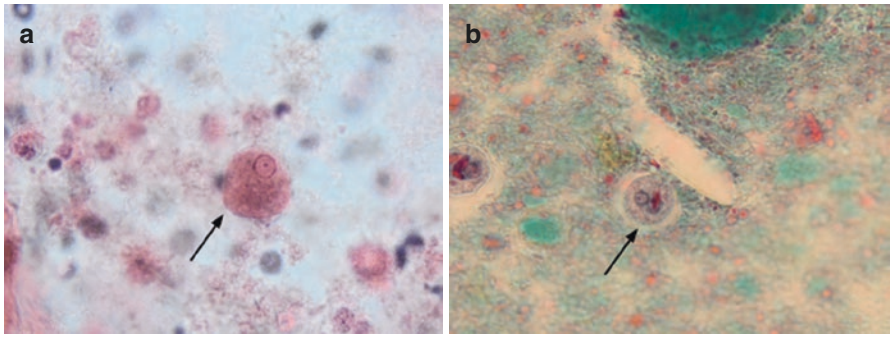


Fig. 3.1 *Entamoeba histolytica.* (**a**) Trophozoite, (**b**) Cyst

Its nucleus is spherical and contains central karyosome. The nuclear membrane is lined by a rim of evenly distributed chromatin. It reproduces by binary fission. It is killed by drying, heat and chemical sterilization.

The trophozoites undergo encystment in the intestinal lumen. Before encystment, the trophozoite extrudes its food vacuoles and rounds up to form a precystic stage, measuring 10–20 μm in size. It contains a large glycogen vacuole and chromatoid bars. It secretes a cyst wall to become cyst.

The cyst is spherical in shape. Immature cyst contains a single nucleus, a glycogen vacuole and chromatoid bars which are cigar shaped with rounded ends. The chromatoid bars are visible in saline. With iron haematoxylin stain, nuclear chromatin and chromatoid bodies appear deep blue or black. When stained with iodine, the glycogen mass appears golden brown while the nuclear chromatin and karyosome bright yellow. Mature cyst contains 4 nuclei. It measures 10–20 μm in size (Fig. 3.1b). The glycogen mass and chromatoid bars disappear in mature cyst. The cyst wall is highly resistant to gastric juice and unfavourable environmental conditions.

Life Cycle (Fig. 3.2)

(*1*) The cysts (usually found in formed stools) and trophozoites (in loose stools) are passed out in faeces of infected human. (*2*) Cysts are ingested via contaminated food or water. (*3*) In the intestine, the cysts undergo excystation and form trophozoites (*4*). (*5*) As the trophozoite passes down the intestine, it undergoes encystation and is excreted in the faeces.

Entamoeba histolytica completes its life cycle in human host. In the majority of cases, *E. histolytica* remains as a commensal in the large intestine. They are carriers or asymptomatic cyst passers and are responsible for maintenance and transmission of infection in the community.

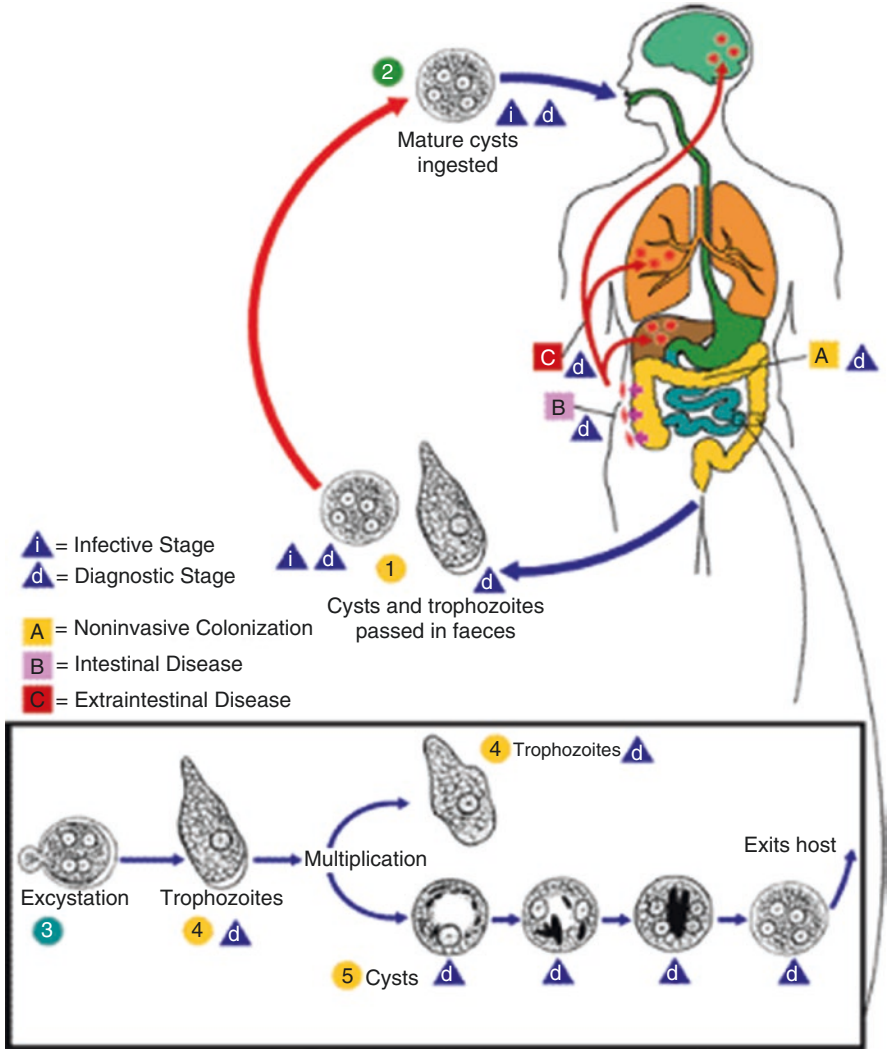


Fig. 3.2 Life cycle of *Entamoeba histolytica* (Reproduced from https://www.cdc.gov/dpdx/amebiasis/index.html)

Pathogenesis and Clinical Features

Entamoeba histolytica causes intestinal and extraintestinal amoebiasis.

The lumen-dwelling amoebae do not cause any illness. They cause disease only when trophozoites invade the intestinal tissues. The trophozoite penetrates the epithelial cells in the colon, aided by its movement and histolysin, a tissue lytic enzyme, which damages the mucosal epithelium. Amoebic lectin mediates adherence.

Table 3.1 Other complications of intestinal amoebiasis

• Amoebic cerebral abscess
• Amoebic peritonitis
• Genitourinary amoebiasis
• Perianal ulceration
• Pulmonary amoebiasis
• Splenic abscess
• Toxic megacolon

Mucosal penetration produces discrete ulcers with pinhead centre and raised edges. Sometimes, the invasion remains superficial and heals spontaneously. The ulcers are multiple and are confined to the colon, being most numerous in the caecum and recto-sigmoidal region. The intervening mucous membrane between the ulcers remains healthy.

The amoebic ulcer is flask shaped in cross-section. Multiple ulcers may coalesce to form large necrotic lesions with ragged and undermined edges and are covered with brownish slough. The ulcers generally do not extend deeper than submucosal layer. Amoebae are seen at the periphery of the lesions and extending into the surrounding healthy tissues. Clinical manifestations are diarrhoea, vague abdominal symptoms and dysentery. This may resemble bacillary dysentery. The ulcers may involve the muscular and serous coats of the colon, causing perforation and peritonitis. Blood vessel erosion may cause haemorrhage. Deep ulcers form scars and may lead to strictures and partial obstruction. A granulomatous pseudotumoral growth may develop on the intestinal wall from a chronic ulcer. This amoebic granuloma or amoeboma may be mistaken for a malignant tumour. The incubation period for intestinal amoebiasis varies from 1 to 4 months.

Liver involvement is the most common extraintestinal complication of intestinal amoebiasis. About 5–10% of patients with intestinal amoebiasis will develop amoebic liver abscess (ALA). ALA arises from haematogenous spread of amoebic trophozoites from colonic mucosa or by direct extension. Often, ALA patients do not present with bowel symptoms. Liver damage may not be directly caused by the amoebae, but by lysosomal enzymes and cytokines from the inflammatory cells surrounding the trophozoites. The centre of the abscess contains thick brown pus (anchovy sauce), which is liquefied necrotic liver tissue free of amoeba. The trophozoite is in the wall of the abscess. Liver abscess may be multiple or more often solitary, usually located in the upper right lobe of the liver. Jaundice develops only when lesions are multiple or when they press on the biliary tract. Large, untreated abscess may rupture into the lungs and pericardium. The incidence of liver abscess is more common in adult males. Other complications of intestinal amoebiasis are as shown in Table 3.1.

Immunity

Infection with invasive strains will activate both humoral and cellular immune responses. Systemic antibodies can be demonstrated within a week of invasive infection. Infection confers some degree of protection against the recurrence of invasive colitis and liver abscess in endemic areas.

Diagnosis

1. Diagnosis of intestinal amoebiasis
   (a) *Microscopic examination*
   Demonstration of cysts or trophozoites in stool sample. Since excretion of cysts in the stool is often intermittent, at least 3 consecutive specimens should be examined. Trophozoite and cyst of *E. histolytica* have similar morphology to *E. dispar* and *E. moshkovskii* which are non-pathogens. Molecular technique can differentiate these 3 species. Fixed stool smear can be stained with trichrome to demonstrate cysts and trophozoites.
   (b) *Sigmoidoscopy for mucosal scrapings*
   Direct wet mount and iron haematoxylin staining to demonstrate trophozoites.
   (c) *Stool culture*
   Stool culture is a sensitive method in diagnosing chronic and asymptomatic intestinal amoebiasis. However, it is not a routine method of diagnosis.
   (d) *Serodiagnosis*
   Serological test is positive only in invasive amoebiasis.
   (e) *Molecular diagnosis*
   Polymerase chain reaction (PCR) to detect *E. histolytica* in stool and to differentiate between the other species that are non-pathogens (*E. dispar* and *E. moshkovskii*).
2. Diagnosis of extraintestinal amoebiasis
   (a) *Microscopic examination*
   Demonstration of trophozoites in pus aspirated from the wall of liver abscess. The pus obtained from the centre of the abscess may not contain amoebae as they are confined to the wall of the abscess. Cysts are not found in extraintestinal lesions. Stool examination rarely can detect *E. histolytica* cyst.
   (b) *Molecular diagnosis*
   PCR of pus aspirated from ALA
   (c) *Serodiagnosis*

Treatment

1. Luminal amoebicides: Diloxanide furoate, iodoquinol, paromomycin and tetracycline act in the intestinal lumen but not in tissues.
2. Tissue amoebicides: Emetine and chloroquine are effective in systemic infection, but less effective in the intestine.
3. Both luminal and tissue amoebicides: Metronidazole (750–800 mg 3 times daily for 5–10 days), tinidazole and ornidazole act on both sites.

Carriers should also be treated because of the risk of transmitting the infection to others. Paromomycin or iodoquinol should be used in these cases. Although

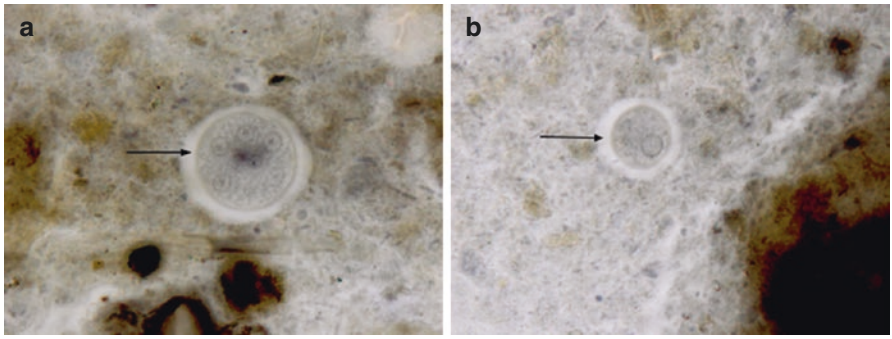


Fig. 3.3 *Entamoeba coli.* (**a**) Cyst, (**b**) Trophozoite

metronidazole and tinidazole are both luminal and tissue amoebicides, neither of them reach adequate levels in the gut lumen. Therefore, patients with ALA should also receive treatment with a luminal agent to ensure eradication of infection. Paromomycin (25–35 mg/kg/day, divided into 3 doses for 7 days) is the drug of choice.

Prevention and Control

1. Boil drinking water
2. Wash fruits and vegetables in clean water before eating
3. Detection and treatment of carriers and prohibit them from food handling
4. Health education

Note: It is important to distinguish between *Entamoeba histolytica* and *Entamoeba coli* cyst and trophozoite. *Entamoeba coli* is a commensal intestinal protozoa and it is non-pathogenic. The cyst of *E. coli* is large, 10–30 μm in size and mature cyst has 8 nuclei (Fig. 3.3a). Its chromatoid bodies are splinter like. The trophozoite of *E. coli* is large, measuring 20–50 μm**,** does not contain ingested red blood cells and does not invade tissues (Fig. 3.3b). Its life cycle is the same as that of *E. histolytica*.

Pathogenic Free-Living Amoebae (FLA)

Among the numerous types of FLA found in water and soil, a few are potentially pathogenic and can cause human infections.

1. *Naegleria fowleri* causes primary amoebic meningoencephalitis (PAM)
2. *Acanthamoeba* spp. cause granulomatous amoebic encephalitis (GAE) and amoebic keratitis (AK).

A few instances of GAE caused by *Balamuthia* spp. have also been reported. While PAM and AK occur in previously healthy individual, GAE has been associated with immunodeficient patients.

Naegleria fowleri

Distribution

Naegleria fowleri is a thermophilic amoeba that thrives in warm water (e.g. hotsprings) and soil. It has a worldwide distribution.

Habitat

In human, *N. fowleri* is found in the central nervous system (CNS).

Morphology

It occurs in 3 forms:

1. Trophozoite (2 forms)
   (a) Amoeboid (Fig. 3.4a)
   (b) Flagellate
2. Cyst (Fig. 3.4b)

The trophozoites can withstand moderate heat (45 °C), but die at chlorine levels of 2 ppm and salinity of 0.7%. The amoeboid form is about 10–20 μm with rounded pseudopodia (lobopodia), a spherical nucleus and a big endosome. It is the invasive and the infective form of the parasite. The flagellate form is biflagellated, pear-shaped and occurs when trophozoites are transferred to distilled water. The flagellate can revert to the amoeboid form.

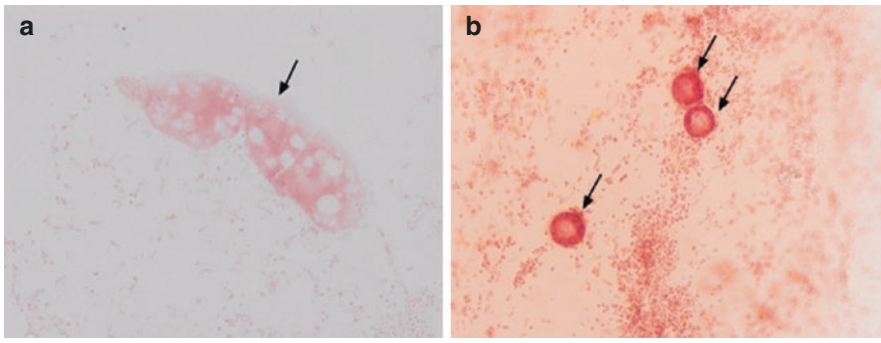


Fig. 3.4 *Naegleria fowleri.* (**a**) Trophozoite (amoeboid), (**b**) Cysts

Trophozoites encyst due to unfavourable conditions like food deprivation, desiccation and cold temperature. The cyst is 7–10 μm in diameter and has a smooth double wall. They are the resting or the dormant form and can resist unfavourable conditions, such as drying and chlorine up to 50 ppm. Cysts of *N. fowleri* have never been found in cerebrospinal fluid (CSF).

Life Cycle (Fig. 3.5)

(*1*) Cyst. (*2*) Trophozoite. (*3*) Flagellated form showing flagella. (*4*) The trophozoite replicates by promitosis. (*5*) The trophozoite penetrates the nasal mucosa. (*6*) The trophozoite migrates to the brain via the olfactory nerves.

Infection occurs when humans go swimming or diving in warm freshwater (lakes and rivers), hotsprings, heated pools, or nasal irrigation using contaminated tap water.

Pathogenesis and Clinical Features

Primary amoebic meningoencephalitis (PAM) is usually reported in previously healthy young adults or children. During contact with contaminated water, the amoebae invade the nasal mucosa and pass through the olfactory nerves in the cribriform plate into the meninges and brain to initiate an acute meningitis and encephalitis. The incubation period varies from 2 days to 2 weeks. The disease progresses rapidly, causing fever, headache, vomiting, stiff neck, ataxia, seizure and coma and is almost always fatal.

Diagnosis

1 *Cerebrospinal fluid (CSF) examination*

The CSF is cloudy to purulent, with prominent neutrophils, elevated protein and low glucose, resembling pyogenic meningitis. Wet film examination of CSF may show motile trophozoites. Fixed smear can be stained with Giemsa or a modified trichrome stain for identification. Cysts are not found in CSF or brain. Histological examination of the brain following autopsy may show the presence of trophozoites.

2 *Culture*

Naegleria fowleri in CSF can be grown on non-nutrient agar plates coated with *Escherichia coli*. Both trophozoites and cysts can be detected in culture.

3 *Molecular diagnosis*

PCR on CSF specimen.

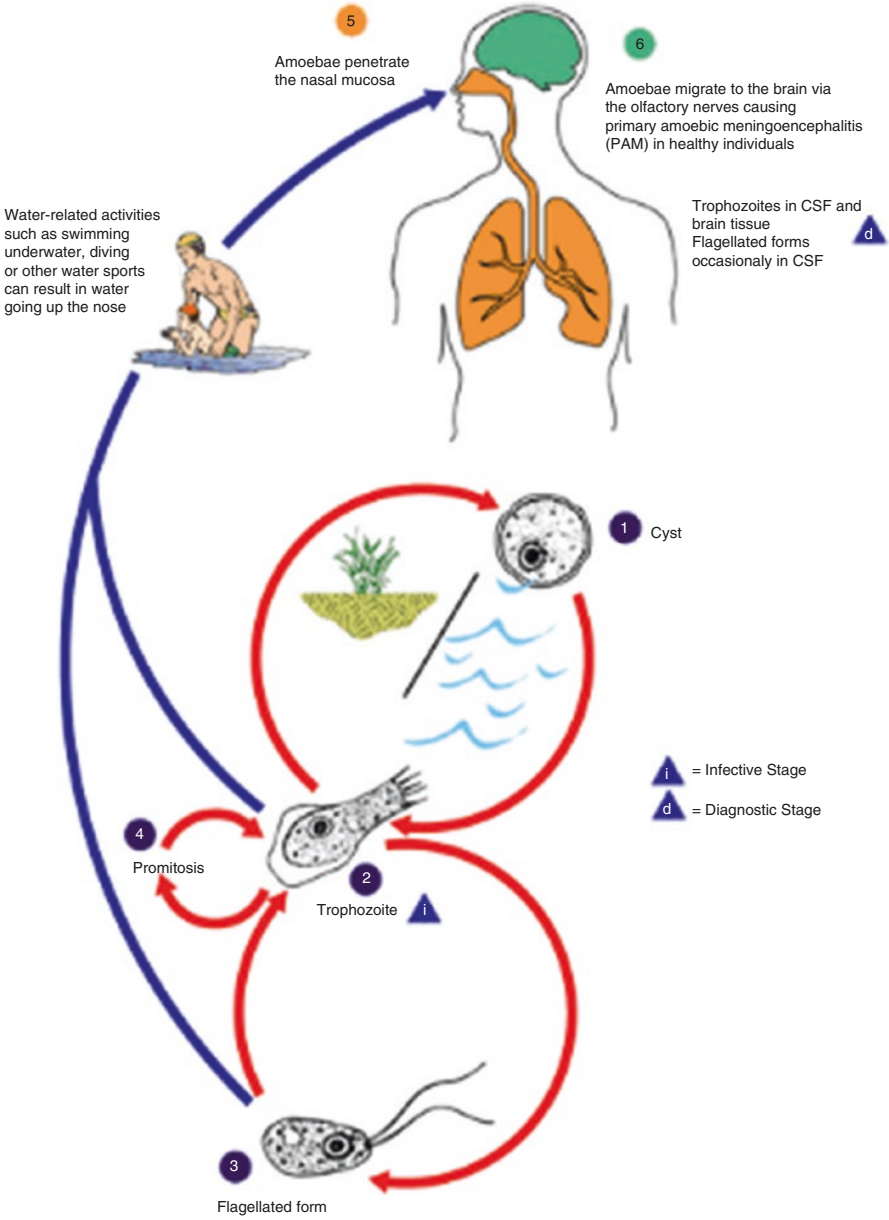


Fig. 3.5 Life cycle of *Naegleria fowleri* (Reproduced from https://www.cdc.gov/dpdx/freeliving-amebic/index.html)

Treatment

The drug of choice is intravenous amphotericin B (1.5 mg/kg/day in 2 divided doses for 3 days followed by 1 mg/kg/day once daily for 11 days). It can also be given intrathecally. Treatment combining miconazole and sulfadiazine has shown limited success. Majority of cases are fatal despite treatment.

Prevention and Control

1. Chlorination of swimming pools

Acanthamoeba Species

Acanthamoeba culbertsoni is the species most often responsible for human infection. Other species like *A. polyphaga*, *A. castellanii,* and *A. astronyxis* have also been reported.

Distribution

It is an opportunistic pathogen found worldwide in the environment, water and soil.

Habitat

In human, it is found in the CNS and eye.

Morphology

It occurs in 2 forms:

1. Trophozoite
2. Cyst (Fig. 3.6)

Trophozoite measures 20–50 μm in size and is characterized by spine-like pseudopodia (acanthopodia). It does not have a flagellate stage. The cyst has a polygonal double walled and is highly resistant. It measures 10–20 μm. Cyst is found in brain tissue.

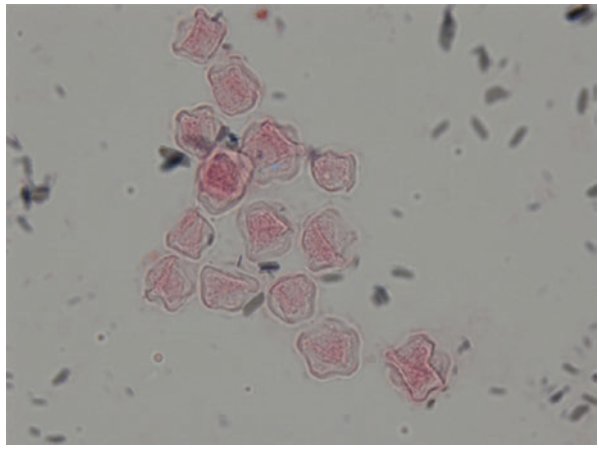


Fig. 3.6 *Acanthamoeba* cysts

Life Cycle (Fig. 3.7)

(*1*) Cyst. (*2*) Trophozoite showing spinous acanthopodia. (*3*) The trophozoite replicates by mitosis. (*4*) The cyst and trophozoite enter humans (*5*) through the eye, (*6*) through nasal passages and (*7*) through ulcerated or broken skin.

Both trophozoites and cysts are infective. Humans acquire infection by inhalation of cyst or trophozoite, or via broken skin or eyes. Upon reaching the lungs after inhalation, the trophozoites enter the blood circulation and invade the CNS, producing granulomatous amoebic encephalitis (GAE).

Pathogenesis and Clinical Features

1. Granulomatous amoebic encephalitis (GAE)

   GAE usually occurs in patients who are immunodeficient. The parasite spreads haematogenously to the CNS. Invasion of the connective tissue and induction of proinflammatory responses lead to neuronal damage that can be fatal within days. Clinical features are that of intracranial space-occupying lesions with seizures, paresis and mental deterioration. Autopsy of the brain reveals severe oedema and haemorrhagic necrosis. In immunocompromised states like AIDS, disseminated disease occurs with a widespread infection affecting skin, lungs, sinuses and other organs.

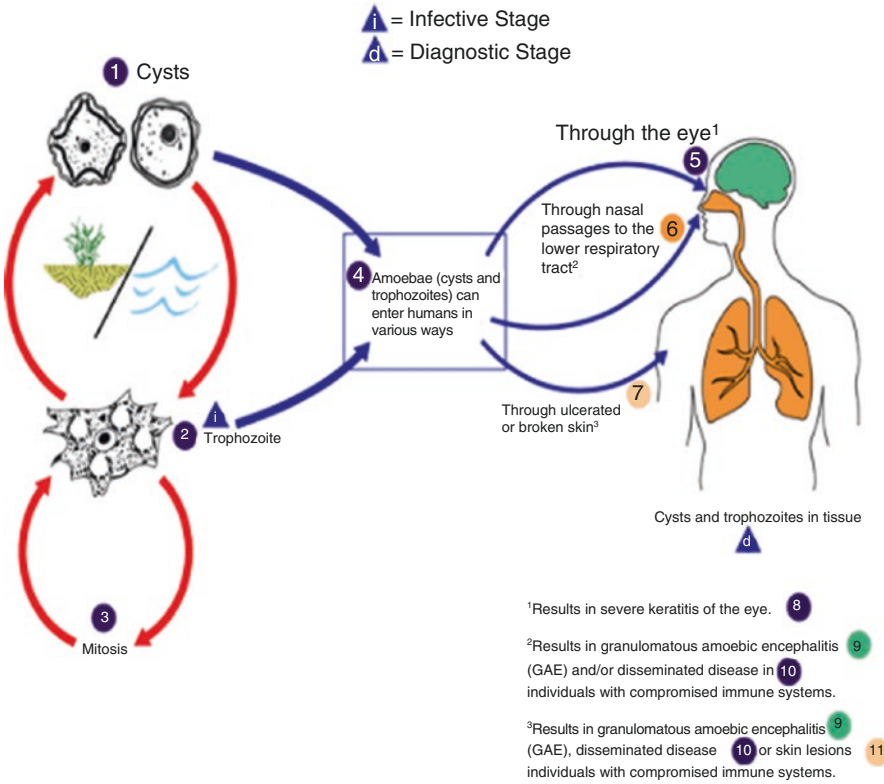


Fig. 3.7 Life cycle of *Acanthamoeba* species (Reproduced from https://www.cdc.gov/dpdx/free-livingamebic/index.html)

2. Acanthamoeba keratitis

   An infection of the eye that occurs in healthy persons and develops from the entry of the amoebic cyst through abrasions on the cornea. Most cases have been associated with the use of contact lenses. The clinical features resemble that of severe herpetic keratitis. The eye is severely painful in amoebic infection. Unilateral photophobia, excessive tearing, redness and foreign body sensation are the early signs and symptoms. Keratitis can result in permanent visual impairment or blindness.

Diagnosis

1. Diagnosis of GAE

Demonstration of trophozoites and cysts in brain biopsy, culture (non-nutrient agar plate coated with *E. coli*), or immunofluorescence microscopy using monoclonal antibodies. CSF examination can reveal motile trophozoite forms.

2. Diagnosis of amoebic keratitis

Demonstration of the cyst in corneal scrapings by wet mount, histology or culture.

Treatment

No effective treatment is available for GAE. In acanthamoeba keratitis, therapy involves topical application of biguanide or chlorhexidine. When vision is threatened, keratoplasty can be done. Multidrug combinations which include pentamidine, sulfadiazine, rifampicin and fluconazole are being used with limited success.

Prevention and Control

1. Tap water should not be used to rinse contact lenses

Balamuthia mandrillaris

Balamuthia mandrillaris is a newly identified FLA species reported to cause GAE. It is an emerging opportunistic protozoan pathogen.

Distribution

Balamuthia mandrillaris is found in the soil and was first discovered in 1986 in the brain of a baboon that died in the San Diego Wild Animal Park.

Habitat

In human, it is found in CNS.

Morphology

It occurs in 2 forms:

1. Trophozoite
2. Cyst

Trophozoite measures 12–60 μm, irregular in shape and actively motile by broad pseudopodia. Cyst is spherical, measuring 6–20 μm. Under light microscopy, it appears to have an outer irregular wall and an inner smooth wall. Infection to human is transmitted through respiratory tract, skin lesions or eyes.

Life Cycle

Life cycle is similar to that of *Acanthamoeba* spp.

Pathogenesis and Clinical Features

It causes GAE in both healthy and immunocompromised hosts particularly in children and elderly. There is a lack of information regarding the pathogenesis of *B. mandrillaris.*

Diagnosis

1. *Microscopy and histology*
   Identification of trophozoites in the CSF and trophozoites and cysts in brain tissue.
2. *Molecular diagnosis*
   PCR on CSF
   The amoeba cannot be cultured on an agar plate coated with *E. coli* because *B. mandrillaris* does not feed on bacteria.

Treatment

Drugs used in treating GAE caused by *Balamuthia* have included a combination of flucytosine, pentamidine, fluconazole, sulfadiazine and either azithromycin or clarithromycin.

Prevention and Control

Currently, there are no known ways to prevent infection with *Balamuthia*.

Intestinal and Genital Flagellates

4

Giardia lamblia

Distribution

It has a global distribution. It is endemic in the tropics and subtropics where sanitation is poor. Visitors to such areas develop traveller's diarrhoea.

Habitat

Giardia lamblia lives in the duodenum and upper jejunum.

Morphology

It exists in 2 forms:

1. Trophozoite
2. Cyst

Trophozoite is pyriform in shape, rounded anteriorly and pointed posteriorly. It measures 15 μm × 9 μm. Dorsally, it is convex and ventrally, it has a concave sucking disc for its attachment to the intestinal mucosa. It is bilaterally symmetrical, possesses 2 nuclei, 4 pairs of flagella, 1 pair of axostyles running along the midline and 2 parabasal or median bodies (Fig. 4.1a).

Cyst is the infective form of the parasite. The cyst is oval, measuring 12 μm × 8 μm. A young cyst contains 2 nuclei. A mature cyst contains 4 nuclei. The axostyle lies diagonally. Remnants of the flagella may be seen in the cyst (Fig. 4.1b).

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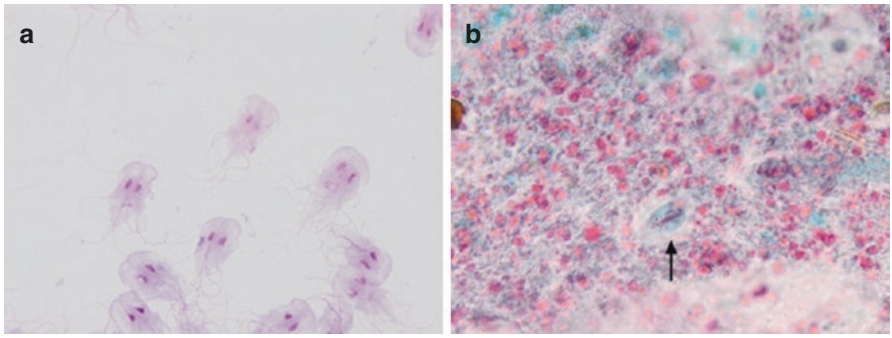


Fig. 4.1 *Giardia lamblia.* (**a**) Trophozoites, (**b**) Cyst

Life Cycle (Fig. 4.2)

(*1*) Cysts are passed out in stool of an infected human. (*2*) Infective cysts are ingested. (*3*) The cyst excysts to release trophozoite in the small intestine. (*4*) The trophozoites multiply by binary fission. (*5*) The trophozoite encysts to become cyst which is passed out in the stool. Trophozoites are passed in loose stools.

Giardia completes its life cycle in 1 host. Infective stage is the mature cyst. Human acquires infection by ingestion of cysts in contaminated water and food. Direct person to person transmission may also occur in children, male homosexuals, and institutional occupants.

Pathogenesis and Clinical Features

Trophozoite does not invade the tissue, but remains adhered to intestinal epithelium by means of the sucking disc causing stunting and shortening of the villi. Patients are usually asymptomatic, but in some cases, giardiasis may cause diarrhoea, fat malabsorption (steatorrhea), dull epigastric pain and flatulence. The stool contains excess mucus and fat. Children may develop chronic diarrhoea, malabsorption of fat and vitamin A and weight loss. Incubation period is about 2 weeks.

Diagnosis

1. *Microscopic examination*
   Detection of cysts and trophozoites in stools by direct saline, iodine wet preparations and use of concentration technique like formal ether. Often, multiple stool specimens need to be examined. In asymptomatic carriers, only the cysts are seen. Fixed stool smear can be stained with trichrome to identify cysts and trophozoites.
2. *Enterotest (String test)*
   A useful method for obtaining duodenal specimen to detect parasites.

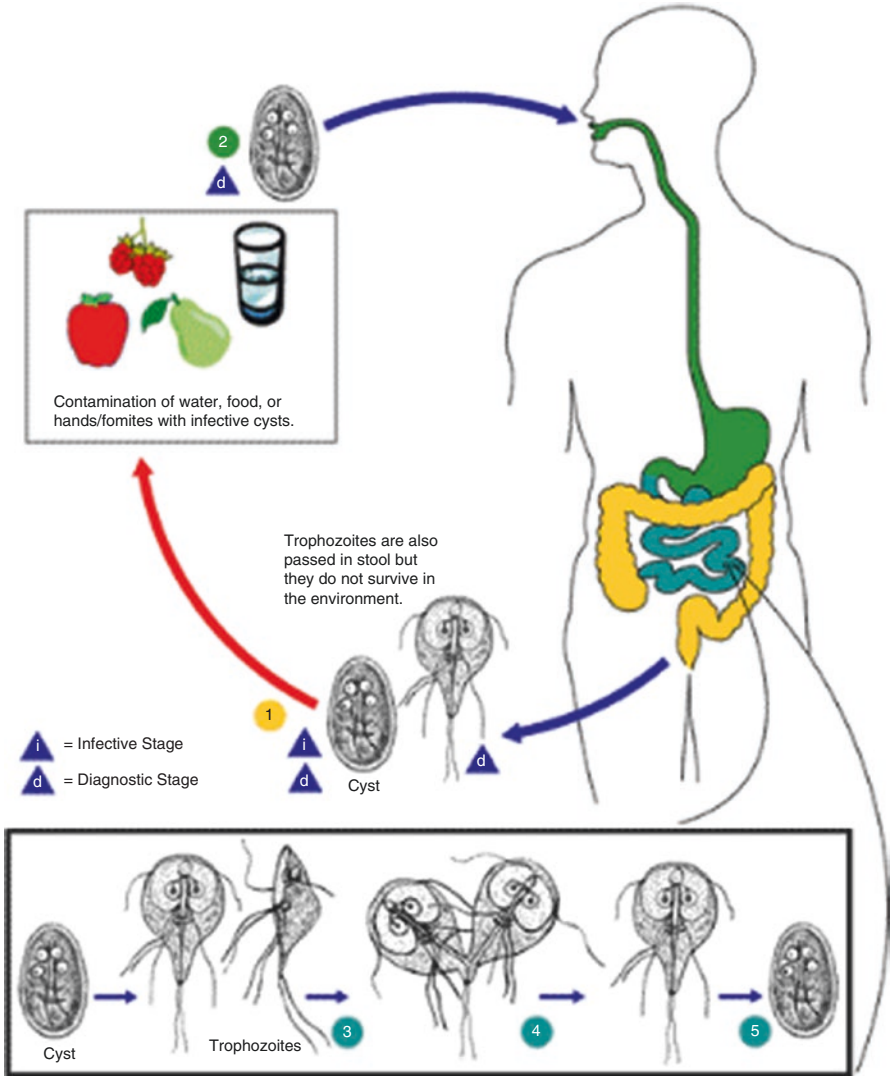


Fig. 4.2 Life cycle of *Giardia lamblia* (Reproduced from https://www.cdc.gov/dpdx/giardiasis/index.html)

3. *Molecular diagnosis*
   PCR on stool specimen.

Treatment

Metronidazole (250 mg 3 times daily for 5 days) or tinidazole is the drug of choice. Paromomycin can be given to symptomatic pregnant woman.

Prevention and Control

1. Proper faecal disposal
2. Personal hygiene
3. Boiling of drinking water
4. Filtration of drinking water
5. Wash fruits and vegetables with clean water before eating
6. Health education

Trichomonas vaginalis

Distribution

It is distributed worldwide.

Habitat

In human, it lives mainly in the vagina and cervix of females. In males, it occurs mainly in the anterior urethra.

Morphology

It only exists in the trophozoite stage (Fig. 4.3). Trophozoite is pear shaped or ovoid and measures 10–30 μm in length and 5–10 μm in breadth with a short undulating membrane reaching up to the middle of the body. It has 4 anterior flagella and a fifth running along the outer margin of the undulating membrane. A prominent axostyle runs throughout the length of the body and projects posteriorly.

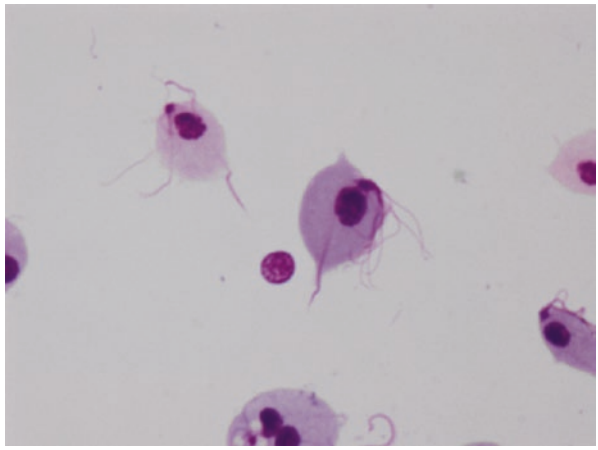


Fig. 4.3 *Trichomonas vaginalis* trophozoites

Life Cycle (Fig. 4.4)

(*1*) Trophozoites live in the vagina and cervix and may also be found in Bartholin's glands, urethra and urinary bladder in females. In males, it occurs mainly in the anterior urethra, but may also be found in the prostate. (*2*) Trophozoites multiply by longitudinal binary fission. (*3*) Trophozoites in vagina or orifice of urethra can be found in the vaginal and prostatic secretions and urine

Life cycle of *T. vaginalis* is completed in a human host. There is no cystic stage. The trophozoite is transmitted directly from person to person. Sexual transmission is the usual mode of infection. Trichomoniasis often coexists with other sexually transmitted diseases; like candidiasis, gonorrhoea, syphillis, or human immunodeficiency

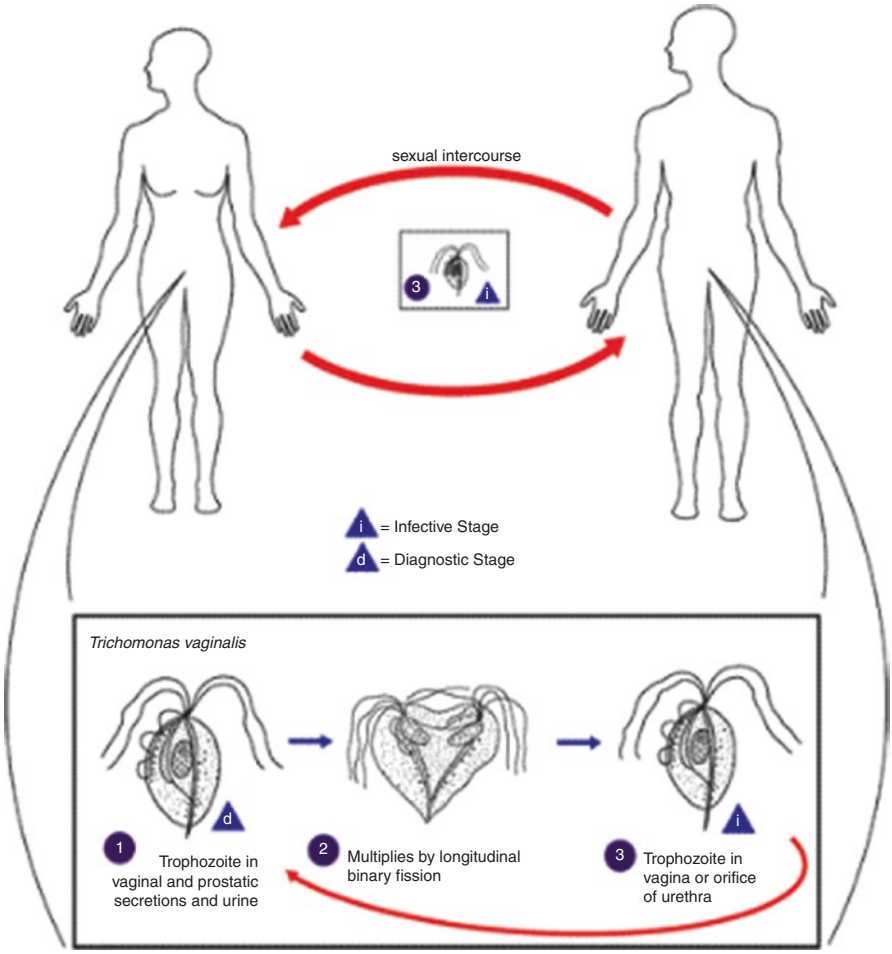


Fig. 4.4 Life cycle of *Trichomonas vaginalis* (Reproduced from https://www.cdc.gov/dpdx/trichomoniasis/index.html)

virus (HIV). Babies may acquire infection during birth from infected mothers. Fomites such as towels have been implicated in transmission.

Pathogenesis and Clinical Features

Trichomonas vaginalis infects the vagina and secretes cysteine, proteases, lactic acid and acetic acid, which disrupt the glycogen levels and lower the pH of the vaginal fluid. Trophozoite does not invade the vaginal mucosa. The infection can range from mild irritation to severe inflammation. Infection is often asymptomatic, particularly in males, although some may develop urethritis, epididymitis and prostatitis. In females, it may produce severe itching in the genital area with foul smelling yellowish green frothy discharge, dysuria, burning sensation with urination and dyspareunia. Cervical erosion is common. The incubation period is 4 days to 4 weeks.

Diagnosis

1. *Microscopic examination*
   Vaginal or urethral discharge is examined microscopically in saline wet mount preparation for the characteristic jerky and twitching motility of the trophozoite. In males, trophozoites may be found in urine or prostatic secretions. Fixed smears can be stained with acridine orange, Papanicolaou or Giemsa stains. Direct fluorescent antibody (DFA) is another method of parasite detection.
2. *Culture*
   Culture of clinical specimens in Johnson's and Trussel's medium is recommended when direct microscopy is negative.
3. *Molecular diagnosis*
   PCR on clinical specimens.

Treatment

Treatment of both sexual partners is recommended. Metronidazole is the drug of choice (250 mg 3 times daily for 10 days). In pregnancy, metronidazole is safe to be given in second and third trimesters.

Prevention and Control

1. Treatment of sexual partner
2. Patients should be advised to abstain from sexual intercourse until they and their partners have completed treatment and follow-up

Hemoflagellates

5

Trypanosoma brucei gambiense

Distribution

It is endemic in scattered foci in West and Central Africa. The principal vectors are *Glossina palpalis* and *Glossina tachynoides* (riverine tsetse flies).

Habitat

Trypanosomes live in human and other vertebrate hosts. From the blood, they invade regional lymph nodes and finally CNS.

Morphology

1. In vertebrate host
   Trypomastigote form, which is highly pleomorphic (long slender form, stumpy short broad form and an intermediate form), is about 15–40 μm long and 1.5–3.5 μm broad (Fig. 5.1). In fresh blood films, trypomastigotes are extracellular, colourless, spindle shaped bodies moving rapidly and spinning around the red cells.
2. In vector (tsetse fly)

Occurs in 2 forms:

(a) Epimastigotes
(b) Metacyclic trypomastigotes

Life Cycle (Fig. 5.2)

Trypanosoma brucei gambiense completes its life cycle in 2 hosts. Vertebrate hosts are humans. Game and other domestic animals can also be infected. (*1*) Tsetse fly (the

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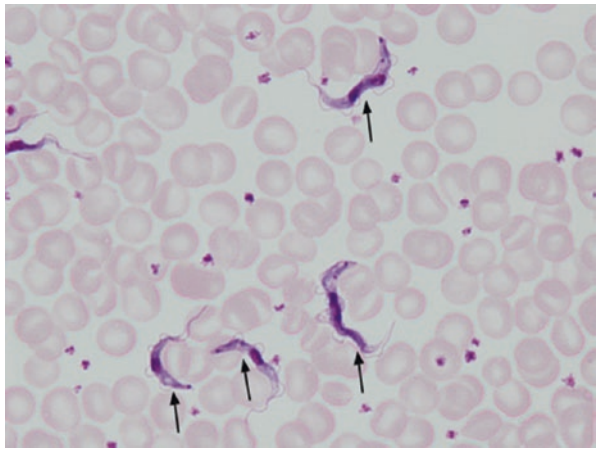


Fig. 5.1 *Trypanosoma brucei gambiense* trypomastigotes

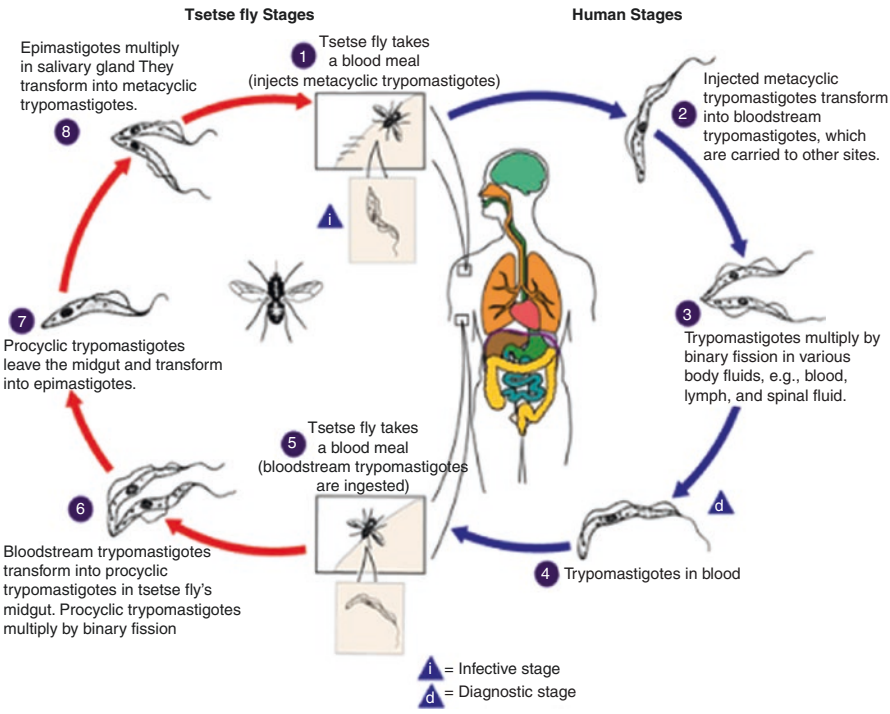


Fig. 5.2 Life cycle of *Trypanosoma brucei gambiense* (Reproduced from https://www.cdc.gov/dpdx/trypanosomiasisafrican/index.html)

invertebrate host) takes a blood meal and injects the infective metacyclic trypomastigotes. (*2*) Injected metacyclic trypomastigotes transform into trypomastigotes and are carried to other sites via blood stream. (*3*) Trypomastigotes multiply by binary fission. (*4*) Trypomastigotes are found in blood extracellular. (*5*) Trypomastigotes in the blood are ingested by tsetse fly and transform into procyclic trypomastigotes in the midgut of the fly (*6*). (*7–8*) Procyclic trypomastigotes transform into epimastigotes before transforming into metacyclic trypomastigotes in the fly's salivary gland.

Modes of transmission are via bite of infected tsetse fly and congenital transmission.

It is endemic in scattered foci in West and Central Africa.

Pathogenesis and Clinical Features

Trypanosoma brucei gambiense causes African trypanosomiasis (West African sleeping sickness). The illness is chronic and can persist for many years. There is an initial period of parasitaemia, followed by localization of parasites in the lymph nodes. A painless chancre appears on the skin at the site of bite by tsetse fly, followed by fever, chills, rash, anaemia and weight loss. There is high levels of immunoglobulins mainly IgM. Patient presents with hepatosplenomegaly and lymphadenopathy, particularly in the posterior cervical region (Winterbottom's sign). Invasion of CNS occurs after several months later and is marked by increasing headache, mental dullness, apathy and daytime sleepiness. The patient may fall into coma followed by death from other infections and physical weakness. Histopathology examination of the brain shows chronic meningoencephalitis. The meninges are heavily infiltrated with lymphocytes, plasma cells and morula cells (atypical plasma cells containing mulberry-shaped masses of IgA). Vessels in the brain show perivascular cuffing. There is cellular infiltration of the brain and spinal cord, neuronal degeneration and microglial proliferation. Intracranial pressure is raised and CSF shows pleocytosis with increased protein.

Antigenic Variation

Trypanosomes exhibit antigenic variation of their glycoproteins. There is a cyclical fluctuation in the trypanosomes in the blood of infected vertebrates. Trypanosomes have many variant surface glycoprotein (VSG) genes that help to evade immune response.

Trypanosoma brucei rhodesiense

Distribution

It is found in Eastern and Central Africa. The principal vectors are *Glossina morsitans, Glossina palpalis* and *Glossina swynnertoni.* It is a zoonotic disease, with the reservoir hosts being game and domestic animals. It is usually transmitted by the

vector from human to human. Its morphology, habitat and life cycle are similar to that of *T. brucei gambiense*.

Pathogenesis and Clinical Features

Trypanosoma brucei rhodesiense causes East African sleeping sickness. It is more acute than the Gambian form and appears after an incubation period of 4 weeks. It may end fatally within a year of onset, before the CNS symptoms develop. Pathological features are similar in both diseases with some variations. Lymphadenitis is less prominent and typical sleeping sickness picture is seldom seen in East African trypanosomiasis.

Diagnosis

The diagnosis of both types of human African trypanosomiasis (HAT) is similar.

1. *Microscopic examination*
   Wet mount preparation of lymph node aspirates, CSF, and chancre fluid are used for demonstration of trypomastigotes. These specimens can be fixed and stained with Giemsa.
2. *Culture*
   Culture is not routinely used.
3. *Animal inoculation*
   Inoculation of specimens from suspected cases to rats/mice is a highly sensitive procedure.
4. *Serodiagnosis*
   Specific antibodies or antigens can be detected in serum and CSF.
5. *Molecular diagnosis*
   PCR on clinical specimens.

Treatment

Before CNS involvement, pentamidine (i.m. 4 mg/kg daily for 10 days) is the drug of choice for gambiense human African trypanosomiasis (HAT). This drug does not cross the blood–brain barrier and hence is ineffective during the CNS stage of the disease. Suramin (1 g i.v. on days 1, 3, 5, 14 and 21) is the drug of choice for rhodesiense HAT. In patients with CNS involvement, melarsoprol (2–3.6 mg/kg/day i.v. for 3 days, a week later, 3.6 mg/kg/day for 3 days followed by a third series of 3.6 mg/kg/day after a week) is the drug of choice, as it can cross the blood–brain barrier.

Prevention and Control

1. Early diagnosis and early treatment of cases
2. Control of tsetse fly population using insecticides
3. Minimize contact with tsetse flies

Trypanosoma cruzi

Distribution

It is limited to South and Central America and it causes Chagas' disease, which is a zoonotic disease.

Habitat

In human, trypomastigotes are in the blood and amastigotes are in tissue.

Morphology

In humans, *Trypanosoma cruzi* exists in 2 forms, amastigote and trypomastigote. Amastigotes are intracellular, oval bodies measuring 2–4 μm in diameter having a nucleus and kinetoplast (Fig. 5.3a). Morphologically, it resembles the amastigote of *Leishmania* spp. Multiplication of the parasite occurs in this stage. This form is found in muscles, nerve cells and reticuloendothelial systems. In reduviid bugs, amastigotes are found in the midgut.

Trypomastigote is a non-multiplying form found in the peripheral blood of human and other mammalian hosts. In stained blood smears, they are 'C' or 'U' shaped, having a free flagellum of about one third the length of the body and a big kinetoplast (Fig. 5.3b). In reduviid bugs, metacyclic trypomastigotes are present in hindgut and faeces.

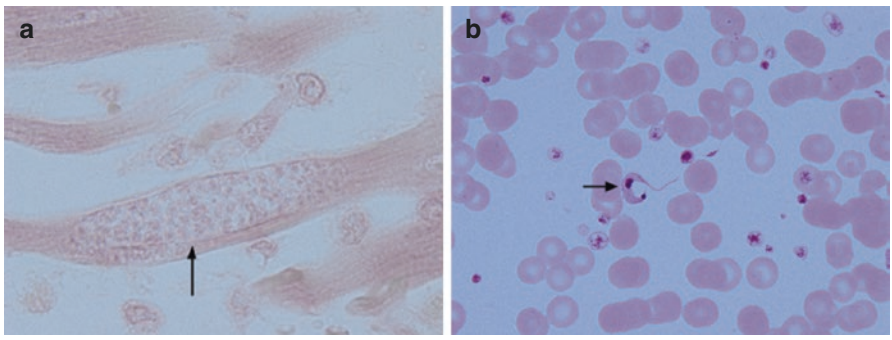


Fig. 5.3 *Trypanosoma cruzi.* (**a**) Amastigotes in heart muscle, (**b**) Trypomastigote in blood

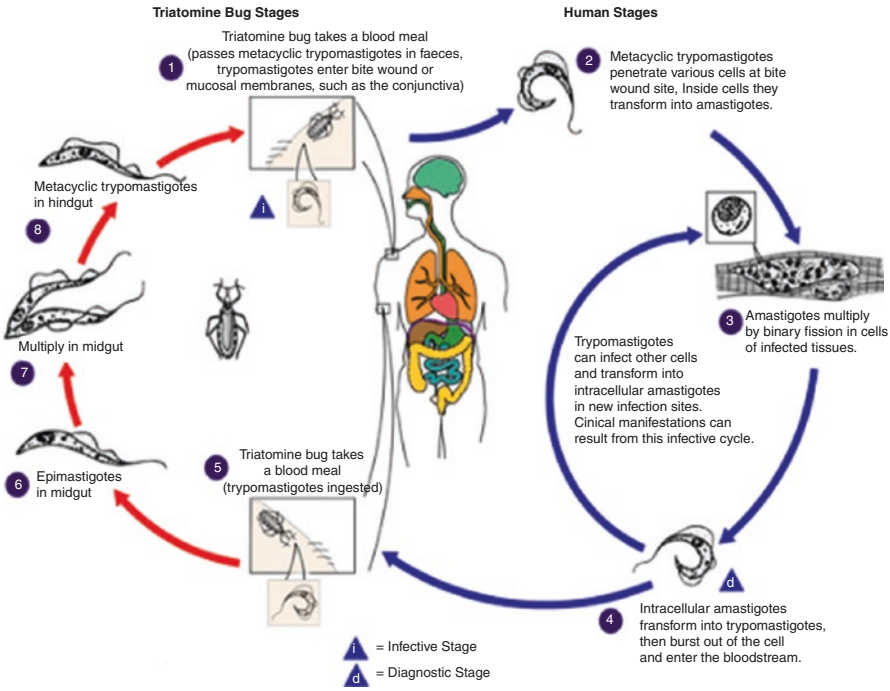


Fig. 5.4 Life cycle of *Trypanosoma cruzi* (Reproduced from https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html)

Life Cycle (Fig. 5.4)

Trypanosoma cruzi completes its life cycle in 2 hosts. Human is the vertebrate host. Its invertebrate host (vector) is reduviid bug or triatomid bug (*Triatoma infestans, Rhodnius prolixus* and *Panstrongylus megistus*). Its reservoir hosts are armadillos, cats, dogs and pigs. The infective stage to human is metacyclic trypomastigotes which are found in faeces of reduviid bugs. This bug defaecates while feeding. The parasite enters human at the biting site. Transmission of infection to human and other reservoir hosts takes place when mucus membranes, conjunctiva, or wound on the surface of the skin is contaminated by faeces of the bug containing metacyclic trypomastigotes. Other modes of transmission are blood transfusion, organ transplantation and vertical transmission.

Development in Human

The metacyclic trypomastigotes in faeces of reduviid bug enter human body and invade the myocardium, skeletal muscles, neuroglial cells and cells of the reticuloendothelial system. Inside these cells, they transform into amastigotes form which divide by binary fission. The amastigotes will pass through promastigotes and

epimastigotes forms, before becoming trypomastigotes again, which are released into the blood stream and are the infective stage for reduviid bug. No multiplication occurs in this stage.

Development in Reduviid Bugs

Bugs acquire infection by feeding on an infected mammalian host. The trypomastigotes are transformed into epimastigotes in the midgut, from where they migrate to the hindgut and multiply. These, in turn, develop into non-dividing metacyclic trypomastigotes, which are excreted in faeces. The development of *T. cruzi* in the vector takes 8–10 days.

Pathogenesis and Clinical Features

The incubation period of *T. cruzi* in human is 1–2 weeks. The disease manifests in acute and chronic forms.

1. Acute Chagas' disease

   Acute phase occurs soon after infection and may last for 1–4 months. It is seen often in children under 2 years of age. First sign appears within a week after invasion of parasite. 'Chagoma' is the subcutaneous lesion occurring at the site of inoculation. Inoculation of the parasite in conjunctiva causes unilateral, painless oedema of periorbital tissues known as Romana's sign. This is a classical finding in acute Chagas' disease. There may be generalized infection with fever, lymphadenopathy and hepatosplenomegaly. The patient may die of acute myocarditis and meningoencephalitis. Usually within 4–8 weeks, acute signs and symptoms resolve. Then, patient progresses into asymptomatic or chronic phase of *T. cruzi* infection.

2. Chronic Chagas' disease

   The chronic form is found in adults and older children and becomes apparent years or even decades after the initial infection. In chronic phase, *T. cruzi* produces inflammatory response, cellular destruction and fibrosis of muscles and nerves which can present with cardiac myopathy, megaoesophagus and megacolon.

Diagnosis

1. *Microscopic examination*

   Demonstration of trypomastigotes in thick and thin Giemsa-stained peripheral blood smears in acute infection.
2. *Culture*

   Novy, McNeal, and Nicolle (NNN) medium is used for growing *T. cruzi.*
3. *Animal inoculation and xenodiagnosis*

4. *Histopathology*
   Biopsy specimens may reveal amastigotes of *T. cruzi.*
5. *Serodiagnosis*
6. *Intradermal test*
7. *Molecular diagnosis*
   PCR on clinical samples.

Treatment

No effective specific treatment is available for treating Chagas' disease. Nifurtimox (5–7 mg/kg daily in 4 divided doses and is increased by 2 mg/kg daily at 2 week intervals up to a daily dose of 15–17 mg/kg, a total of 120 days treatment is given) and benznidazole have been used with limited success in both acute and chronic Chagas' disease. These drugs kill only the extracellular trypanosomes but not the intracellular form.

Prevention and Control

1. Insecticide to control the vector bug
2. Insect repellant and use of insect netting
3. Improvement in housing to eliminate breeding places of bugs

Leishmania donovani

Distribution

It causes visceral leishmaniasis or kala azar which is a major public health problem in many parts of the world.

Habitat

In human, the amastigotes are found in the reticuloendothelial system.

Morphology

The parasite exists in 2 forms.

1. Amastigote form is found in humans and other mammals. The amastigote form of the parasite seen in human samples is called Leishman Donovan (LD) body and it is intracellular.
2. Promastigote form is found in the sandfly and in culture.

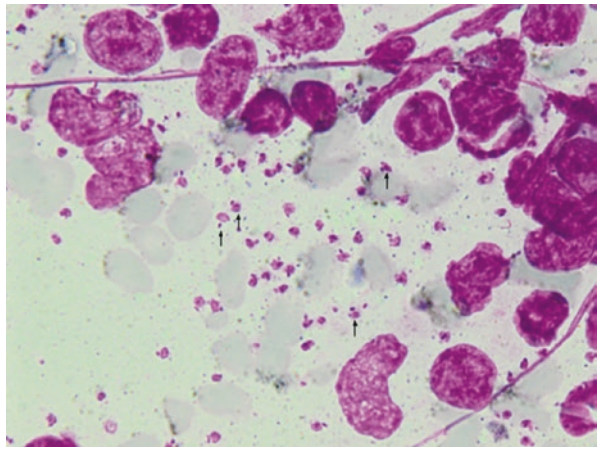


Fig. 5.5 *Leishmania donovani* amastigotes (arrows) which break free when the macrophages rupture

The amastigote form (LD body) is an ovoid or rounded cell, about 2–4 μm in size (Fig. 5.5). It is intracellular, found inside macrophages in the reticuloendothelial system. Promastigote is a flagellate and is present in sandfly and in culture. It is long, spindle shaped, 15–25 μm in length and 1.5–3.5 μm in breadth.

Life Cycle (Fig. 5.6)

Leishmania donovani completes its life cycle in 2 hosts. The vertebrate hosts are human, dog and other mammals. Its vector is the female sandfly (*Phlebotomus* species). Promastigote is the infective stage to humans. Humans acquire infection by bite of an infected female sandfly. Incubation period is 2–6 months. Other modes of transmission are congenital transmission, blood transfusion and accidental inoculation in the laboratory.

Pathogenesis and Clinical Features

Leishmania donovani causes visceral leishmaniasis or kala azar. The parasitized macrophages disseminate the infection to all parts of the body. In the reticuloendothelial system, the amastigotes multiply in the fixed macrophages. This causes a marked proliferation and destruction of reticuloendothelial tissue in these organs. It causes hepatosplenomegaly and lymphadenopathy. The bone marrow is heavily infiltrated with parasitized macrophages causing pancytopenia. Severe anaemia may occur in kala azar, as a result of infiltration of the bone marrow as well as by the increased destruction of erythrocytes due to hypersplenism. Autoantibodies to red blood cells, white blood cells, and platelets may contribute to pancytopenia. Patients usually present with fever and weight loss.

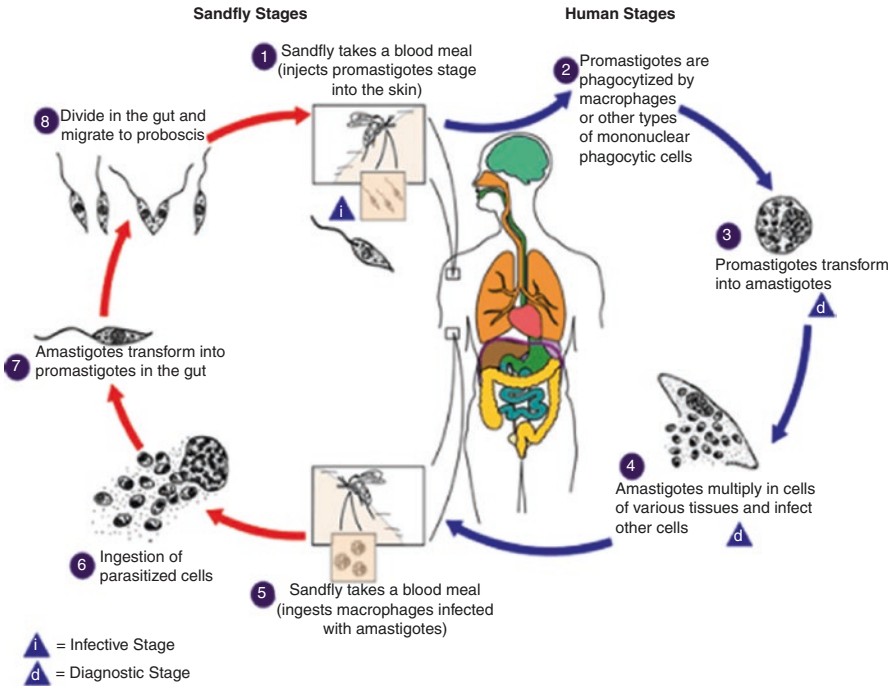


Fig. 5.6 Life cycle of *Leishmania donovani* (Reproduced from https://www.cdc.gov/dpdx/leishmaniasis/index.html)

Some patients with visceral leishmaniasis in endemic areas may develop post kala azar dermal leishmaniasis (PKDL), about a year or 2 after recovery from the systemic illness. PKDL is seen mainly in India and East Africa and is a nonulcerative skin lesion.

Visceral leishmaniasis has emerged as an important opportunistic infection associated with HIV.

Immunity

Recovery from visceral leishmaniasis and cutaneous leishmaniasis will give lasting immunity to the respective disease but may not provide cross-protection.

Diagnosis

1. *Microscopic examination*

   Demonstration of amastigotes in blood smears and tissue aspirates (bone marrow, spleen, lymph nodes) is the gold standard for diagnosis. Fixed smears can be stained with Giemsa to demonstrate amastigotes.

2. *Culture*
   Tissue specimens or blood are cultured in NNN medium.
3. *Animal inoculation*
4. *Serodiagnosis*
5. *Molecular diagnosis*
   PCR on clinical specimens.
6. *Skin test*
   Leishmanin skin test (Montenegro test).

Diagnosis of PKDL

Biopsy of nodular lesions to demonstrate amastigotes in stained sections. The biopsy material can be cultured or inoculated into animals.

Treatment

1. Pentavalent antimonials compound given intravenously or intramuscularly. Sodium stibogluconate (20 mg/kg daily for 28 days) and meglumine antimoniate are the drugs of choice.
2. Amphotericin B
3. Paromomycin
4. Miltefosine

Treatment of PKDL is the same as that for visceral leishmaniasis.

Prevention and Control

1. Early detection and treatment of cases
2. Insecticide spraying
3. Control of animal reservoir hosts in cases of zoonotic kala azar
4. Use of protective clothing, bed nets, window mesh or insect repellants

Leishmania tropica Complex

It includes 3 species:

1. *Leishmania tropica*
2. *Leishmania major*
3. *Leishmania aethiopica*

These species cause old world cutaneous leishmaniasis (oriental sore).

Distribution

Leishmania tropica and *L. major* are found in Middle East, India, Afghanistan, eastern Mediterranean countries and North Africa. *L. aethiopica* occurs in Ethiopia and Kenya.

Habitat

In human, the amastigotes are found in the skin.

Morphology

Morphology of amastigote and promastigote of *L. tropica* complex is indistinguishable from that of *L. donovani.* The amastigotes are present in the skin, within large mononuclear cells and neutrophils.

Life Cycle

The life cycle of *L. tropica* complex is similar to that of *L. donovani.* Incubation period varies from 2 to 8 months. Modes of transmission is via bite of sandflies from human to human or animal to human by direct inoculation of amastigotes.

Pathogenesis and Clinical Features

Early lesions are papular, followed by ulceration necrosis. Papule and ulcer are the main pathological lesions. Amastigotes are found in histiocytes. There is an inflammatory granulomatous reaction with infiltration of lymphocytes and plasma cells. They heal over months to years, leaving scars. The anthroponotic urban type causes painless dry ulcerating lesions (oriental sore or Delhi boil) caused by *L. tropica.* The zoonotic rural type causes moist ulcers which are inflamed, often multiple, caused by *L. major.* Lesions due to *L. major* heal more rapidly than *L. tropica.* The non-ulcerative and often diffuse lesions caused by *L. aethiopica* is known as diffuse cutaneous leishmaniasis.

Diagnosis

1. *Microscopic examination*
   Smear made from the indurated edge of nodule or sore and stained by Giemsa or Leishman stains to detect amastigotes.
2. *Culture*
   Culture of the aspirated material in NNN medium.

3. *Skin test*
   Leishmanin skin test.
4. *Serodiagnosis*
   Of limited value as the patient shows no detectable levels of circulating antibodies.
5. *Molecular diagnosis*
   PCR on clinical specimens.

Treatment

The specific treatment of cutaneous leishmaniasis is the same as for visceral leishmaniasis. Antimony resistant diffuse cutaneous leishmaniasis can be treated with pentamidine. Topical treatment consists of a paste of 10% charcoal in sulphuric acid or liquid nitrogen.

Prevention and Control

1. Insecticide spraying
2. Use of protective clothing and insect repellants
3. Control of mammalian reservoir

Leishmania braziliensis Complex and *L. mexicana* Complex

Distribution

Leishmania braziliensis complex and *L. mexicana* complex cause new world leishmaniasis in Central and South America.

Habitat

In human, amastigotes are found in the naso-oral mucosa.

Morphology

Morphology of amastigote and promastigote forms of both the parasites is the same as that of the other 2 species of *Leishmania.*

Life Cycle

The life cycle of *Leishmania* species causing the new world cutaneous and mucocutaneous leishmaniasis is similar to that of *L. donovani.* The infection is transmitted to human

from animals by bite of sandfly vectors of genus *Lutzomyia.* Sylvatic rodents and domestic animals are the common sources and reservoir of infection. Direct transmission also occurs from human to human.

Pathogenesis and Clinical Features

Leishmania mexicana complex causes cutaneous leishmaniasis which closely resembles the old world cutaneous leishmaniasis. However, a specific lesion caused by *L. mexicana* is chiclero ulcer which is characterized by ulcerations in pinna. *L. braziliensis* complex causes both cutaneous and mucocutaneous leishmaniasis.

Diagnosis

1. *Microscopic examination*
   Stained smears from skin lesions and mucous membrane to demonstrate amastigotes.
2. *Biopsy*
   Skin biopsy to demonstrate amastigotes.
3. *Culture*
   Culture of specimens obtained from ulcers in NNN medium.
4. *Skin test*
   Leishmanin test.
5. *Molecular diagnosis*
   PCR on clinical specimens.

Treatment

Pentavalent antimonials compound is moderately effective for mild mucocutaneous leishmaniasis. Amphotericin B (i.v. 0.25–1.0 mg/kg daily or every other day for up to 8 weeks) is the best alternative drug.

Prevention and Control

1. Insect repellants, insecticide spraying
2. Use protective clothing

Due to sylvatic and rural nature of the disease, control is often difficult.

Malaria Parasites and Babesia

6

Causative agents of human malaria:

1. *Plasmodium vivax*
2. *Plasmodium falciparum*
3. *Plasmodium malariae*
4. *Plasmodium ovale*
5. *Plasmodium knowlesi*

Distribution

Plasmodium vivax is the predominant malaria parasite in most parts of the world. *P. falciparum* is mostly confined to the tropics and subtropics. It is well known to be the fatal form of human malaria and is also known as malignant tertian. *Plasmodium malariae* occurs in subtropical and temperate areas. It is less frequently seen than *P. vivax* or *P. falciparum*. *Plasmodium ovale* is confined to West Africa. *Plasmodium knowlesi,* a monkey malaria is distributed in Southeast Asia where the reservoir macaques are prevalent.

Habitat

In human, the parasites are found in the erythrocytes and hepatocytes.

Vectors

Human malaria is transmitted by over 60 species of female *Anopheles* mosquito.

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Types of Malarial Parasites and Their Morphology

1. *Plasmodium falciparum* (Malignant tertian)

   This is the most pathogenic of all the plasmodia and unless treated, is often fatal. The species is responsible for almost all deaths caused by malaria. They infect both young and old erythrocytes. The early ring form is fine, measuring 1/6 the size of red blood cell (RBC). Rings are often seen attached along the margin of the red cell (appliqué or accole form). Double chromatins are common. Multiple rings may be seen within a single erythrocyte (Fig. 6.1a). Late trophozoites and schizonts are not usually seen in the peripheral blood. These stages are sequestrated in the internal capillaries. The mature schizont has 8–24 (usually 16) merozoites. The erythrocytic schizogony takes about 36–48 h. The infected erythrocytes are not enlarged. A good staining will show coarse dots which are called Maurer's clefts. The mature gametocytes are crescent or banana shaped (Fig. 6.1b).
2. *Plasmodium vivax* (Benign tertian)

   Merozoites of *P. vivax* prefer reticulocytes. All erythrocytic stages can be seen in peripheral smears. The infected erythrocytes are enlarged and with good staining will show granules known as Schuffner's dots in the cytoplasm of the RBC. The ring is about 1/3 the size of RBC (Fig. 6.1c). The ring develops rapidly into trophozoite which is amoeboid shape and accumulates malarial pigment. There are about 12–24 (usually 18) merozoites per schizont (Fig. 6.1d). The erythrocytic schizogony takes 48 h. Both male and female gametocytes are large, filling almost the enlarged RBC (Fig. 6.1e).
3. *Plasmodium malariae* (Quartan malaria)

   Plasmodium malariae prefers older erythrocytes. The ring forms resemble those of *P. vivax* but the cytoplasm is thicker. The infected erythrocytes may be of the normal size or slightly smaller. Fine stippling, called Ziemann's stippling may be seen with special stains. The trophozoites stretch across the diameter of the erythrocyte and is seen as a band form (Fig. 6.1f). The mature schizont has an average of 8 merozoites, which usually present as a rosette appearance (Fig. 6.1g). Erythrocytic schizogony takes 72 h. Both male and female gametocytes occupy nearly the entire RBC (Fig. 6.1h).
4. *Plasmodium knowlesi* (Quotidian malaria)

   The ring stage resembles *P. falciparum*. Accole form, double chromatins and multiple infections are common in an infected RBC (Fig. 6.1i). The infected RBC is not enlarged. The trophozoite stage has a band form resembling *P. malariae*. The mature schizont has an average of 10 merozoites, with a maximum of 16 (Fig. 6.1j). Pigment collects into 1 or more yellowish-black masses and eventually into a single mass in the mature schizont. The erythrocytic schizogony takes 24 h. Both male and female gametocytes occupy nearly the entire RBC (Fig. 6.1i).
5. *Plasmodium ovale* (Tertian malaria)

   It is the rarest of all plasmodia infecting humans. The trophozoites resemble those in *P. vivax*, but are usually more compact, with less amoeboid appearance (Fig. 6.1k). Schuffner's dots are present in the cytoplasm of the infected RBC

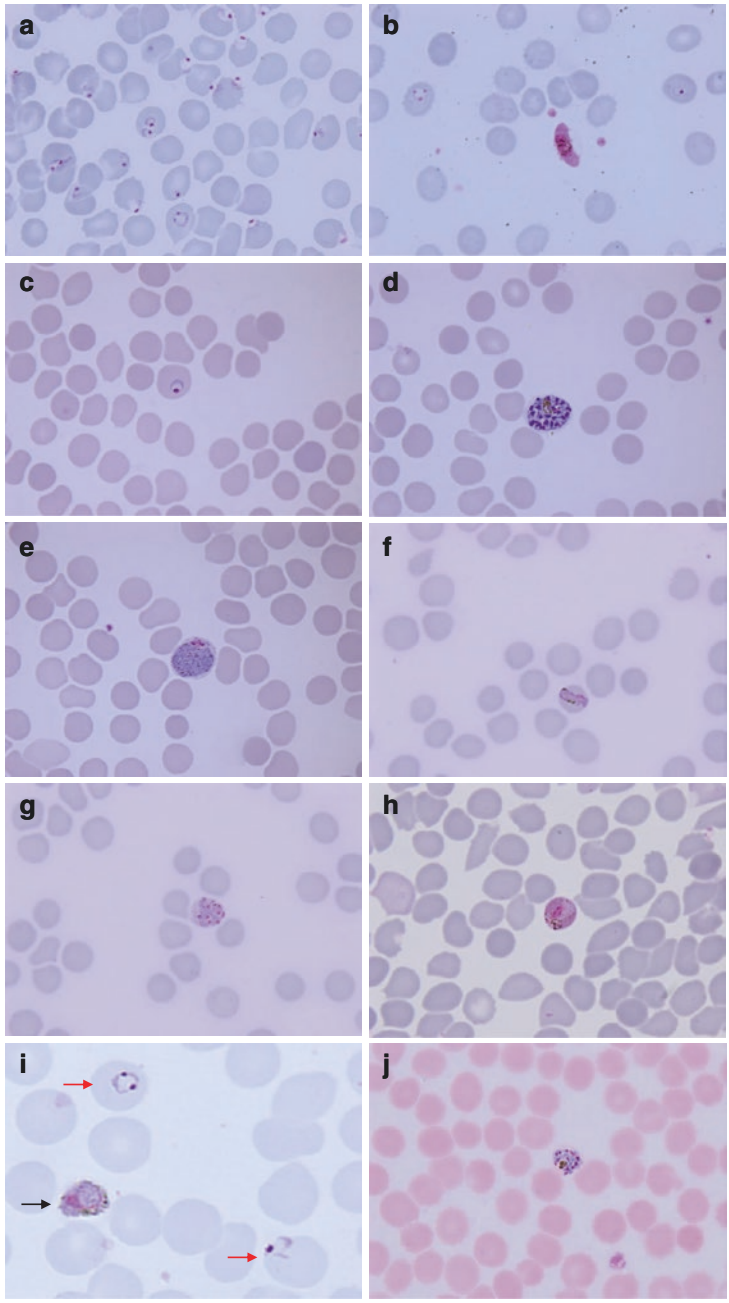


Fig. 6.1 *Plasmodium falciparum*; (**a**) Rings, (**b**) Gametocytes. *P. vivax*; (**c**) Ring, (**d**) Schizont, (**e**) Gametocyte. *P. malariae*; (**f**) Trophozoite, (**g**) Schizont, (**h**) Gametocyte. *P. knowlesi*; (**i**) Ring (red arrow) and gametocyte (black arrow), (**j**) Schizont. *P. ovale*; (**k**) Trophozoite, (**l**) Schizont, (**m**) Gametocyte.

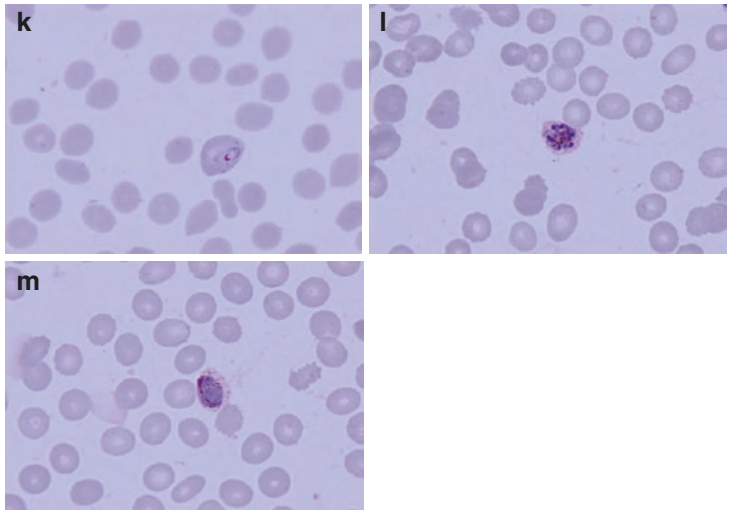


Fig. 6.1 (continued)

and are seen under good staining. The infected erythrocytes are slightly enlarged. In thin films, many of them appear oval shape with fimbriated margins. The schizonts resemble those of *P. malariae,* except that the pigment is darker (Fig. 6.1l). The erythrocytic schizogony takes 48 h. Both male and female gametocytes occupy nearly the entire RBC (Fig. 6.1m).

Life Cycle (Fig. 6.2)

Malaria parasite completes its life cycle in 2 hosts. Its definitive host is the female *Anopheles* mosquito. Humans are the intermediate host. Modes of transmission are via bite of infected *Anopheles* mosquito, blood transfusion, congenital transmission and shared syringes.

1. Asexual phase (in intermediate host)
   The asexual multiplication is known as schizogony. It takes place in the red blood cells (erythrocytic schizogony) and in the liver cells (exoerythrocytic or pre-erythrocytic schizogony).
2. Sexual phase (in definitive host)
   Maturation and fertilization of the gametocytes take place in the mosquito, giving rise to a large number of sporozoites (sporogony).
3. Human cycle (schizogony)
   Humans acquire infection from the bites of infective female *Anopheles* mosquito. The sporozoites, which are the infective forms of the parasite, are present in the salivary gland of the mosquito. They are injected into blood capillaries when the mosquito takes a blood meal. The sporozoites circulate in the blood stream and enter the liver parenchymal cells (hepatocytes).

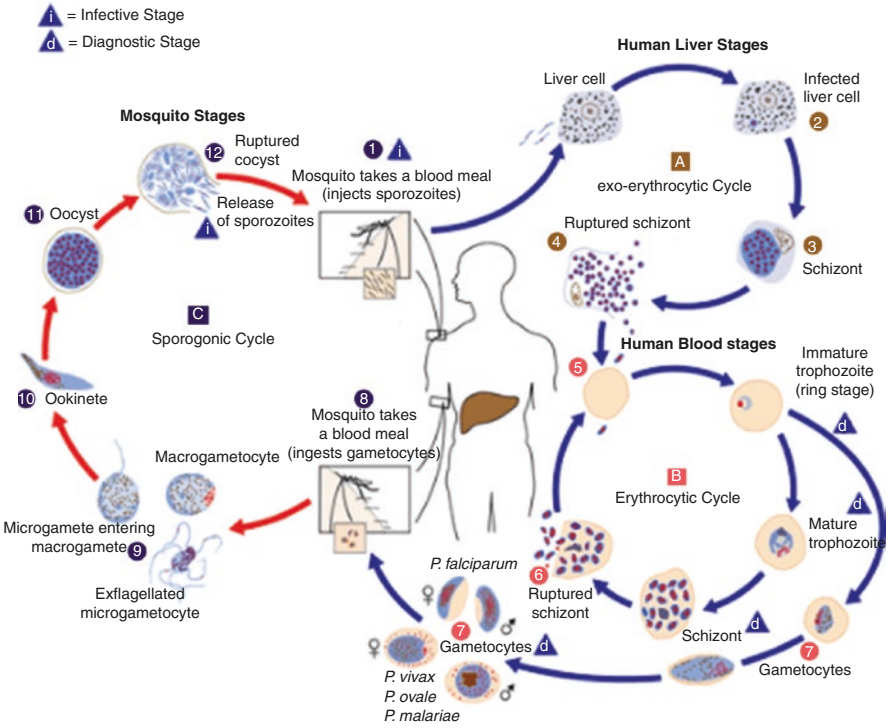


Fig. 6.2 Life cycle of malaria (Reproduced from https://www.cdc.gov/dpdx/malaria/index.html)

4. Exoerythrocytic cycle

   Within 30 min, the sporozoites reach the liver and enter the hepatocytes to initiate the stage of pre-erythrocytic schizogony. In *P. vivax* and *P. ovale*, they form schizonts which persist and remain dormant (hypnozoite). From time to time, the dormant schizonts are reactivated and release merozoites, which go on to infect RBCs causing clinical relapse.

5. Erythrocytic cycle

   The merozoites released by pre-erythrocytic schizonts in the liver invade the RBCs and form rings or young trophozoites. The parasite feeds on the haemoglobin. It does not metabolize haemoglobin completely and leaves behind haemozoin or malaria pigment.

6. Sporogonic cycle

   When a female *Anopheles* mosquito ingests parasitized erythrocytes along with its blood meal, the asexual forms of malaria parasite are digested. The gametocytes undergo further development in the midgut (stomach) of mosquito. The nuclear material and cytoplasm of the male gametocytes divide to produce 8 microgametes (exflagellation). The female gametocyte (macrogamete) is fertilized by the microgamete to form zygote. The zygote develops into a motile form called ookinete. It penetrates the epithelial lining of the mosquito stomach wall and comes to lie beneath the basement membrane. It forms an oocyst within

which numerous sporozoites are formed. The mature oocyst ruptures releasing sporozoites into the body cavity, from where some find their way to the salivary glands. The mosquito is now infective and when it feeds on humans, the sporozoites are injected into skin capillaries to initiate infection. The time taken for completion of sporogony in the mosquito is about 1–4 weeks, depending on the species and environmental temperature.

Pathogenesis and Clinical Features

The disease process in malaria occurs due to local or systemic response of the host to parasite antigens. The typical presentation of malaria is periodic bouts of fever with chills and rigors. The febrile paroxysm follows the completion of erythrocytic schizogony when the mature schizont ruptures, releasing red cell fragments, merozoites, malaria pigments and other parasitic debris. It is commonly associated with severe headache, nausea, and vomiting.

Liver is enlarged and congested. Haemozoin pigments are found in the parenchymal cells. Spleen is soft, moderately enlarged, and congested in acute infection. In chronic infection, the spleen undergoes fibrosis and the sinusoids are dilated. Anaemia is caused by rupture of infected red blood cells and other causes of anaemia are by complement-mediated, autoimmune haemolysis and hypersplenism. A decreased erythropoiesis in the bone marrow may also contribute to anaemia.

Complications

Cerebral malaria is the most serious complication of *P. falciparum* infection. The brain in *P. falciparum* infection is congested. Late stage schizonts of *P. falciparum* secrete a protein on the surface of RBCs to form knobs. This knob produces specific adhesive proteins, which promote adhesion of infected RBCs to other non-infected RBCs and adhere to the receptors on capillary endothelial cells. These sequestrated RBCs cause obstruction of cerebral microvasculature, which results in anoxia, ischaemia and haemorrhage causing cerebral malaria. It is the most common cause of death in malignant malaria. Cerebral malaria is manifested by headache, hyperpyrexia, confusion and finally coma. The pathogenesis of cerebral malaria is likely a multi-factorial process with sequestration, inflammation and endothelial dysfunction in the microvascular of the brain leading to coma.

Pulmonary oedema may develop secondary to parenteral fluid administration or as a result of anoxia affecting the pulmonary microcirculation. Acute respiratory distress syndrome (ARDS) is a complication of severe, complicated falciparum malaria and has also been described in vivax and knowlesi malaria. Non-immune individuals are more prone to develop this condition. There is increased alveolar-capillary permeability resulting in intravascular fluid loss into the lungs.

Blackwater fever is sometimes seen in falciparum malaria, in patients who have experienced repeated infections and inadequate treatment with quinine. Clinical manifestations include bilious vomiting and prostration, with passage of dark red or blackish urine (blackwater).The pathogenesis is due to massive intravascular haemolysis caused by anti-erythrocyte antibodies, giving rise to haemoglobinuria. Complications of blackwater fever include renal failure, acute liver failure, and circulatory collapse.

Acute renal failure may occur in severe falciparum malaria most likely due to tubular necrosis. Acute renal failure has also been described in severe malaria caused by other species. Nephrotic syndrome has been reported in malariae malaria. Immune complexes may cause structural glomerular damage and the associated nephrotic syndrome.

Tropical splenomegaly syndrome (TSS) or hyper-reactive malarial splenomegaly is a chronic benign condition seen in some adults in endemic areas. This results from abnormal immunological response to malaria and is characterized by splenomegaly, high titres of anti-malaria antibodies and absence of malaria parasites in peripheral blood smears. Hypergammaglobulinemia (IgM) is its other feature. Liver is also enlarged, congested, with marked lymphocytic infiltration. TSS responds to anti-malarial treatment.

Other complications of malaria are hypoglycemia and hyperparasitaemia.

Immunity

Immunity in malaria may be classified as innate immunity and acquired immunity.

1. Innate immunity

   It is an inherent, non-immune mechanism of host resistance against malarial parasite. It could be due to Duffy-negative RBCs. The invasion of red cells by merozoites requires the presence of specific glycoprotein receptors on the erythrocyte surface. Persons negative with Duffy blood group antigen are found to be refractory to infection by *P. vivax.* This genetically determined blood group antigen is a specific receptor for *P. vivax* and *P. knowlesi.*

   Nature of haemoglobin like haemoglobin E provides natural protection against *P. vivax. Plasmodium falciparum* does not multiply properly in sickled red cells containing HbS. Sickle cell anaemia trait is very common in Africa, where falciparum malaria is hyperendemic and offers a survival advantage. HbF present in neonates protects them against all *Plasmodium* species.

   Innate immunity to malaria has also been related to glucose-6-phosphate dehydrogenase (G6PD) deficiency found in Mediterranean coast, Africa, Middle East and India. G6PD-deficient cells are more resistant to *P. falciparum*.
2. Acquired immunity

   Malaria induces specific immunity involving both humoral and cellular immunity, which brings about clinical cure, but cannot eliminate parasites

from the body. It can prevent superinfection, but not reinfection. This type of immunity associated with asymptomatic infection is called premunition and disappears once the infection is eliminated. Acquired antibody-mediated immunity is transferred from mother to foetus across the placenta and is evident in endemic areas where infants below the age of 3 months are protected by passive maternal antibodies. Young children are highly susceptible to malaria. As they grow up, they acquire immunity by subclinical or clinical infections. Incidence of malaria is low in older children and adults.

Recrudescence

Recrudescence occurs when parasites persist although the level of parasitaemia is below the fever or microscopic threshold. Erythrocytic schizogony continues in the body at low levels and parasitaemia gradually increase to cross the fever threshold. New malarial attacks then occur. These malaria attacks appear within 8 weeks after the primary attack. Recrudescence may be due to waning immunity of the host or to antigenic variation and is seen in all human malaria.

Relapse

It is seen in *P. vivax* and *P. ovale* infections, caused by the reactivation of hypnozoite stage in the liver. This leads to initiation of erythrocytic cycles and new attacks of malarial fever. Reactivation of hypnozoite stage usually occurs from 24 weeks to 5 years after the primary attack.

Diagnosis

1. *Microscopic examination (Gold standard)*
   Demonstration of malarial parasite in the peripheral blood in thin and thick smears. Thin smear is used for detecting the parasites and determining the species by studying its morphological details. The thick smear is more sensitive and is used for detection of malarial parasite when there is low parasitaemia. Species identification is not easy in thick smear. Both thin and thick smears can be used to determine the parasitaemia level.
2. *Rapid diagnostic tests (RDT)*
   The tests aid in the diagnosis of malaria by detecting malaria parasite antigens in human blood.
3. *Molecular diagnosis*
   PCR on blood.
4. *Serodiagnosis*
   It is used mainly for seroepidemiological survey and to identify the infected donors in transfusion malaria.

5. *Culture*
   This method is rarely used for diagnostic purposes. It is mainly used for research.

Treatment

1. Treatment of uncomplicated malaria
   In areas with chloroquine-susceptible infections, adults, and children are treated with either artemisinin-based combination therapy (ACT) (except women in first trimester of pregnancy) or chloroquine. In cases of chloroquine resistance, ACT is given. In uncomplicated *P. falciparum* infection, ACT is used for treatment (except women in first trimester of pregnancy). Infected pregnant women in their first trimester in areas of chloroquine resistance are treated with quinine. For prevention of relapse in vivax and ovale, primaquine is given for 14 days under supervision. G6PD status of the patient must be determined before starting primaquine. Primaquine is contraindicated in pregnant women.
2. Treatment of complicated malaria
   All patients (including infants, pregnant women in all trimesters and lactating mothers) with severe malaria should be treated with intravenous or intramuscular artesunate for at least 24 h or until they can tolerate oral medication. Artemether or quinine is given as an alternative if parenteral artesunate is not available.
   ACT consists of an artemesinin derivative combined with a long-acting antimalarial drug (amodiaquine, lumefantrine, mefloquine, or sulfadoxine-pyrimethamine). Artemesinin derivative must never be given as monotherapy to prevent development of parasite resistance to these drugs (Table 6.1).

Prevention and Control

1. Chemoprophylaxis
   For travellers visiting endemic areas, chemoprophylaxis provides effective protection. The drugs recommended are proguanil, chloroquine or mefloquine weekly or doxycycline daily. Prophylaxis should begin 1 week before travelling and be continued while in the endemic area and for 4–6 weeks after departure from endemic area.
2. Vector Control Strategies
   (a) Insecticide residual spraying (IRS): The spraying of the indoor surfaces of house with residual insecticides
   (b) Insecticide treated bed nets (ITN)
   (c) Use of repellants, protective clothing, mosquito coils and screening of house
3. Anti-larval Measures

Table 6.1 Treatment for malaria

	First line	Alternative
Uncomplicated malaria	Riamet (1 tablet: 20 mg artemether/120 mg lumefantrine) A 3-day treatment schedule with a total of 6 doses is recommended The patient should receive an initial dose followed by the 2nd dose 8 h later, then 1 dose BD for the following 2 days 5–<15 kg: 1 tablet per dose 15–<25 kg: 2 tablets per dose 25–<35 kg: 3 tablets per dose ≥35 kg: 4 tablets per dose In *P. vivax* and *P. ovale* infection, primaquine 0.5 mg/kg (max 30 mg) OD for 14 days	Artesunate/Mefloquine (AS + MQ Fixed Dose Combination (FDC) Tablet) 2 FDC strength—25 mg AS/55 MQ and 100 mg AS/220 mg MQ A 3-day treatment schedule, once daily regime 5–8 kg: 1 tablet of 25 mg AS/55 mg MQ 9–17 kg: 2 tablets 25mg AS/55 mg MQ 18–29 kg: 1 tablet of 100 mg AS/220 mg MQ ≥30 kg: 2 tablets of 100mg AS/220 mg MQ *Or* Oral Quinine (10 mg/kg) 8 hourly with oral Doxycycline 100 mg BD for 7 days
Complicated malaria	Day 1 IV Artesunate 2.4 mg/kg at 0, 12, 24 h, and daily subsequently till day 7[a] *And* Oral Doxycycline 100 mg BD (given together with IV Artesunate)	Day 1 (Loading dose) IV Quinine 20 mg salt/kg over 4 hours in D5% *Or* IV Quinine 7 mg salt/kg over 1 h followed by 10 mg salt/kg over 4 h *Then*, IV Quinine 10 mg/kg 8 hourly (can give orally if tolerated) for 7 days *And* Oral Doxycycline 100 mg BD for 7 days

Adapted from Management Guidelines of Malaria in Malaysia 2013, Ministry of Health Malaysia

This guideline has been revised and updated based on previous national guidelines (published in year 1993) and the 2nd edition of WHO guidelines)

[a]Parenteral artesunate should be given for a minimum of 24 h (3 doses) or until patient can tolerate orally then it can be switched to a complete course of oral ACT either Riamet or AS + MQ. For all stages of pregnancy: IV Artesunate is given as for normal adults.

Babesia

Babesia are intraerythrocytic sporozoan parasites that morphologically resemble *P. falciparum.* It is a tick-borne parasite.

Distribution

Most human cases were reported from the USA and are mainly caused by *Babesia microti*.

Habitat

In human, the parasites are found in the erythrocytes.

Morphology

Trophozoites are 2–5 μm in diameter found inside the red cells. The shape may be pyriform, amoeboid, or spindle-like, usually in pairs and are often mistaken as ring form of *Plasmodium.*

Life Cycle (Fig. 6.3)

The definitive host is *Ixodid* ticks. Humans and rodents are the intermediate hosts. Modes of transmission to human are through bite of *Ixodid* ticks and via blood transfusion.

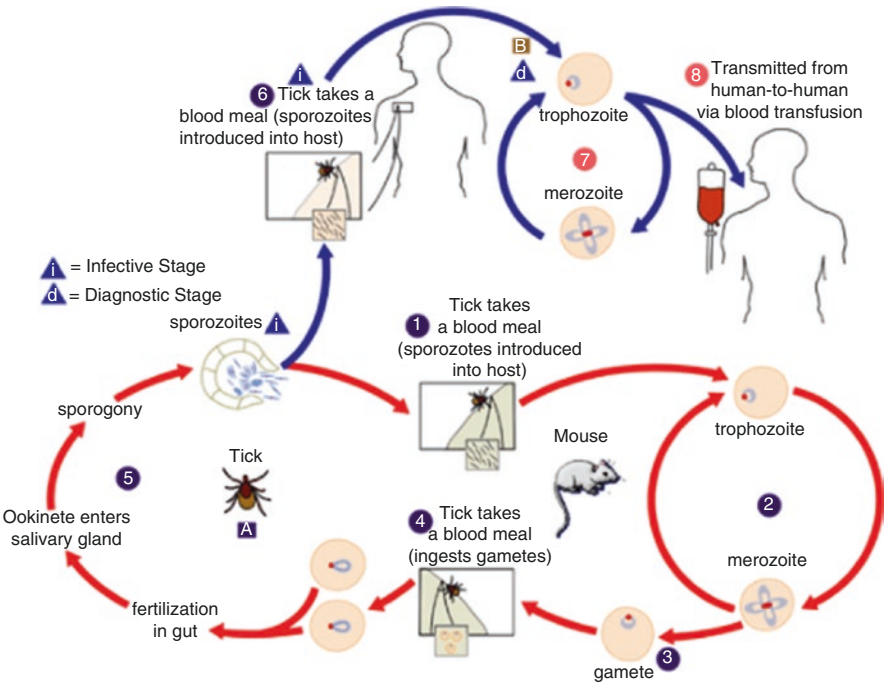


Fig. 6.3 Life cycle of *Babesia* (Reproduced from https://www.cdc.gov/dpdx/babesiosis/index.html)

In its life cycle, merogony takes place in the vertebrate host and sporogony in the invertebrate host. Man acquires infection by bite of the infected ticks. Sporozoites present in the salivary glands of tick are introduced into human or other mammals. Sporozoites transform to trophozoites in the circulation, which then invade the RBCs and multiply asexually by binary fission. The organisms frequently occur in pairs or in tetrads. Trophozoites are released when erythrocytes rupture and invade new erythrocytes. It can be differentiated from malarial parasites by the absence of pigments in the infected RBCs. Female ticks become infected by feeding on the infected rodents' blood which contains gametocytes. In the digestive tract of tick, the gametocytes undergo sexual development to produce sporozoites which then migrate to the salivary glands. The sporozoite is the infective form for human. In humans, liver is not involved in the life cycle of *Babesia*. Gametocyte and schizont stages are not found in humans. Humans usually are dead-end hosts. However, human-to-human transmission is well recognized to occur via contaminated blood transfusions.

Pathogenesis and Clinical Features

Haemolysis of the infected erythrocytes is primarily responsible for many clinical manifestations. The infection may be subclinical, self-limiting or acute, resembling malaria. In acute disease, there is malaise, fatigue, fever, headache, chills, sweating, myalgia, arthralgia and anorexia. Fever shows no periodicity. Mild hepatosplenomegaly and haemolytic anaemia have been reported. Severe babesiosis is associated with high parasitaemia. Fatality rate is higher among immunocompromised patients. Complications of acute babesiosis are renal failure, disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS) and congestive cardiac failure (CCF).

Diagnosis

1. *Microscopic examination*
   Absence of schizonts and gametocytes and presence of tetrads (maltese cross) in peripheral blood smear.
2. *Molecular diagnosis*
   PCR on blood.
3. *Serodiagnosis*
   There are no serologic kits available.
4. *Animal inoculation*
   Blood from suspected cases are inoculated into hamsters to be examined later for infected RBCs.

Treatment

Babesia microti infection is often mild and self-limiting. Most of the patients recover with only symptomatic care and do not require treatment. In acute cases, chemotherapy is required for at least 7–10 days. Atovaquone (750 mg orally twice a day) in combination with azithromycin (total dose in the range of 500–1000 mg orally on day 1; on subsequent days, a total daily dose in the range of 250–1000 mg) is effective. Alternatively, combination of clindamycin with quinine may be given. In fulminant cases, exchange transfusion is recommended.

Prevention and Control

1. Protective clothing when going into tick infested areas
2. Tick repellents
3. Individuals with history of symptomatic babesiosis should be prevented from donating blood

Coccidia

7

Toxoplasma gondii

Distribution

Toxoplasma gondii is cosmopolitan in distribution, with the widest range of hosts ranging from birds and warm-blooded animals including humans.

Habitat

In human, the parasites are found in the tissue, commonly in the musculoskeletal, brain and eye.

Morphology

Toxoplasma gondii is an obligate intracellular coccidian parasite and it occurs in 3 forms:

1. Oocyst
2. Tachyzoite
3. Tissue cyst

All 3 forms occur in cat which is the definitive host. Tachyzoites and tissue cysts are present in the intermediate hosts (other animals including humans). All the 3 forms are infectious to human.

Oocysts develop only in the intestine of cat. It is oval in shape and measures 10–12 μm in diameter. The oocysts are formed by sexual reproduction (gametogony). Cats shed millions of oocysts per day in faeces for about 2 weeks during the primary infection. The freshly passed oocysts are not infectious. They undergo

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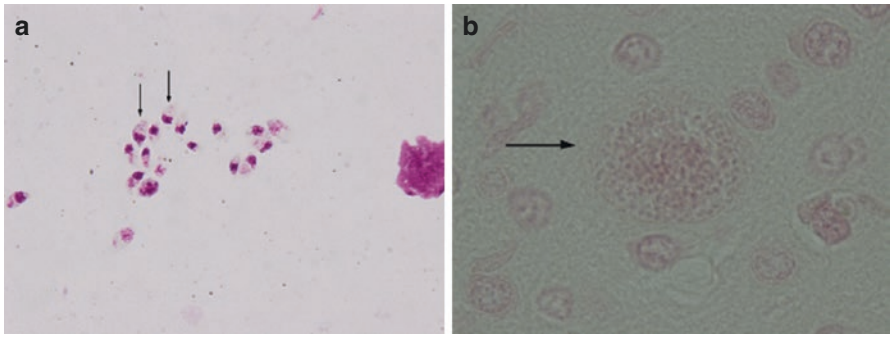


Fig. 7.1 *Toxoplasma gondii.* (**a**) Zoites, (**b**) Tissue cyst

sporulation in the soil with formation of 2 sporocysts, each containing 4 sporozoites. The sporulated oocyst is infective. Oocyst is very resistant to environmental conditions and can remain infective in soil for about a year. When the infective oocyst is ingested, it releases sporozoites in the intestine, which initiates infection.

The zoite is crescent shaped, with one end pointed and the other end rounded (Fig. 7.1a). It measures 3–7 μm in length. The nucleus is situated at the round end of the parasite. It can invade any nucleated cell and multiply by a process called endodyogeny (internal budding). The rapidly proliferating zoites in acute infection are called tachyzoites. The tachyzoites are susceptible to drying, freeze thawing and gastric digestion.

Tissue cyst is the dormant form of the parasite (Fig. 7.1b). Tissue cysts are found during chronic stage of the infection in the brain, eye, skeletal muscles and other organs. The slowly multiplying parasites within the cyst are called bradyzoites. The cyst is round or oval, 10–20 μm in size and contains numerous bradyzoites. When raw or undercooked meat containing the cysts is ingested, infection occurs. The cyst wall is destroyed by gastric digestion and zoites which are released initiate infection by invading intestinal epithelial cells. The zoites reach various tissues and organs through blood and lymphatic dissemination and form tissue cysts. Cysts are susceptible to freezing, thawing and heat above 60 °C.

Life Cycle (Fig. 7.2)

(*1*) Oocysts are passed out in faeces of cat. (*2*) The oocysts are ingested by rodents and follow the life cycle to (*3*) form tissue cysts. (*4*) The definitive host (cat) ingests tissue cyst present in intermediate host. (*5*) The oocysts ingested by other intermediate hosts (e.g. sheep and pig) will follow the life cycle and become tissue cysts. (*6*) Humans acquire infection when they ingest uncooked meat containing tissue cysts or ingestion of oocysts via (*7*) drinking contaminated water or eating unwashed fruits and vegetables. (*8*) Humans can also acquire infection via blood transfusion, (*9-10*) organ transplant or (*11*) congenital infection.

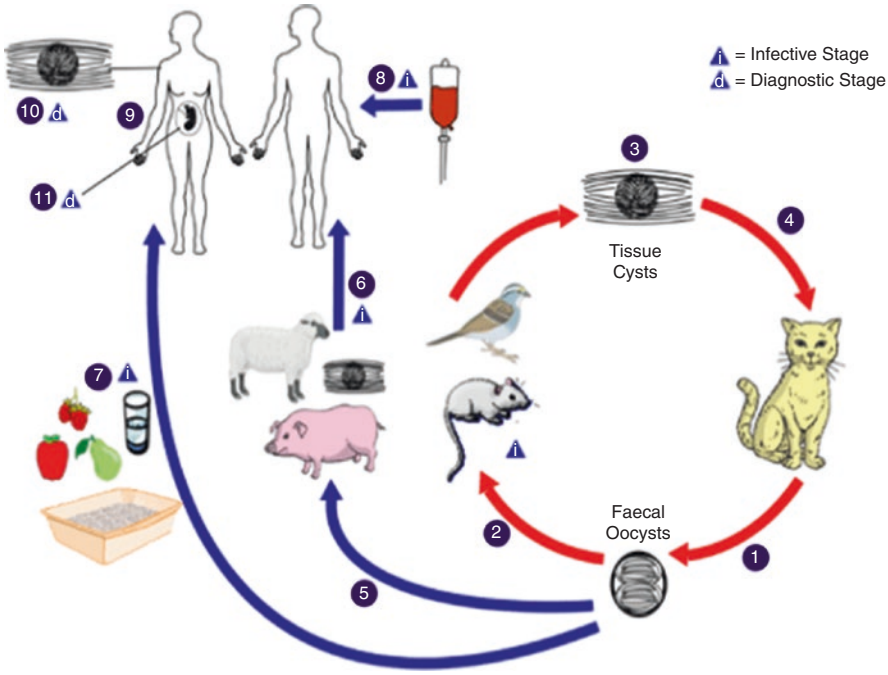


Fig. 7.2 Life cycle of *Toxoplasma gondii* (Reproduced from https://www.cdc.gov/dpdx/toxoplasmosis/index.html)

Toxoplasma gondii completes its life cycle in 2 hosts. Definitive host is where both sexual and asexual cycles takes place. In the intermediate hosts, only asexual cycle occurs. Modes of transmission to human are by eating uncooked or undercooked infected meat containing tissue cysts, ingestion of infective oocysts (through food, water or fingers contaminated with oocysts), intrauterine infection from mother to foetus (congenital toxoplasmosis) and blood transfusion or organ transplantation from infected donors.

Both sexual reproduction (gametogony) and asexual reproduction (schizogony) occur within the epithelial cells of the small intestine of the cat. Cat acquires infection by ingestion of tissue cysts in rats and other animals or by ingestion of oocysts passed in its faeces. The zoites released in the small intestine undergo asexual multiplication (schizogony) leading to formation of merozoites. Some merozoites are carried to extraintestinal tissues or organs and form tissue cysts. Some merozoites transform into male and female gametocytes and initiate sexual cycle (gametogony) with the formation of microgamete and macrogamete. A macrogamete is fertilized by motile microgamete and develops into oocyst which sporulates in the soil after being excreted in faeces of cat. An oocyst with 8 sporozoites is the infective form.

In humans, after ingestion of oocysts or tissue cyst, sporozoites from oocyst and bradyzoites from tissue cysts enter the intestinal mucosa and multiply asexually by endodyogeny to form tachyzoites. Tachyzoites are carried to other extraintestinal organs via circulation to form tissue cysts. Cysts are formed in many organs

particularly in muscles and brain as a response to developing host immunity. The dormant bradyzoites inside the cyst may be reactivated in immunosuppressed patients causing clinical illness.

Pathogenesis and Clinical Features

Toxoplasma gondii is an opportunistic parasite. Most human infections are asymptomatic. Clinical toxoplasmosis may be congenital or acquired and the manifestations depend on the immune status of the infected person. Toxoplasmosis may cause fatal complications in AIDS patients.

Congenital toxoplasmosis occurs when *T. gondii* is transmitted transplacentally from mother with primary *Toxoplasma* infection to foetus. The risk of foetal infection increases with the progress of pregnancy and severity of foetal damage is highest when infection is transmitted in the first trimester of pregnancy. Most infected newborns are asymptomatic at birth and may remain so throughout. Some develop clinical manifestations of toxoplasmosis weeks, months and even years after birth. The manifestations of congenital toxoplasmosis include chorioretinitis, intracerebral calcifications, psychomotor disturbances and hydrocephalus.

Acquired toxoplasmosis is mostly asymptomatic. The most common manifestations of acute acquired toxoplasmosis are cervical lymphadenopathy, fever, headache, myalgia and splenomegaly. The illness may resemble viral infection and is self-limiting. Rarely but some may present with pneumonitis, myocarditis and meningoencephalitis which can be fatal.

Toxoplasmosis in immunocompromised patients may be due to reactivation of chronic or latent infection. Involvement of the brain is most common, causing toxoplasmic encephalitis. Symptoms may include headache, confusion, ataxia, hemiparesis and seizures.

Immunity

Host defence against *Toxoplasma* infection involves both humoral and cellular responses. *Toxoplasma* infection in healthy adults is asymptomatic because of effective protective immunity involving extracellular antibodies and intracellular T-cell factors.

Diagnosis

1. *Serodiagnosis* (routine laboratory diagnostic method)

   Diagnosis of infection with *T. gondii* can be made by detection of the presence of IgM and IgG antibodies. Tests for detecting antibodies include:

   - Enzyme linked immunosorbent assay (ELISA)
   - Indirect fluorescent antibody test (IFAT)

- Latex agglutination test
- Sabin Feldman dye test (Gold standard). This is not carried out as a routine test because it involves use of live zoites which are maintained in culture.

IgM appears first about 1–2 weeks after infection. It peaks at about 8 weeks. IgG appears after IgM, typically reaching maximal levels at about 4 months, then declines to a lower level over the next 12–24 months. IgG persists for decades.

Toxoplasma IgG avidity testing was developed to help discriminate between past and recently acquired infections. High avidity IgG antibodies indicate past infection. Low avidity IgG antibodies indicate recent infection. This test is useful in pregnancy to establish timing of the infection for management of the pregnancy.

2. *Molecular diagnosis*
   PCR on blood, CSF or amniotic fluid samples.
3. *Microscopic examination*
   Giemsa-stained impression smears of lymph nodes, bone marrow, spleen or brain may occasionally show the trophozoites. Tissue sections may show the cyst form.
4. *Animal inoculation and cell cultures*
5. *CT scan*
   To detect lesions in the brain.

Treatment

Only symptomatic cases are treated. Combination drugs of choice are pyrimethamine (25–50 mg daily for 1 month) and sulfadiazine (2–6 g daily for 1 month) with folinic acid to prevent bone marrow suppression. Pyrimethamine is teratogenic. Pregnant mother in first trimester can be given spiramycin in replacement of pyrimethamine. For congenital toxoplasmosis, daily oral pyrimethamine and sulfadiazine with folinic acid are given for 1 year. Systemic corticosteroid may be added to reduce chorioretinitis.

Patients with ocular toxoplasmosis are treated for 1 month with pyrimethamine plus either sulfadiazine or clindamycin.

AIDS patients who are seropositive for *T. gondii* and have a CD4+ T lymphocyte count below <100/μL, should receive primary prophylaxis against toxoplasmic encephalitis. Trimethoprim-sulfamethoxazole (Bactrim) (160 mg trimethoprim; 800 mg sulfamethoxazole orally once daily) is the drug of choice. If trimethoprim-sulfamethoxazole cannot be tolerated by patients, dapsone-pyrimethamine is the recommended alternative drug of choice. Prophylaxis against toxoplasmic encephalitis should be discontinued in patients who have responded to anti-retroviral therapy (ART) and whose CD4+ T lymphocyte count is above 200/μL for 3 months.

Prevention and Control

1. Individuals at risk, particularly pregnant women, children and immunocompromised persons should avoid contact with cat and its faeces
2. Proper cooking of meat
3. Proper washing of hands, washing of vegetables and fruits before eating
4. Screening for *T. gondii* antibody on all blood donors
5. Pet cats should be fed with canned or cooked food
6. Cats' faeces should be discarded daily

Currently, there is no effective vaccine available for humans.

Cystoisospora belli (Formerly Known as *Isospora belli)*

Distribution

It is more common in tropical and subtropical countries. *Cystoisospora belli* is a coccidian parasite which causes diarrhoea in humans.

Habitat

In human, the parasites reside in the epithelial cells of the small intestine.

Morphology

Oocysts of *C. belli* are elongated, ovoid and measure 25 μm × 15 μm. Each oocyst is surrounded by a thin smooth cyst wall (Fig. 7.3). Immature oocyst seen in the faeces of patients contains 2 sporoblasts. On maturation, the sporoblasts become sporocysts. Each sporocyst contains 4 sporozoites. The sporulated oocyst is the infective stage of the parasite.

Life Cycle (Fig. 7.4)

(*1*) Unsporulated oocysts are passed out in faeces of infected person. (*2*) Humans acquire infection by ingesting the mature oocysts containing sporozoites via contaminated food or water. (*3*) The mature oocyst ruptures in the intestine releasing 8 sporozoites which invade the intestinal epithelial cells. (*4*) In the epithelium, the sporozoites transform into trophozoites, which multiply asexually (schizogony) to produce merozoites. The merozoites invade adjacent epithelial cells to repeat the asexual cycle. (*5*) Some of the trophozoites undergo sexual cycle

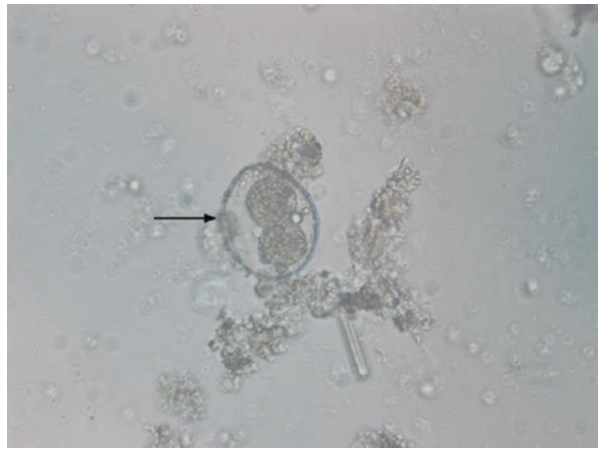


Fig. 7.3 *Cystoisospora belli* oocyst

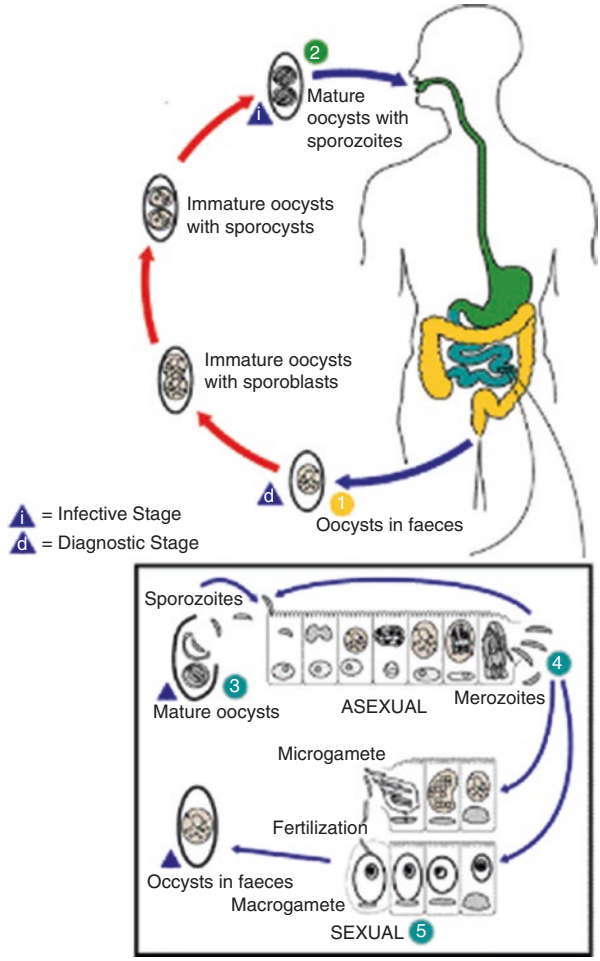


Fig. 7.4 Life cycle of *Cystoisospora belli* (Reproduced from https://www.cdc.gov/dpdx/cystoisosporiasis/index.html)

(gametogony) in the cytoplasm of enterocytes and transform into macrogametocytes and microgametocytes. After fertilization, a zygote is formed and develops into an immature oocyst. These immature oocysts are excreted with faeces and mature in the soil

Cystoisospora belli completes its life cycle in 1 host. Incubation period ranges from 1 to 4 days.

Pathogenesis and Clinical Features

Once mature *C. belli* oocysts are ingested, they liberate sporozoites which invade the enterocytes of the proximal small intestine. They become trophozoites, and asexual multiplication (schizogony) produces merozoites which invade other uninfected cells.

Infection is usually asymptomatic. Clinical illness includes abdominal discomfort, mild fever, diarrhoea and malabsorption. Diarrhoea is usually watery with no blood or pus and is self-limiting. Protracted diarrhoea can be seen in immunocompromised persons, particularly in HIV patients.

Diagnosis

1. *Microscopic examination*
   To detect the oocysts in saline preparation of stool. Stool concentration technique may be required when direct wet mount is negative. The staining technique used is modified Ziehl Neelsen stain or Kinyoun acid fast. Pink-coloured acid fast oocyst can be demonstrated. Samples from duodenal aspirates and intestinal biopsy can also be obtained for diagnosis.
2. *Molecular diagnosis*
   PCR of the stool sample.

Treatment

Infection is self-limiting, hence, no treatment is indicated in immunocompetent persons. Immunosuppressed patients with diarrhoea are treated with co-trimoxazole (160 mg trimethoprim/800 mg sulfamethoxazole orally or i.v. 4 times/day for 10 days). Relapses can occur in persons with AIDS and co-trimoxazole is given for maintenance therapy.

Prevention and Control

1. Proper faecal disposal
2. Personal hygiene

3. Boiling of drinking water
4. Filtration of drinking water
5. Wash fruits and vegetables with clean water before eating
6. Health education

Cryptosporidium parvum

Distribution

It has a ubiquitous distribution. Two species, *Cryptosporidium hominis* (humans are the only natural host) and *C. parvum* (infects various species of mammals) can cause human infections. *Cryptosporidium* causes intractable diarrhoea in AIDS patients and immunocompromised persons.

Habitat

Cryptosporidium parvum inhabits the small intestine. It may also be found in stomach, large intestine and lungs.

Morphology

The infective form is the thick-walled oocyst. The oocyst is small, spherical, or oval and measures about 4–6 μm in diameter (Fig. 7.5). Oocysts do not stain with iodine and is acid fast. Some oocysts have thin wall, and they are responsible for autoinfection. Oocysts contain 4 crescent shaped sporozoites and can remain viable in the environment for prolonged period and resistant to most disinfectants and temperature up to 60 °C. It can survive chlorinated water, but application of ozone is effective in killing the oocysts.

Life Cycle (Fig. 7.6)

(*1*) Thick-walled sporulated oocysts are passed out in faeces of infected host. (*2–3*) Humans acquire infection via ingestion of contaminated water and food.

The parasite completes its life cycle, sexual and asexual phases in a single host. Besides humans, the parasite can infect other animals. Reservoir hosts include mammals, birds and reptiles. Sporulated oocyst is the infective stage to humans. Mode of transmission is through ingestion of food and water contaminated with oocysts or by direct contact with infected animals.

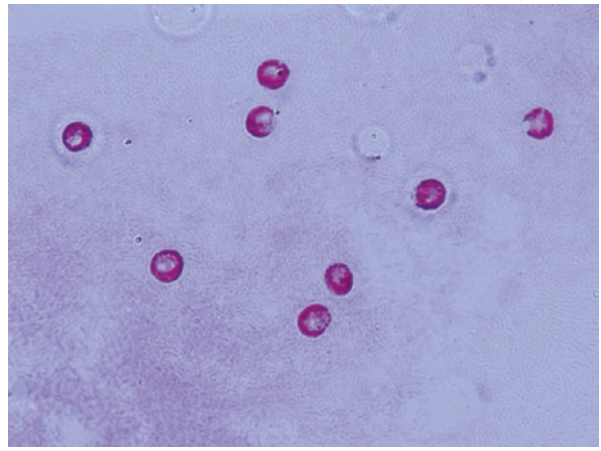


Fig. 7.5 *Cryptosporidium parvum* oocysts

Pathogenesis and Clinical Features

Clinical manifestations of cryptosporidiosis depend on the immune status of the host. Infection in immunocompetent persons may be asymptomatic or cause self-limiting watery diarrhoea, nausea, abdominal cramping and weight loss. It can also cause traveller's diarrhoea, as well as waterborne outbreaks. In immunocompromised hosts and AIDS patients, diarrhoea can be profuse, chronic and persistent causing severe fluid and electrolyte depletion and weight loss. The small intestine may show villous atrophy, crypt hyperplasia and lymphocyte infiltration. Incubation period is 2–14 days.

Diagnosis

1. *Microscopic examination*
   Diagnosis is made by the detection of oocysts in faeces. Stool concentration methods facilitate detection of oocysts. The oocysts are small and difficult to visualize in unstained wet preparations. Modified acid fast Ziehl Neelsen staining is the method of choice and oocysts appear as pink spheres. Definitive identification can be made by indirect immunofluorescence microscopy using specific antibody.
2. *Molecular diagnosis*
   PCR on stool sample.
3. *Antigen detection test*
   Enzyme immunoassays for detection of *Cryptosporidium* antigens in stool samples.
4. *Biopsy*
   Histopathological examination of biopsied small bowel specimen.

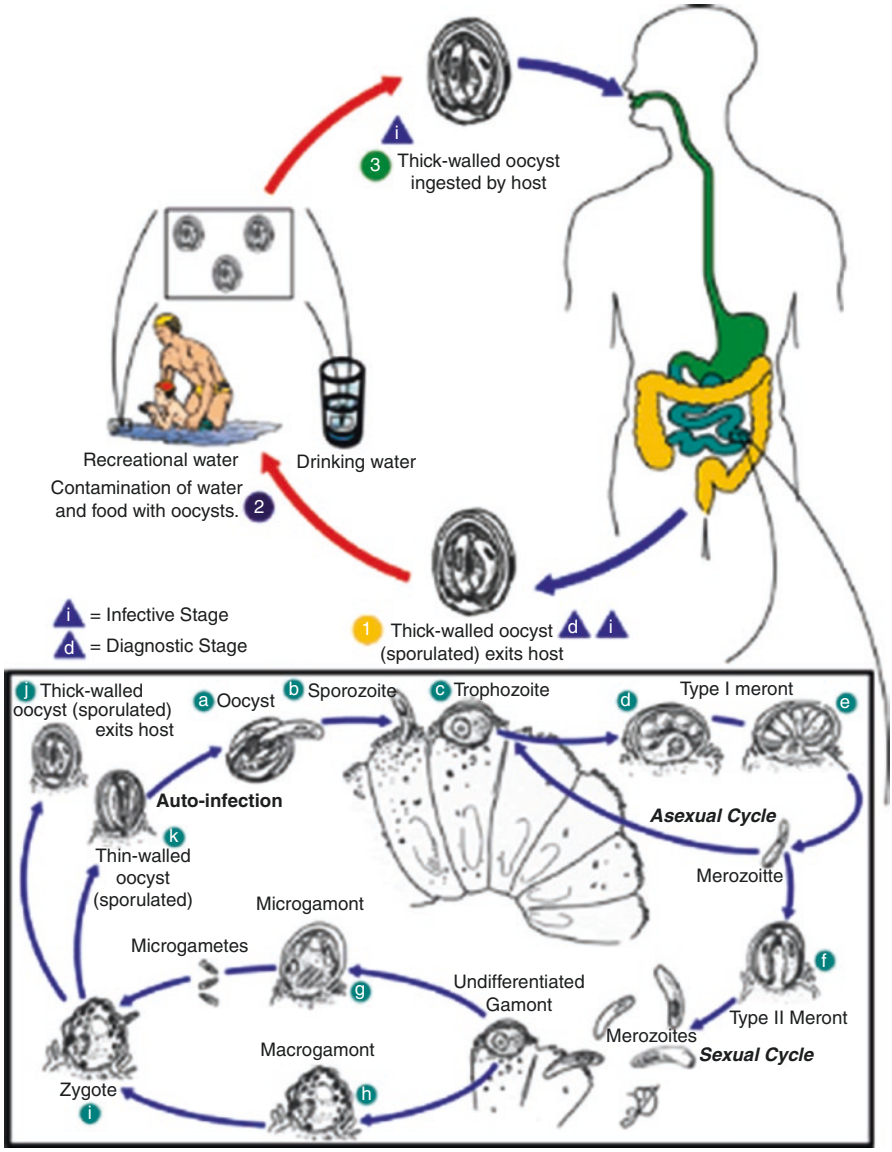


Fig. 7.6 Life cycle of *Cryptosporidium parvum* (Reproduced from https://www.cdc.gov/dpdx/cryptosporidiosis/index.html)

Treatment

There is no effective treatment for cryptosporidiosis. Nitazoxanide (500 mg twice/day for 3 days) or paromomycin may be effective in AIDS patients. Anti-retroviral therapy (ART) improves cryptosporidiosis by increasing the host's immune status. Supportive therapy includes fluid, electrolytes and nutrient replacement.

Prevention and Control

1. Proper faecal disposal
2. Personal hygiene
3. Boiling of drinking water
4. Filtration of drinking water
5. Wash fruits and vegetables with clean water before eating
6. Health education

Cyclospora cayetanensis

Distribution

It was first reported from Nepal, where it caused outbreaks of prolonged diarrhoea. It is most common in tropical and subtropical areas.

Habitat

In human, the parasite is present in the small intestine.

Morphology

Sporulated oocyst is the infective form to humans. The oocyst measures 8–10 μm in diameter. It contains 2 sporocysts and each sporocyst contains 2 sporozoites.

Life Cycle (Fig. 7.7)

(*1*) Excretion of unsporulated oocysts in stool of infected humans. (*2–3*) Oocysts contaminate and sporulate in the environment. (*4*) Sporulated oocysts enter the food chain. (*5*) Human acquires infection by ingestion of food and water contaminated with oocysts. (*6*) Excystation of the sporocyst releases sporozoites which infect enterocytes of the small intestine where sexual and asexual phases occur. (*7*) After the sexual phase, unsporulated oocysts develop and are excreted in faeces.

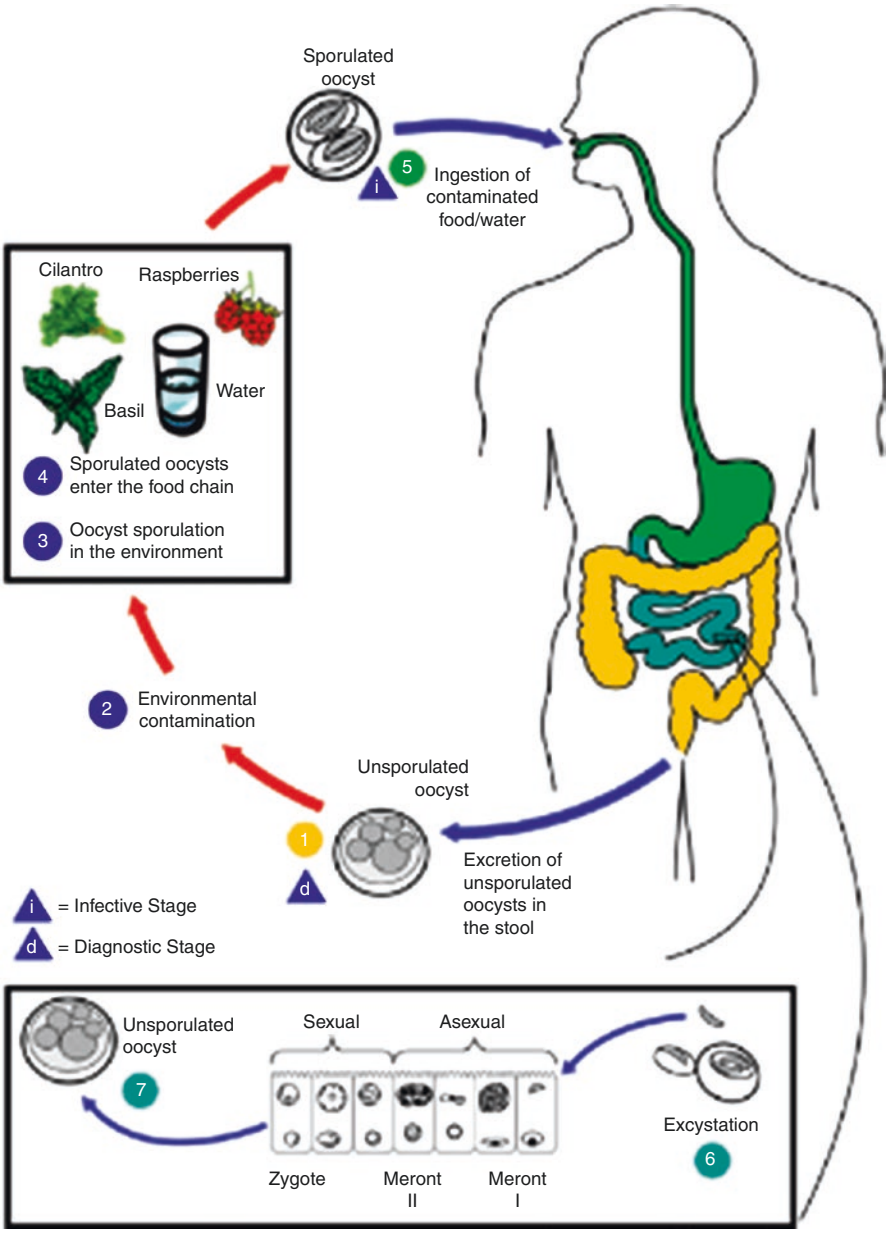


Fig. 7.7 Life cycle of *Cyclospora cayetanensis* (Reproduced from https://www.cdc.gov/dpdx/cyclosporiasis/index.html)

Pathogenesis and Clinical Features

Infection is through faecal oral route by ingestion of contaminated water and vegetables. Enterocytes show features of acute and chronic inflammation with blunting and atrophy of villi and hyperplasia of crypts. It causes prolonged diarrhoea with abdominal pain, low-grade fever and fatigue. The infection is more severe in immunocompromised hosts, especially AIDS patients. Incubation period is 1–7 days.

Diagnosis

1. *Microscopic examination*
   Direct wet mount to detect oocysts in faeces. Oocyst stains pink with Ziehl Neelsen.

2. *Biopsy*
   Histopathology examination of biopsied specimen from jejunum.

Treatment

Co-trimoxazole (160 mg trimethoprim/800 mg sulfamethoxazole twice/day for 7 days) is used for its treatment. Long term suppressive maintenance therapy is given to HIV-infected patients.

Prevention and Control

1. Proper faecal disposal
2. Personal hygiene
3. Boiling of drinking water
4. Filtration of drinking water
5. Wash fruits and vegetables with clean water before eating
6. Health education

Sarcocystis

Distribution

It is worldwide in distribution. The 3 species that can infect humans are *Sarcocystis hominis* (transmitted through cattle), *Sarcocystis suihominis* (transmitted through pig) and *Sarcocystis lindemanni* (unknown mode of transmission).

Habitat

When human is the intermediate host, sarcocysts are found in the striated muscles. When human is the definitive host, oocysts are found in stools.

Morphology

The sporocysts of *S. hominis* measure 13.1 to 17.0 by 7.7 to 10.8 μm. Sporocysts of *S. suihominis* measure 11.6 to 13.9 by 10.1 to 10.8 μm. Four sporozoites can be found within each sporocyst.

Life Cycle (Fig. 7.8)

(*1*) Oocysts (fully developed) and sporocysts are shed in human faeces, which contaminate grass and are ingested by cows and pigs. In the intermediate hosts, the sporocyst ruptures and releases sporozoites which invade the intestinal mucosa and reaches the vascular endothelial walls, where they undergo schizogony producing merozoites. These are carried to muscle fibres and develop into sarcocysts. Cattle is the intermediate host for *S. hominis* and pig is the intermediate host for *S. suihominis*. (*2*) Human infection is acquired by ingesting raw or undercooked beef or pork containing sarcocyst. (*3–5*) When sarcocyst is ingested by human (the definitive host), the merozoites are released in the intestine, and enter intestinal cells where they develop into male and female gametes. (*6*) After fertilization, the zygote develops into an oocyst containing 2 sporocysts, each having 4 sporozoites. (*7*) These oocysts are shed in faeces and are ingested by intermediate host.

Human is the intermediate host in *S. lindemanni*; the definitive host is unknown. Human acquires infection by ingestion of oocysts. Sarcocysts develop in the striated muscles of human.

Pathogenesis and Clinical Features

Intestinal sarcocystosis is usually mild. Patients may have nausea, abdominal pain and diarrhoea. Muscular sarcocystosis is usually asymptomatic but in some cases, the early phase of infection may cause fever, eosinophilia, muscle pain, weakness or myositis.

Diagnosis

1. Intestinal sarcocystosis
   (a) *Microscopic examination*
   To detect oocysts or sporocysts in faecal samples.

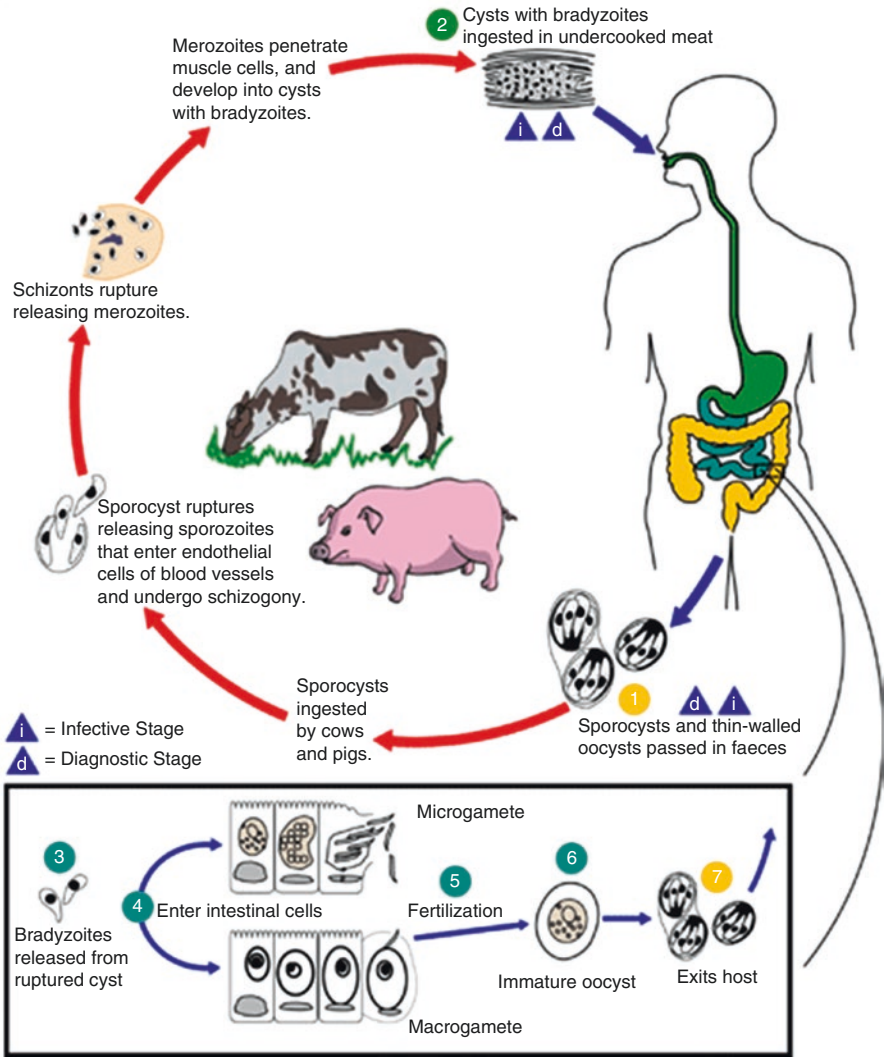


Fig. 7.8 Life cycle of *Sarcocystis* (Reproduced from https://www.cdc.gov/dpdx/sarcocystosis/index.html)

(b) *Molecular diagnosis*

PCR of stool specimen.

2. Muscular sarcocystosis

(a) *Biopsy/autopsy*

Histopathological examination to demonstrate sarcocysts in the striated muscles. PCR of biopsy/autopsy specimens.

(b) *Serodiagnosis*

Not commercially available for human infection.

Treatment

No specific treatment is available for sarcocystosis. For myositis, albendazole, metronidazole and co-trimoxazole have been used. Corticosteroids have been used for symptomatic relief.

Prevention and Control

1. Ingestion of cooked beef or pork
2. Freezing meat at −5 °C for several days will kill the sarcocysts
3. Boiling of drinking water

Other Intestinal Protozoa

Blastocystis hominis

Distribution
It is globally distributed.

Habitat
It is a protozoa found in the large intestine of humans, belonging to the Stramenopiles.

Morphology
Blastocystis hominis has 4 morphological forms:

1. Vacuolated form is usually seen in stool specimen. It measures 8 μm in diameter and is characterized by its large central vacuole, which pushes the cytoplasm and the nuclei to the periphery (Fig. 7.9). It multiplies by binary fission.
2. Amoeboid form is polymorphous, slightly larger than the vacuolated form and is occasionally seen in the faeces. It multiplies by sporulation.

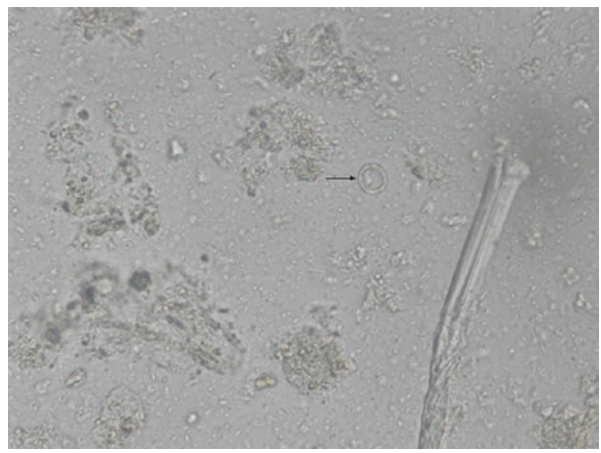


Fig. 7.9 *Blastocystis hominis* vacuolated form

3. Granular form measures 10–60 μm in diameter and is seen in old cultures.
4. Cystic form is generally smaller in size and has a thick multilayered cyst wall.

Life Cycle

Thick-walled cysts are passed out in the stool of infected human. Humans acquire infection via ingestion of contaminated water and food. In the intestine of human, the cyst ruptures and trophozoite undergoes asexual reproduction and the parasite may exist in vacuolar form or amoeboid form. The amoeboid form develops into the thick-walled cyst and is excreted in the faeces of the host.

The parasite completes its life cycle in a single host.

Pathogenesis and Clinical Features

Recent studies have shown the parasite to be associated with diarrhoea. Other clinical manifestations include abdominal pain, abdominal distension, nausea and vomiting. Pathogenicity has been shown to be subtype related. Many carriers are asymptomatic.

Diagnosis

1. *Microscopic examination*
   Demonstration of the organism in stool smear.
2. *Culture*
   In vitro culture in Jones medium.
3. *Molecular diagnosis*
   PCR on stool samples.

Treatment

If diarrhoea is present, metronidazole (250–750 mg orally 3 times/day for 10 days) can be given. Treatment should be considered when no other infectious agent can be identified.

Prevention and Control

1. Proper faecal disposal
2. Personal hygiene
3. Boiling of drinking water
4. Filtration of drinking water
5. Wash fruits and vegetables with clean water before eating
6. Health education

Microsporidia

8

Microsporidia

Distribution

Microsporidia have a wide host range which includes invertebrates and vertebrates. Microsporidia are being recognized as opportunistic infectious agents worldwide.

Habitat

In human, the organisms are found in intestinal epithelium (intracellular). Other sites of infection include cornea, biliary tract and muscle.

Morphology

Microsporidia are unicellular, obligate intracellular organism. They reproduce in host cells by producing spores (sporogony). Spores are 2–4 μm in size and oval to cylindrical in shape, with a polar filament or tubule (Fig. 8.1). The polar tubule is an extrusion mechanism for injecting infective spore contents into the host cell. Spores are surrounded by thick double-layered wall and are the infective stage of microsporidia.

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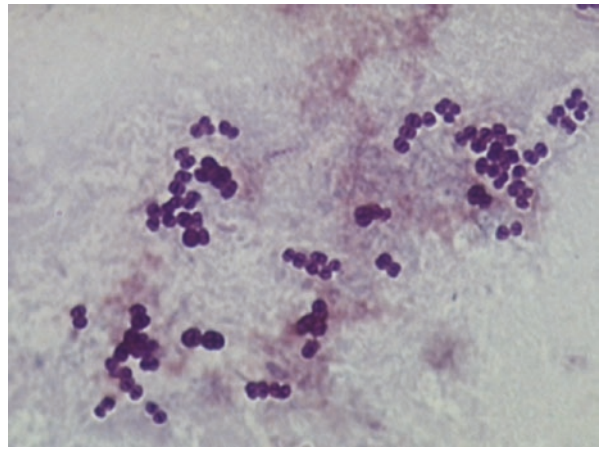


Fig. 8.1 Microsporidia spores (band is seen across the microsporidia spore stained with Gram Chromotrope Kinyoun)

Life Cycle (Fig. 8.2)

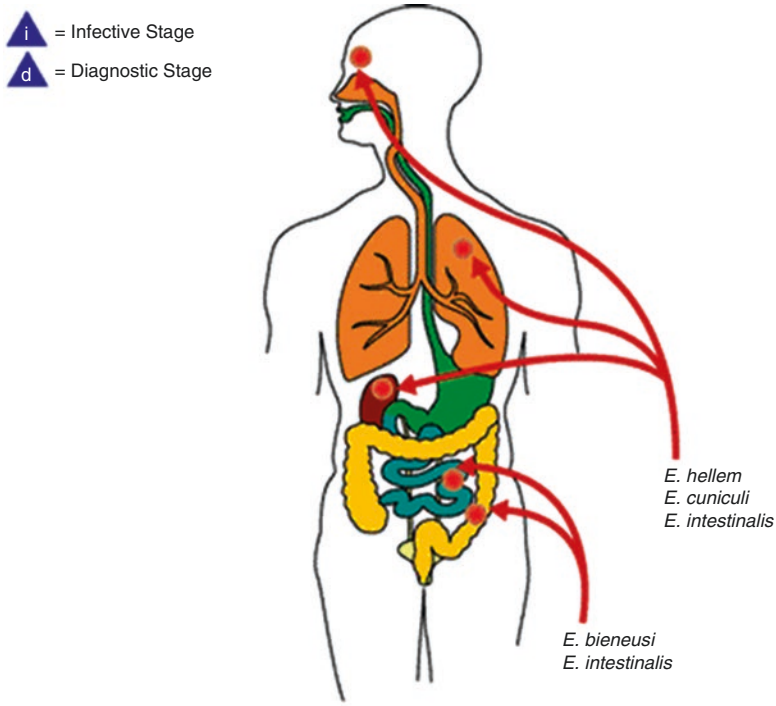
(*1*) Infection in host is acquired by ingestion or inhalation of spores. (*2–3*) In the duodenum, the spore with its nuclear material is injected through the polar tubule into the host cell. (*4–5*) Inside the cell, the microsporidia multiply by repeated binary fission and produce large number of spores. (*6*) The spores are then liberated free from the host cell and infect other cells.

Pathogenesis and Clinical Features

Microsporidia can cause a wide range of illness in patients with HIV, organ transplant recipient, and other immunocompromised diseases. In patients with AIDS, *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* cause protracted and debilitating diarrhoea. *E. intestinalis* may also cause sinusitis, cholangitis and bronchiolitis. Modes of transmission are foodborne, waterborne and zoonosis.

Diagnosis

1. *Microscopic examination*
   Diagnosis is made by detection of spores in stool or small intestine biopsy specimen. The spores can be stained with modified trichrome stain or Gram-chromotrope kinyoun. Although spores can be visualized by light microscopy, electron microscopy is the gold standard.
2. *Immunofluorescent method using monoclonal antibody*
   Detection of microsporidia in clinical samples.
3. *Molecular diagnosis*
   PCR on stool specimen.



Intracellular development of *E. bieneusi* and *E. intestinalis* spores.

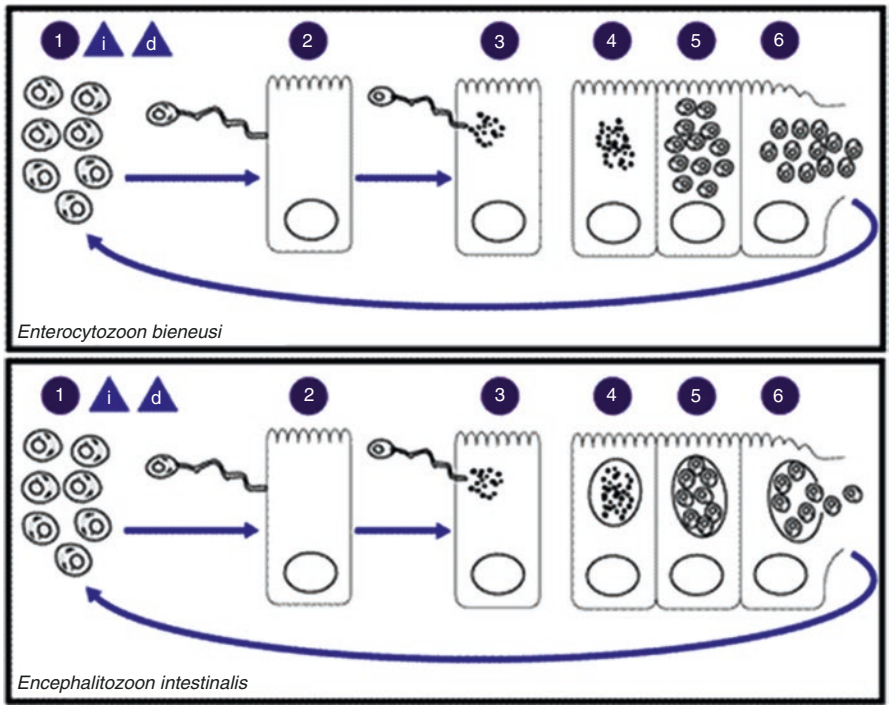


Fig. 8.2 Life cycle of microsporidia (Reproduced from https://www.cdc.gov/dpdx/microsporidiosis/index.html)

Treatment

There is no specific and effective drug for microsporidia. Intestinal microsporidiosis may be treated with albendazole (400 mg orally 3 times/day for 2 weeks or 400 mg twice/day for 1 month). HIV-infected patients are given anti-retroviral therapy (ART) to increase the host's immune status.

Prevention and Control

1. Improved personal hygiene and sanitation
2. Adequate water treatment
3. Initiation of combination ART

Ciliate

9

Balantidium coli

Distribution

It is distributed worldwide.

Habitat

Balantidium coli resides in the large intestine of humans, pigs and non-human primates.

Morphology

It is the largest intestinal protozoa of human. *Balantidium coli* exists in 2 stages—trophozoite and cyst.

The cyst is the infective stage of *B. coli.* It is spherical in shape, measuring 40–60 μm in diameter (Fig. 9.1a). It is surrounded by a thick double-layered wall. The cytoplasm is granular with presence of macronucleus, micronucleus and vacuoles. It is found in chronic cases and carriers.

The trophozoite is the invasive stage. It is large, ovoid, measuring about 60–70 μm in length and 40–50 μm in breadth (Fig. 9.1b). There is presence of short cilia over the entire surface of the body. Its anterior end is narrow and posterior end is broad. At the anterior end, there is a groove (peristome) advancing to the mouth (cytostome) and a short funnel-shaped gullet (cytopharynx). Posteriorly, there is a small anal pore (cytopyge). The trophozoite has 2 nuclei—a large kidney-shaped macronucleus and a small micronucleus. The cytoplasm has contractile vacuoles and food vacuoles.

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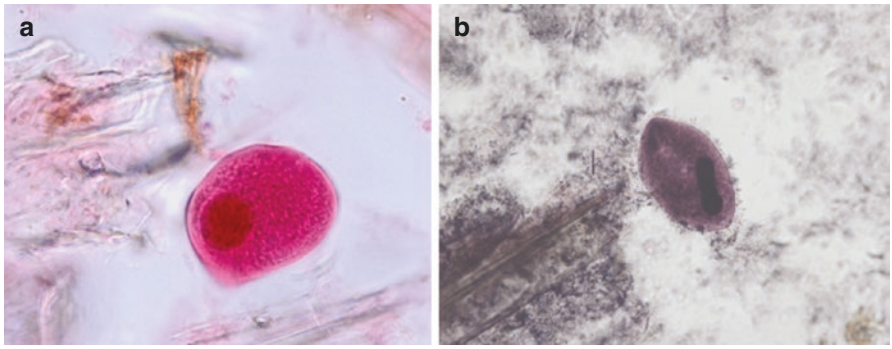


Fig 9.1 *Balantidium coli.* (**a**) Cyst, (**b**) Trophozoite

Life Cycle (Fig. 9.2)

(*1*) Cyst is passed out in the stool of infected human. (*2*) Humans acquire infection by ingesting cyst through contaminated food or water. (*3*) In the intestine, the cyst undergoes excystation to release trophozoite. (*4*) The trophozoites divide by binary fission. (*5*) It encysts as it passes down the colon and is excreted in faeces. Trophozoites can be found in loose stools.

Balantidium coli completes its life cycle in 1 host only. Infection is acquired from pigs and other animal reservoirs or from human carriers. Pig is its reservoir host. Balantidiasis is a zoonosis.

Pathogenesis and Clinical Features

Clinical disease results when the trophozoites burrow into the intestinal mucosa and initiate inflammatory reaction. This leads to mucosal ulcers, resembling lesions in amoebiasis. Unlike *E. histolytica, B. coli* infection does not involve extraintestinal sites.

Most infections are asymptomatic. Symptomatic disease resembles intestinal amoebiasis causing diarrhoea or dysentery with abdominal colic, nausea and vomiting. Occasionally, intestinal perforation and peritonitis may occur.

Diagnosis

1. *Microscopic examination*
   Detection of trophozoites and cysts in stool.
2. *Biopsy*
   When stool examination is negative, biopsy specimens and scrapings from intestinal ulcers can be examined for the presence of trophozoites.

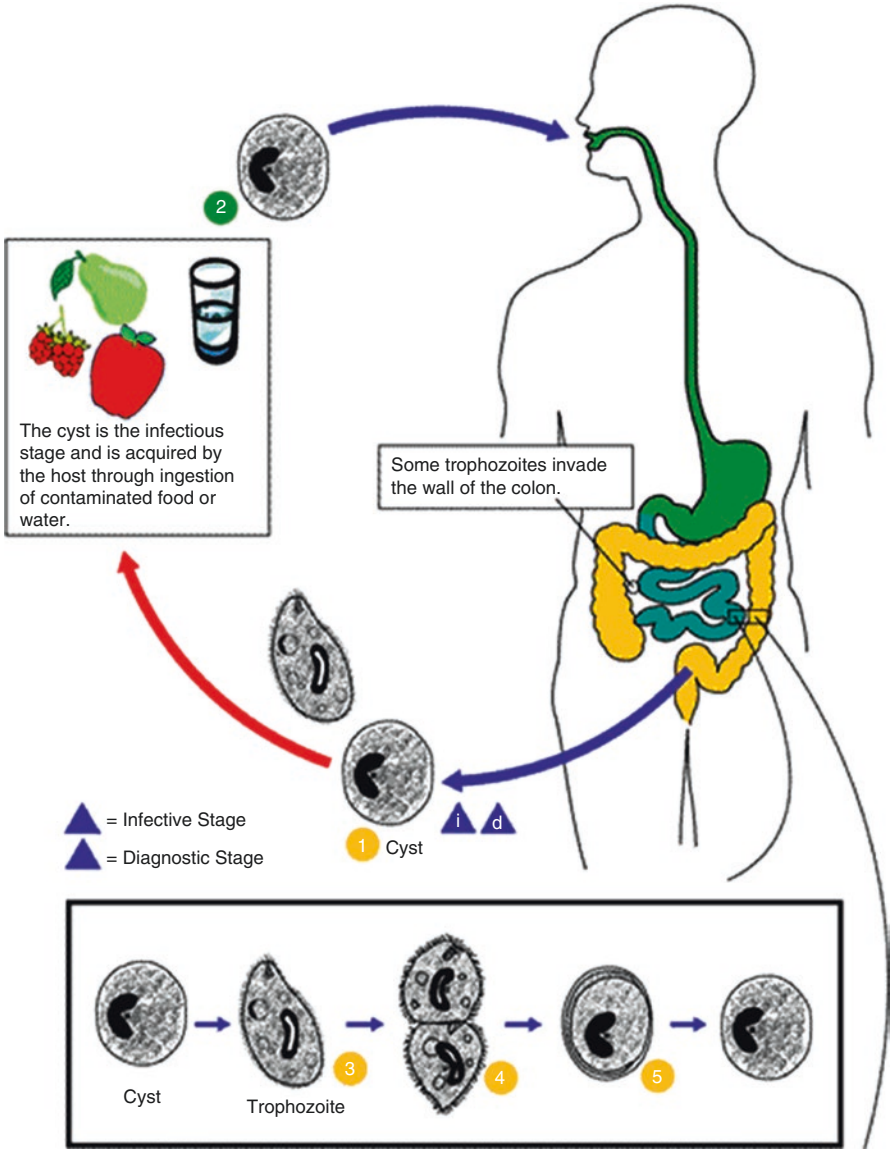


Fig. 9.2 Life cycle of *Balantidium coli* (Reproduced from https://www.cdc.gov/dpdx/balantidiasis/index.html)

Treatment

Tetracycline (500 mg orally 4 times/day for 10 days) is the drug of choice and doxycycline is an alternative drug. Metronidazole and nitroimidazole have been reported to be useful.

Prevention and Control

1. Boil drinking water and eat cooked food
2. Personal hygiene
3. Proper sanitation
4. Treat infected pigs
5. Treat positive cases

Nematodes: Roundworms

10

General Characteristics

Nematodes are cylindrical or filariform in shape and bilaterally symmetrical. The adults vary greatly in size, from a few millimetres to a metre long. Male is generally smaller than female and its posterior end is curved or coiled ventrally. Its body is covered with an outer cuticle. The middle layer is hypodermis and the inner layer is the somatic muscular layer. The nematodes have separate sexes. The male reproductive system consists of testis, vas deferens, seminal vesicle and ejaculatory duct, which opens into the cloaca. It also includes copulatory structures such as spicules or bursa or both. The female reproductive system consists of the ovary, oviduct, seminal receptacle, uterus and vagina. Female nematodes may produce eggs (oviparous), larvae (viviparous) or lay eggs containing larvae, which immediately hatch out (ovoviviparous).

Modes of infection are ingestion of infective eggs or encysted larvae in muscle. Eggs can also be inhaled and swallowed. Infection can occur via skin penetration by infective filariform larvae or transmitted by blood-sucking insects as seen in filarial worm infection. Classification of nematodes of medical importance based on habitat is shown in Table 10.1.

Intestinal Nematodes: Soil-Transmitted Helminths (STH)

Trichuris trichiura

Common name	Whipworm

Distribution

It is distributed globally but more common in the tropics and subtropics.

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Table 10.1 Classification of nematodes of medical importance based on habitat

Habitat of adult nematode	Nematode
Small intestine	1. *Ascaris lumbricoides* 2. *Strongyloides stercoralis* 3. Hookworm 4. *Trichinella spiralis*
Large intestine	1. *Trichuris trichiura* 2. *Enterobius vermicularis*
Lymphatic	1. *Wuchereria bancrofti* 2. *Brugia malayi*
Subcutaneous	1. *Loa loa* 2. *Onchocerca volvulus*

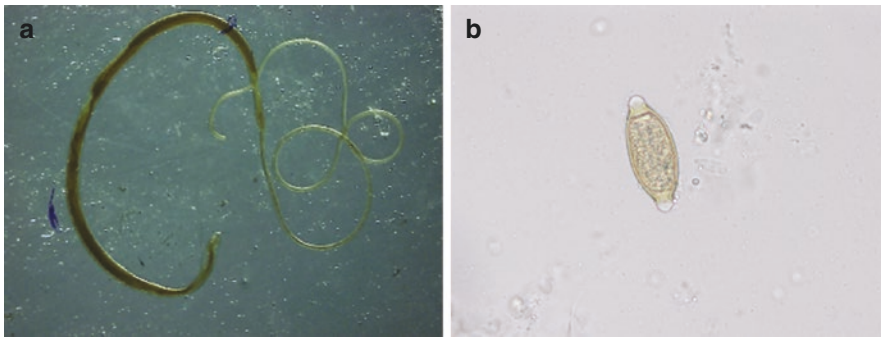


Fig. 10.1 *Trichuris trichiura.* (**a**) Adult, (**b**) Egg

Habitat

Trichuris trichiura lives in the large intestine, mainly in the caecum. The anterior part of the adult worm is found embedded in the mucosa of the large intestine and the posterior part is found hanging in the lumen.

Morphology

The adult male worm is 30–45 mm long, while the female is about 40–50 mm. The worm resembles a whip, with the anterior portion thin and thread-like and the posterior portion thick and fleshy (Fig. 10.1a). The anterior portion, which contains the oesophagus, is embedded in the mucosa. The posterior portion contains the intestines and reproductive organs. The posterior end of the male is coiled ventrally, while in the female it is straight and rounded. The worm has a lifespan of 5–10 years.

Its egg is barrel shaped measuring 50 μm long, with bipolar plugs containing an unsegmented ovum when passed in faeces (Fig. 10.1b). It is brown in colour due to bile-stain.

Life Cycle (Fig. 10.2)

(*1*) Unembryonated eggs are passed out in faeces of infected human. (*2*) In the soil, the egg develops into a two-cell stage. (*3*) It undergoes advanced cleavage. (*4*)

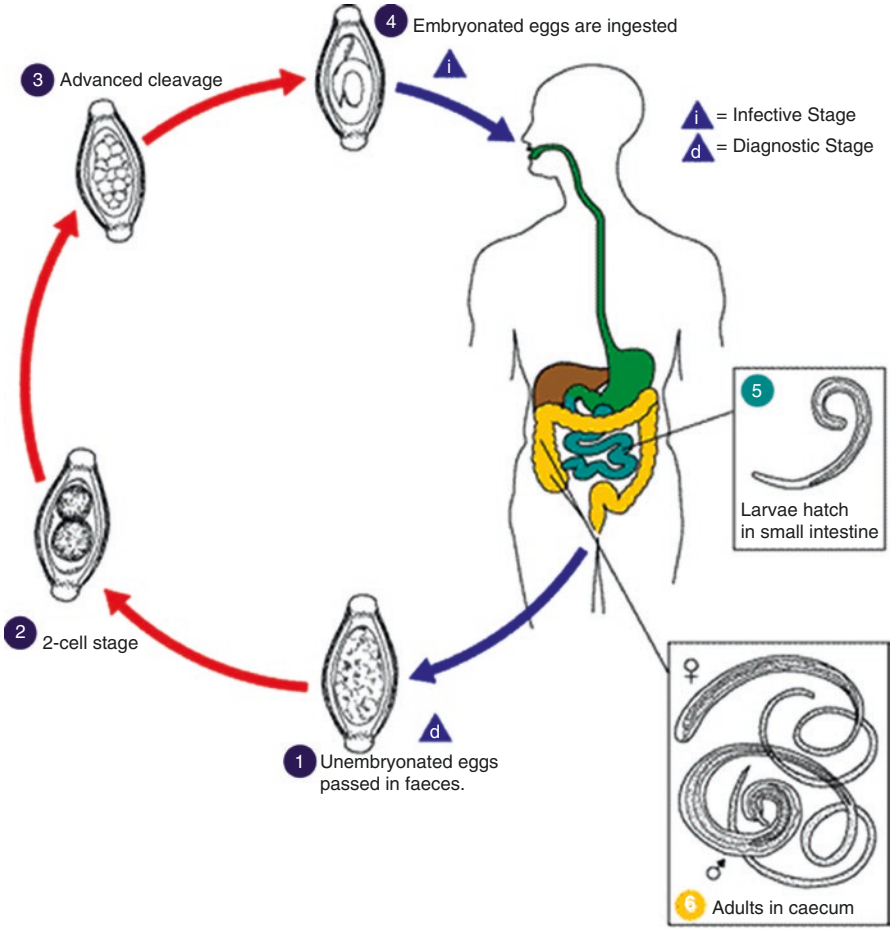


Fig. 10.2 Life cycle of *Trichuris trichiura* (Reproduced from https://www.cdc.gov/dpdx/trichuriasis/index.html)

Humans acquire infection by ingesting the embryonated eggs. (*5*) The egg hatches into larva in the intestine. (*6*) Larva matures into adult in about 2–3 months in the large intestine (caecum). Female worm produces eggs which are passed out in the faeces.

Human is its natural host. No intermediate host is required. The embryonated eggs are the infective stage to human.

Pathogenesis and Clinical Features

Infection with *T. trichiura* (trichuriasis) is usually asymptomatic, except in heavy infection. Blood may ooze out at the site of attachment of the anterior part of the

worm. It is not a blood feeder like hookworm. In heavy and chronic infections, iron deficiency anaemia may develop. Mechanical blockage of the appendix lumen by adult worms may cause acute appendicitis. The worm may be found even up to the rectum in heavy infection. In *Trichuris* dysentery syndrome (TDS), there is heavy colonic infection which causes mucoid diarrhoea, dysentery, rectal prolapse, iron deficiency anaemia and finger clubbing. Children with severe *T. trichiura* infection have growth retardation, impaired mental development and cognitive function.

Diagnosis

1. *Microscopic examination*
   Detection of the characteristic barrel-shaped eggs in stools.
2. *Sigmoidoscopy*
   Sigmoidoscopy is useful in severe infection as worms are found in the rectum.

Treatment

Mebendazole (100 mg orally twice/day for 3 days), albendazole (400 mg orally for 3 days), or ivermectin (200 μg/kg/day orally for 3 days).

Prevention and Control

1. Proper faecal disposal
2. Wash fruits and vegetables before consumption
3. Personal hygiene
4. Treatment of infected persons

Ascaris lumbricoides

Common name	Common roundworm

Distribution

It is distributed worldwide mainly in the tropics and subtropics.

Habitat

Adult worms live in the lumen of the small intestine.

Morphology

The adult *Ascaris* worms are large and cylindrical, with tapering ends (Fig. 10.3a). The adult male worm measures 15–30 cm in length. Its posterior end is curved with 2 copulatory spicules. The female worm measures 20–40 cm in length. Its posterior extremity is straight and conical. The vulva is situated mid-ventrally, near the junction of the anterior and middle thirds of the body. A groove (vulvar waist) is seen surrounding the worm at the vulvar opening and this is to facilitate mating.

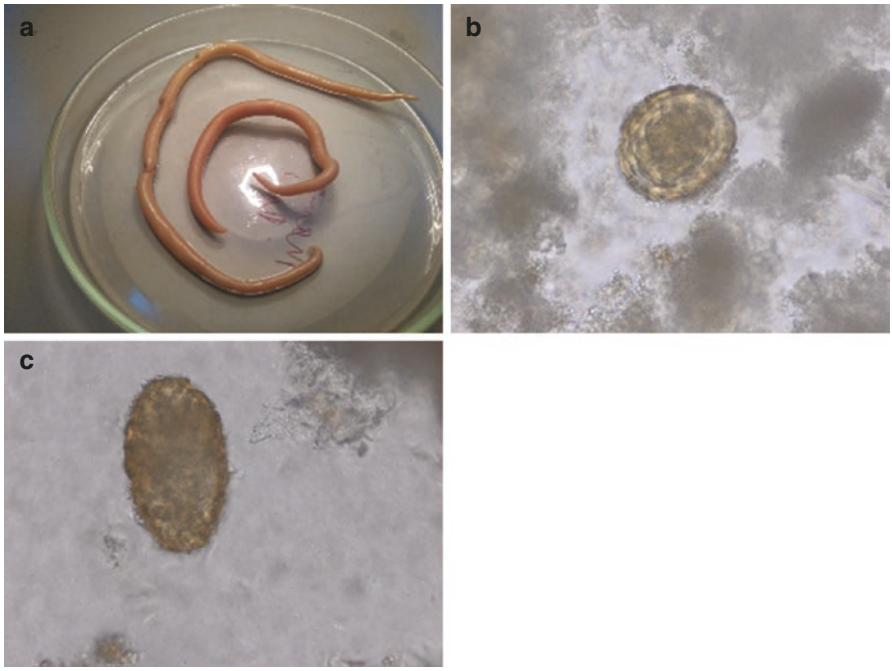


Fig 10.3 *Ascaris lumbricoides.* (**a**) Adults, (**b**) Fertilized egg, (**c**) Unfertilized egg

Two types of eggs are passed by the female worm; fertilized and unfertilized. The fertilized egg is spherical or ovoid, bile stained, measuring 60–75 μm in length with the ovum inside (Fig. 10.3b). The outer layer is coarsely mamillated. The unfertilized egg is longer, more elliptical with a thinner shell, measuring up to 90 μm and contains granules (Fig. 10.3c). It does not develop into the infective stage.

Life Cycle (Fig. 10.4)

(*1*) The adult male and female worms live in the lumen of the small intestine of human. (*2*) The female worm produces both fertilized and unfertilized eggs which are passed out in faeces. (*3*) In the soil, the fertilized egg undergoes development to the infective stage. (*4*) Human acquires infection via ingestion of the infective eggs. (*5*) In the intestine, the eggs hatch into larvae. (*6*) The larvae penetrate the mucosa of the small intestine and enter the portal circulation and are carried to the heart and lungs. (*7*) In the lungs, the larvae rupture out of the alveolar capillaries into the alveolar space and crawl up the bronchiole, bronchi, trachea and pharynx. They are swallowed back into the intestine where they develop into adults in about 3 months.

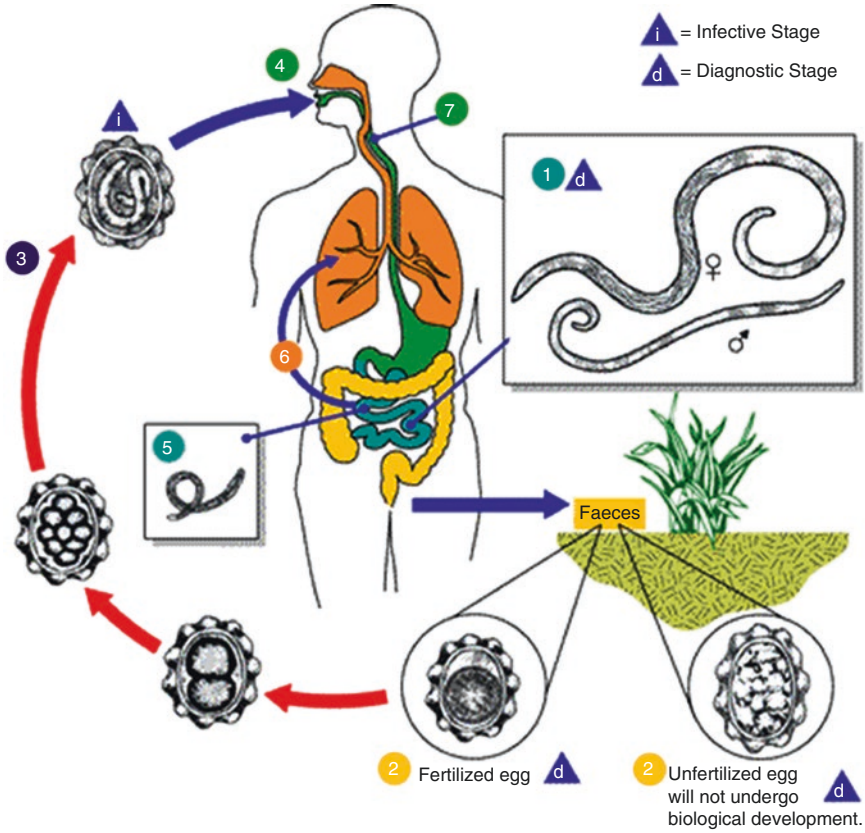


Fig. 10.4 Life cycle of *Ascaris lumbricoides* (Reproduced from https://www.cdc.gov/dpdx/ascariasis/index.html)

Pathogenesis and Clinical Features

Clinical manifestations of ascariasis are caused by the migrating larvae and the adult worms.

The larval migration causes allergic reaction. The initial exposure to larvae during the lung migration phase is usually asymptomatic, except when the larval load is heavy. When reinfection occurs, there may be infiltration of eosinophils and macrophages. Loeffler's syndrome is characterized by low-grade fever, cough, wheezing, dyspnoea, transient eosinophilia and chest X-ray may show lung infiltration. The sputum may contain Charcot-Leyden crystals and larvae. Loeffler's syndrome seen in ascariasis is also known as ascaris pneumonitis. The pulmonary clinical features subside in 1 or 2 weeks after infection.

Intestinal infection by adult worm is usually asymptomatic. The clinical features, if present, are due to nutritional and toxic effects. The nutritional effects are usually seen when there is heavy worm burden. The worms interfere with proper digestion and absorption of food. Ascariasis may contribute to protein-energy malnutrition and vitamin A deficiency. The toxic effects are due to hypersensitivity to the worm antigens and may be manifested as fever, urticarial and angioneurotic oedema. Ascariasis may cause complications due to mechanical effect. Masses of worms may cause intestinal obstruction. Ectopic migration is a complication of ascariasis due to a few factors, e.g. fever and worms seeking mates. The worm may migrate up or down along the intestine. It may block the biliary or pancreatic ducts causing acute biliary obstruction or pancreatitis. It may enter the liver parenchyma causing liver abscesses. The worm may go up the oesophagus and come out through the mouth or nose. It may obstruct the appendix causing appendicitis. It may lead to peritonitis when it perforates the intestine at weak spots such as typhoid or tuberculous ulcers or through suture lines.

Diagnosis

1. *Microscopic examination*
   Detection of eggs in faeces.
2. *Gross examination*
   The adult worm can occasionally be detected in stool.

Treatment

Pyrantel pamoate (11 mg/kg (maximum 1 g) orally once), albendazole (400 mg orally once), mebendazole (100 mg orally twice daily for 3 days or 500 mg orally once), or ivermectin (150–200 μg/kg orally once) can be used. These drugs are contraindicated in pregnancy except for pyrantel pamoate. Complete intestinal obstruction is a surgical emergency.

Prevention and Control

Same as for *T. trichiura*

Strongyloides stercoralis

Distribution

It is found mainly in the tropics, but may also occur in the temperate regions. Another species *S. fullerborni* is prevalent in African monkeys. It causes infection in pygmies in Africa and human infection in Papua New Guinea.

Habitat

The female adult worm is found embedded in the mucosa of the small intestine of human.

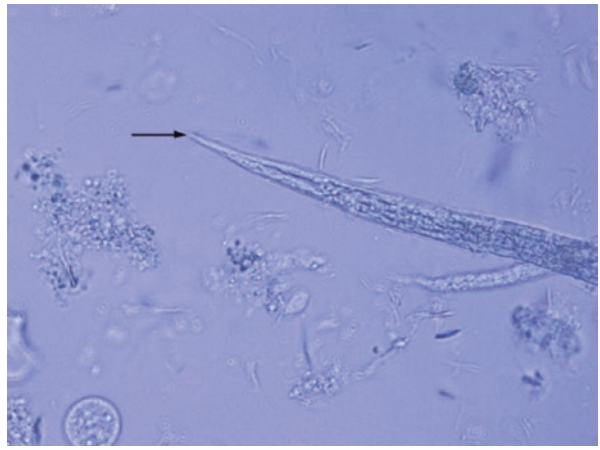


Fig. 10.5 *Strongyloides stercoralis*, notched tail of L3 stage

Morphology

This is the smallest intestinal nematode of human. The female worms live in the mucosa of the small intestine. It is thin, measuring about 2.5 mm long. The worm is parthenogenetic. It reproduces without the presence of a male worm. It is ovoviviparous. The worm causes autoinfection and hence, infection may persist for years. The male worms are not seen in human infection.

Strongyloides stercoralis eggs are visible within the paired uteri of gravid female. As soon as the eggs are laid, they hatch out to rhabditiform larva (L1 stage). Thus, it is the L1 stage and not the egg, which is excreted in faeces and detected in stool examination.

The L1 stage measures 0.25 mm in length. It migrates into the lumen of the intestine and passes down the gut to be excreted out in faeces.

Filariform larva (L3 stage) is the third larval stage (Fig. 10.5). L1 larva moults twice to become the L3 larva. It is long and slender, measuring 0.55 mm in length with a notched tail. It is the infective stage to human.

Life Cycle (Fig. 10.6)

(*1*) Rhabditiform larvae, L1, in the intestine are excreted in stool of infected human. This larva can follow 3 different pathways to complete its life cycle (direct, indirect and autoinfection). In the direct development, the L1 moults twice into L3 in the soil. (*2*) In the indirect development, the L1 larvae develop into the free-living adult worms (male and female) in the soil. (*3*) Eggs are produced by fertilized female worms. (*4*) L1 larvae hatch from embryonated eggs. (*5*) The L1 larvae develop into infective filariform, L3. (*6–7*) The L3 larvae penetrate the intact skin and enter the circulation, ending up in the heart and lungs. In the lungs, the larvae rupture out of the alveolar capillaries into the alveolar space and crawl up the bronchiole, bronchi,

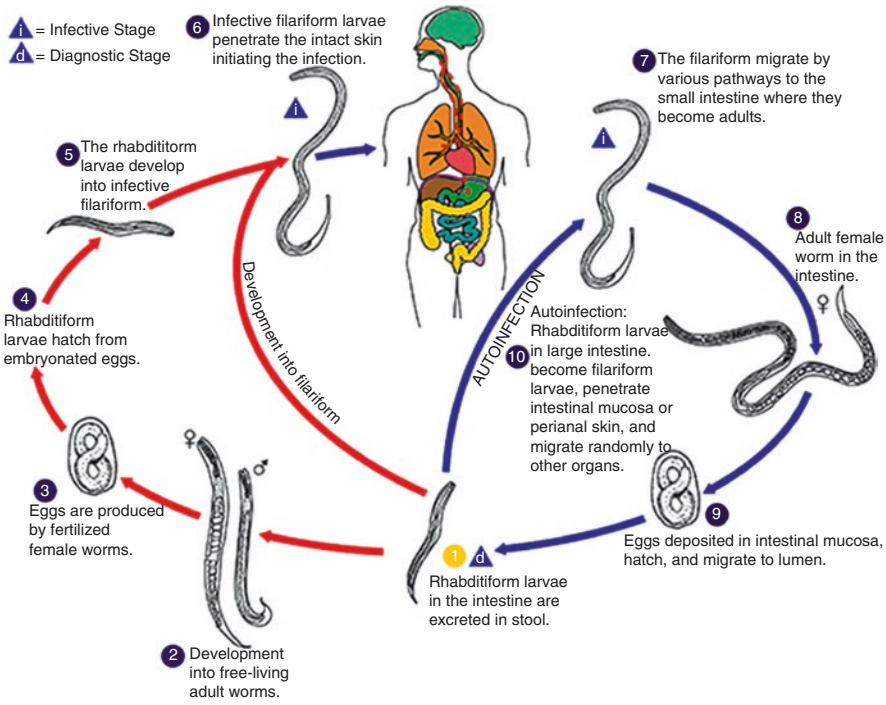


Fig. 10.6 Life cycle of *Strongyloides stercoralis* (Reproduced from https://www.cdc.gov/dpdx/strongyloidiasis/index.html)

trachea and pharynx. (*8*) They are then swallowed and develop into adults in the mucosa of the small intestine. (*9*) The adult female deposits eggs in the intestinal mucosa. The eggs hatch into L1 larvae which migrate to the intestinal lumen and are excreted in the stool. (*10*) The worm may develop internal and external autoinfection. In external autoinfection, the L1 larvae develop into the infective L3 larvae during passage down the intestine. These L3 larvae cause reinfection by penetrating the perianal skin during defaecation. They enter the circulatory system and are carried to the heart and lungs to complete the life cycle. In internal autoinfection seen commonly in immunosuppressed hosts, the L1 larvae develop into infective L3 larvae in the intestine. The L3 larvae penetrate the intestine and are carried in circulation to the heart and lungs to complete the life cycle.

Pathogenesis and Clinical Features

Strongyloidiasis is generally benign and asymptomatic. Eosinophilia and larvae in stool are the only indication of infection. In immunocompromised persons, it may cause clinical manifestations which may be severe and even fatal. The clinical disease may have cutaneous, pulmonary and intestinal manifestations.

There may be dermatitis, with erythema and itching at the site of penetration of the filariform larva, particularly when large numbers of larvae enter the skin. Larva currens has been used to describe the rapidly progressing linear or serpigenous urticarial tracks caused by migrating filariform larvae which are seen following external autoinfection around the perianal region.

In heavy infection, patient may present with Loeffler's syndrome during the larval lung migration phase of the parasite.

Intestinal manifestations may present as malabsorption syndrome. Diarrhoea is often present. In heavy infection, there may be extensive sloughing of the intestinal mucosa. Other manifestations include protein losing enteropathy and paralytic ileus.

In immunocompromised patients, internal autoinfection takes place, resulting in a large number of worms in the intestine and lungs. This is known as hyperinfection. In disseminated strongyloidiasis, the filariform larvae may enter blood circulation and lodge in various organs, e.g. heart, lungs, brain, kidneys, pancreas, liver and lymph nodes. Clinical manifestations depend on the sites affected. Brain abscess, meningitis and peritonitis are major fatal complications.

Diagnosis

1. *Microscopic examination*
   Detection of the rhabditiform larvae in freshly passed stools. Larvae found in old stools have to be differentiated from larvae hatched from hookworm eggs by doing stool culture. Baermann's funnel gauze is a method used for larval examination.
2. *Stool culture*
   When larvae are scanty in stools, diagnosis may be facilitated by stool culture. Culture techniques used include agar plate culture. Serial examinations of faecal samples and the use of agar plate culture improve the sensitivity of stool diagnosis.
3. *Serodiagnosis*
4. *Molecular diagnosis*
   PCR on stool sample.

Note: Patients who are infected with *Strongyloides* and are prescribed corticosteroids or immunosuppressive drugs can develop disseminated strongyloidiasis or hyperinfection syndrome. These conditions are potentially fatal. Thus, it is important to rule out the presence of strongyloidiasis prior to starting steroids or other immunosuppressive therapy.

Treatment

All cases of strongyloidiasis, symptomatic and asymptomatic, should be treated to prevent severe invasive disease. Ivermectin (200 μg/kg/day orally for 1–2 days) is more effective than albendazole (400 mg orally twice/day for 7 days). For disseminated strongyloidiasis, treatment with ivermectin should be extended for at least 5–7 days.

Prevention and Control

1. Proper faecal disposal
2. Use of footwear and gloves to prevent skin penetration by filariform larva
3. Treatment of patients

Hookworm

Distribution

Hookworm disease is prevalent throughout the tropics and subtropics. Two species of human hookworms are *Ancylostoma duodenale* and *Necator americanus.*

Ancylostoma duodenale

Habitat

The adult worms live in the lumen of the small intestines of infected persons.

Morphology

The adult male worm is about 8–11 mm in length. The posterior end of the male is expanded into a copulatory bursa supported by flashy rays. Two copulatory spicules project from the bursa. The female is 10–13 mm long. The mouth has a prominent buccal capsule, with 4 hook-like teeth ventrally and a median cleft dorsally.

Ancylostoma duodenale eggs are oval, colourless and measuring 60 µm by 40 µm (Fig. 10.7). It has a thin transparent shell. When passed in faeces, the egg contains segmented ovum. There is a clear space between the segmented ovum and the egg shell.

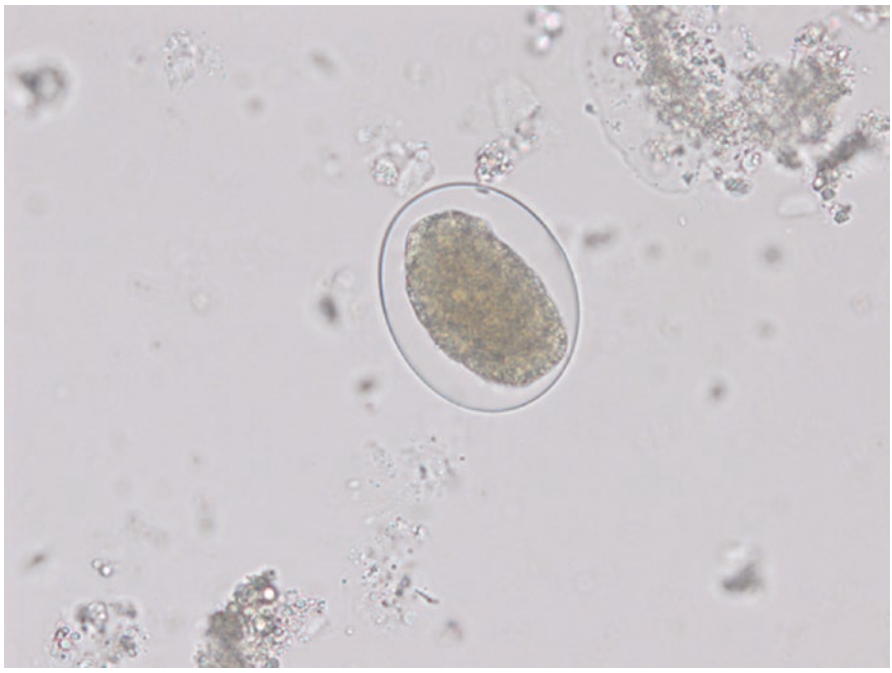


Fig. 10.7 *Ancylostoma duodenale* egg

Necator americanus

Morphology

The adult worms of *Necator americanus* are slightly smaller than *A. duodenale,* the male being 7–9 mm long and the female 9–11 mm long. The anterior end is bent in a direction opposite to the general curvature of the body, while in *A. duodenale,* the bend is in the same direction. The copulatory bursa of the male is long and wide. The copulatory spicules are fused at the ends to form a barbed tip. The buccal capsule has 2 pairs of semilunar cutting plates. The eggs of *N. americanus* are identical to those of *A. duodenale.*

Life Cycle (Fig. 10.8)

(*1*) Eggs are passed out in faeces of infected human. (*2*) The eggs hatch into rhabditiform larvae, L1, in the soil. L1 moults into L2. (*3*) L2 moults into the infective filariform larva, L3. (*4–5*) The L3 larvae penetrate the skin and enter the circulation, ending up in the heart and lungs. In the lungs, the larvae rupture out of the alveolar capillaries into the alveolar space and crawl up the bronchiole, bronchi, trachea and

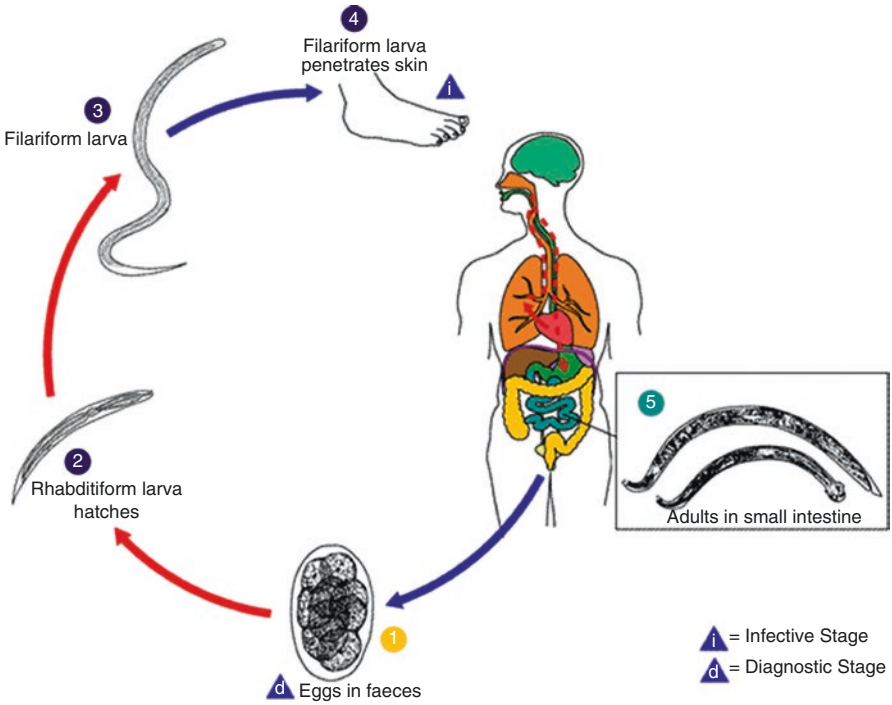


Fig. 10.8 Life cycle of hookworm (Reproduced from https://www.cdc.gov/dpdx/hookworm/index.html)



Fig. 10.9 Hookworm L3 larva (with pointed tail)

pharynx. They are then swallowed and develop into adults in the lumen of the small intestine in 1–2 months. The adult female deposits eggs which are excreted into the faeces.

Both hookworms have similar life cycle. L3 larva is the infective stage (Fig. 10.9). The lifespan of *Necator* is more than 4 years and *Ancylostoma* is 2–7 years.

Pathogenesis and Clinical Features

When the filariform larva penetrates the skin, it causes severe local itching called ground itch. Erythematous papular rash develops when a large number of larvae penetrate the skin.

Loeffler's syndrome may occur in heavy larvae infection.

Hookworm infection is usually asymptomatic. Adult worms suck blood aided by the anticoagulant that they secrete. The worms change feeding sites and the old biting sites will continue to bleed. Stool may become black in colour (malaena). Chronic infection can lead to iron deficiency anaemia. Patients may present with features of anaemia such as exertional dyspnoea, tiredness, palpitations and dizziness. Severe hookworm anaemia may lead to cardiac failure and hypoalbuminaemia.

Diagnosis

1. *Microscopic examination*

   Detection of characteristic hookworm eggs in faeces by direct wet microscopy or by concentration methods. Delayed examination of stool samples may cause eggs to hatch and rhabditiform larvae may be present. These have to be differentiated from *Strongyloides* larvae by doing stool culture. L3 of hookworm has pointed tail whereas L3 of *Strongyloides* has notched tail.

2. *Stool culture*

   Harada Mori method of stool culture is carried out to demonstrate third-stage filariform larvae.

Treatment

Albendazole (400 mg orally once) or mebendazole (100 mg orally twice/day for 3 days or 500 mg orally once). Pyrantel pamoate (11 mg/kg (up to a maximum of 1 g) orally daily for 3 days) is also effective and can be used in pregnancy. Iron supplement is given to correct anaemia. In severe cases, blood transfusion may be needed. When the haemoglobin level is very low, antihelminthic drugs should not be given before correcting the anaemia.

Prevention and Control

Same as for *Strongyloides*

Animal Nematodes That Can Infect Human

Animal nematodes can infect human causing cutaneous larva migrans (CLM) and visceral larva migrans (VLM).

Cutaneous Larva Migrans (CLM)

This condition also known as creeping eruption is caused by animal nematode larvae that penetrate skin of human. The most common cause is dog and cat hookworm (*Ancylostoma braziliense)* and dog hookworm (*Ancylostoma caninum*). Since human is an abnormal host, the parasite cannot develop into adults. The larva will migrate in the human skin till it dies.

Pathogenesis and Clinical Features

Hookworm eggs are passed in the faeces of infected animals into the soil, where the eggs hatch and release larvae. On coming into contact with human skin, the infective larvae penetrate the skin to cause infection. Since human is an abnormal host, the larvae remain confined to the outer layer of the skin. The larvae produce itching papules, which develop into serpigenous tracks in the epidermis. Itchiness causes scratching which may lead to secondary bacterial infection.

Diagnosis

Diagnosis is based mainly on history and clinical manifestations.

Treatment

Albendazole, 400 mg orally once/day for 3–7 days. Thiabendazole ointment is useful in treatment. When the lesions are few, freezing the advancing part of the lesion with ethyl chloride is effective. Symptomatic relief can be given for pruritus.

Prevention and Control

1. Deworming of dogs and cats
2. Wearing shoes when going outdoor

Visceral Larva Migrans (VLM)

This condition is caused by the migration of nematode larvae of dogs and cats in the visceral organs. Human is an abnormal host and the parasite cannot develop into adults. The most common cause is the dog ascarid, *Toxocara canis,* and less often the cat ascarid, *T. cati*. Human acquires infection by the accidental ingestion of *Toxocara* eggs.

Pathogenesis and Clinical Features

When the infective eggs from faeces of dogs and cats are ingested by human, the eggs hatch in the small intestine, releasing larvae which penetrate the gut wall and migrate to the liver. They may migrate via circulation to other organs such as lungs, brain or eyes. Since human is an abnormal host, they do not develop into adults. Granulomatous foci are produced around dead larvae. Clinical manifestations depend on the sites affected and the degree and duration of infection. It is more frequently reported in children due to habit of eating dirt (pica). Fever, hepatomegaly, pneumonitis and hyperglobulinaemia are the common findings. There is persistent high eosinophilia. In ocular larva migrans, patients may also develop retinochoroiditis. Retinochoroiditis may be misdiagnosed as retinoblastoma.

Diagnosis

1. *Serodiagnosis*
2. *Biopsy*
   Not an effective method.

Treatment

Thiabendazole (25 mg/kg twice/day for 5–7 days) is suggested in severe symptomatic cases. Diethylcarbamazine (DEC) has also been recommended.

Prevention and Control

1. Deworming of dogs and cats
2. Personal hygiene
3. Prevent children from eating dirt (pica)

Intestinal Nematodes: Non-Soil Transmitted Helminths

Enterobius vermicularis

Common name	Pinworm

Distribution

It is worldwide in distribution and commonly affects children.

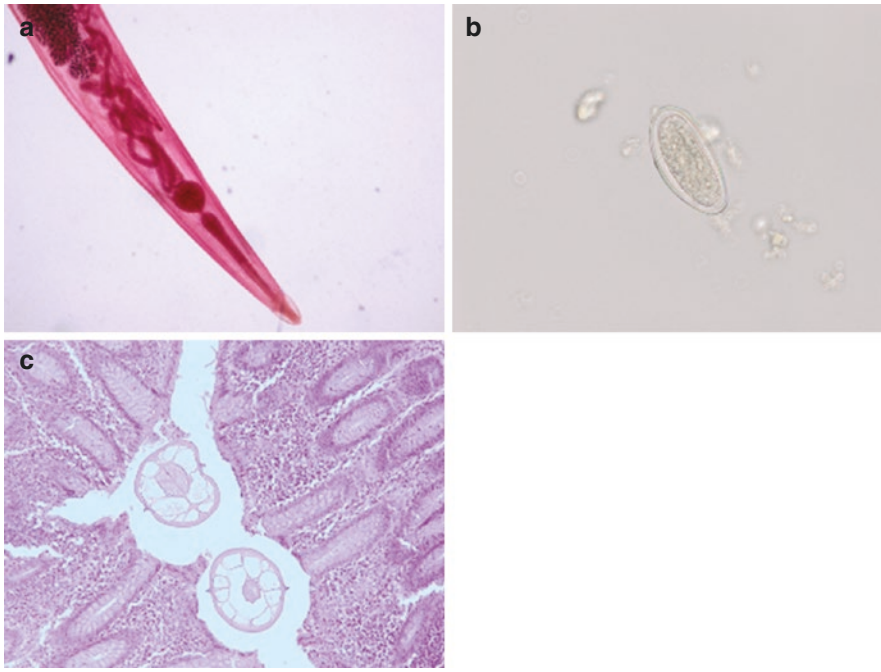


Fig. 10.10 *Enterobius vermicularis.* (**a**) Adult anterior section with bulb shaped oesophagus, (**b**) Egg, (**c**) Cross sections of adult

Habitat

Adult worms are found in the caecum and appendix.

Morphology

The adults are short, white, fusiform worms with pointed ends. The mouth is surrounded by 3 wing-like cuticular expansions (cervical alae). It has a bulb-shaped oesophagus (Fig. 10.10a). The female is 8–13 mm long. Its posterior third is pointed (pin-like). The worm is oviparous. The male worm is 2–5 mm long. Its posterior end is curved ventrally and carries a copulatory spicule. The lifespan of the adults is about 7–8 weeks.

Enterobius vermicularus egg has a characteristic D-shape, flattened on one side and convex on the other measuring 50–60 μm (Fig. 10.10b). The shell is thick and the egg contains a fully formed coiled embryo. It becomes infectious 4–6 h after being deposited on the perianal skin. Under cool moist conditions, the egg remains viable for about 2 weeks.

Life Cycle (Fig. 10.11)

(*1*) Eggs are laid by the gravid female worm in perianal region. Larvae inside the eggs mature within 4–6 h. (*2*) Embryonated eggs are ingested by humans (fingers to anus to mouth or via inhalation). (*3*) Eggs hatch in the intestine. (*4*) Adults develop

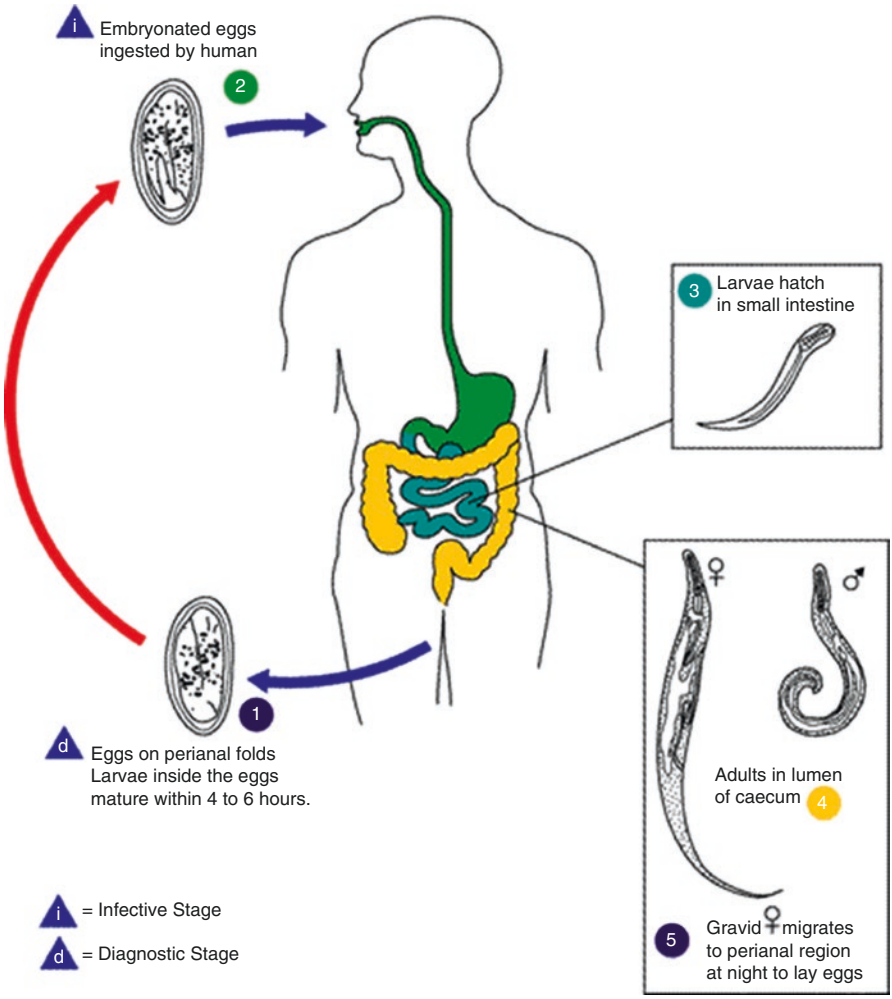


Fig. 10.11 Life cycle of *Enterobius vermicularis* (Reproduced from https://www.cdc.gov/dpdx/enterobiasis/index.html)

in the lumen of the large intestine (caecum). Male worm dies after mating. (*5*) Gravid female migrates to perianal region at night to lay eggs.

Retroinfection occurs when the egg hatches and the larva migrates up the rectum.

Pathogenesis and Clinical Features

Enterobiasis occurs mostly in children. About one-third of infections are asymptomatic. Its main symptom is intense irritation and pruritus of the perianal (pruritus ani) and perineal area, which coincides with laying of eggs by the gravid female

worm at night. The eggs are sticky and stick to the perianal skin. Pruritus ani causes scratching and excoriation of the skin around the anus. In female patients, the worms may cause ectopic migration when they crawl into the vulva and vagina causing irritation. It may migrate up to the uterus and fallopian tubes. This may cause symptoms of cervicitis and chronic salpingitis. The worm is sometimes found in surgically removed appendix.

Diagnosis

Pinworm infection is suspected from the history of pruritus ani. Diagnosis is made on the detection of eggs or adult worms.

1. *Microscopic examination*
   Demonstration of eggs or adult female worms using Scotch tape (adhesive transparent cellophane tape) technique. Specimens are collected from the perianal region during early morning, before going to the toilet or bathing or at night before going to sleep. Eggs are rarely seen in faeces, so faecal examination is not useful in diagnosis.
2. *Gross examination*
   Demonstration of adult female worms by Scotch tape technique or on surface of stool specimen.
3. *Histological examination*
   Identification of adult worms in tissue by demonstration of a pair of cuticular crests (Fig. 10.10c) and typical D-shaped eggs in the uterus.

Treatment

Pyrantel pamoate (single oral dose), albendazole (single oral dose), or mebendazole (single oral dose) can be used. Treatment is to be repeated after 2 weeks to kill worms that might have hatched from eggs ingested following initial treatment. As pinworm infection is usually transmitted by close contact, it is advisable to treat household members.

Prevention and Control

1. Hand washing and keeping finger nails short
2. Washing of bed linen
3. Treatment of infected persons and household members

Trichinella spiralis

Distribution

Its infection occurs in pork-eating countries such as Europe and America.

Habitat

The encysted larvae are present in the striated muscles of pig (reservoir host) and rats. Human is an accidental host.

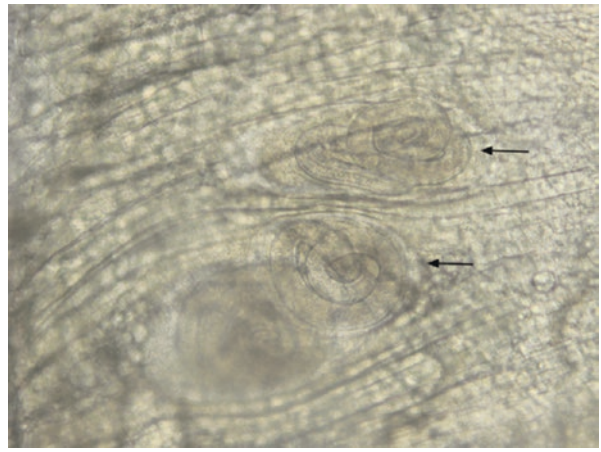


Fig. 10.12 Encysted larvae of *Trichinella spiralis* in striated muscle

Morphology

Trichinella spiralis is one of the smallest nematodes infecting humans. The adult male measures about 1.5 mm by 0.04 mm and the female about 3 mm by 0.06 mm. The female worm is viviparous. The lifespan of the adult worm is very short. The male worm dies soon after fertilizing the female and the female dies after discharging the larvae.

The larva is encysted in the striated muscle fibres. The larva in the cyst is coiled two and a half times (Fig. 10.12).

Trichinella cysts are ovoid measuring 400 μm by 250 μm in size. The cyst is formed by the tissue reaction around the encapsulated larvae. Cysts develop in striated muscles which include diaphragm, biceps, masseter and extraocular muscles. The cyst lies longitudinally along the muscle fibres and larva remains infective inside the cyst for years and eventually calcifies and dies.

Life cycle (Fig. 10.13)

(*1*) Human acquires infection via ingestion of undercooked pork containing encysted larva. (*2*) Following ingestion, the larvae are released in the intestine. (*3*) The larvae penetrate the mucosa of the small intestine and develop into adults. (*4*) After fertilization, the gravid female which is viviparous deposits the larvae in the intestinal mucosa. (*5*) The larva enters the blood circulation and is carried to the striated muscles to be encysted.

The major source of human infection is ingestion of inadequately cooked pork.

Pathogenesis and Clinical Features

Trichinosis is the disease caused by *T. spiralis*. Intestinal invasion occurs when the meat containing the encysted larva excysts. Larva invades the intestinal epithelium of the small intestine and develops into adults. Gastrointestinal symptoms include nausea, diarrhoea, abdominal cramps and vomiting. The onset of illness may last from 20–30 h after ingestion of infective meat and it mimics food poisoning.

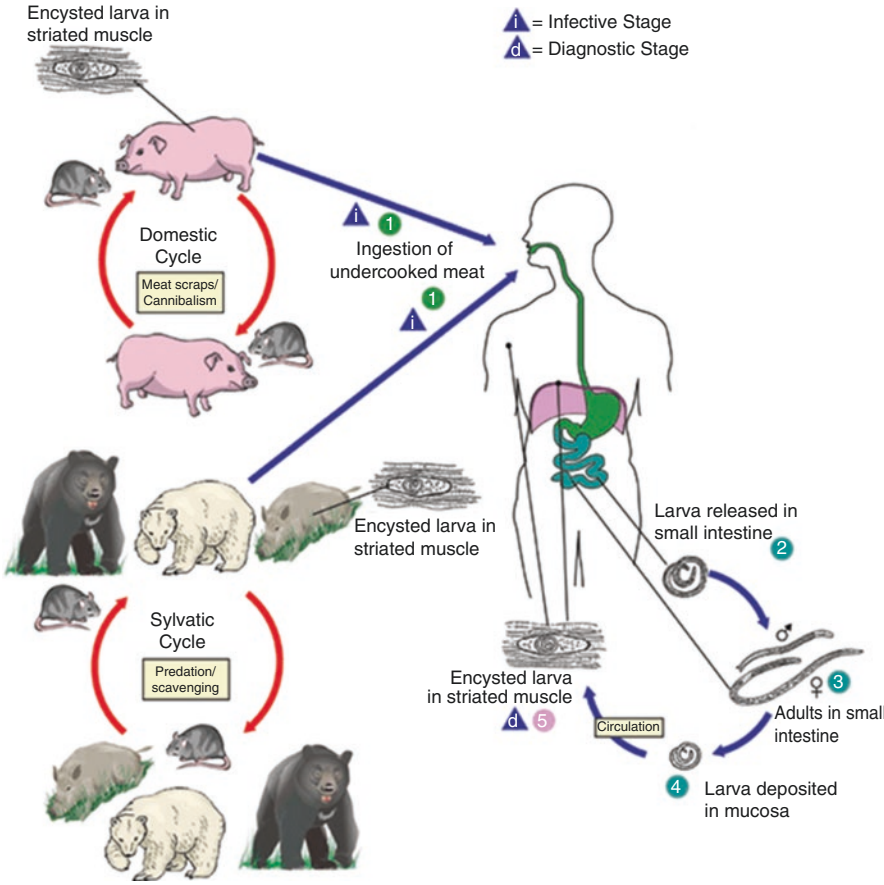


Fig. 10.13 Life cycle of *Trichinella spiralis* (Reproduced from https://www.cdc.gov/dpdx/trichinellosis/index.html)

Muscle invasion occurs after the release of larvae by the female worm at 1–4 weeks of infection. They migrate to the muscle and finally encapsulated in striated muscles. During the migration phase, patients may present with fever, facial oedema, periorbital swelling, myalgia and weakness of affected muscles. Eosinophilia is common. They can infect cardiac muscles causing myocarditis but they do not encyst. They can cause encephalitis but do not encyst in the brain. Myocarditis and encephalitis are serious complications and can be fatal.

Stage of encapsulation last for 1–8 months after infection. Fever and other symptoms subside at this stage. After this stage, calcification of the cyst occurs. The clinical manifestations are self-limiting. Human is a dead-end host.

Diagnosis

1. *Muscle biopsy of the infected muscle*

   Detection of encysted larvae in muscle tissue.

2. *Xenodiagnosis*
   Biopsy bits of infected muscle are fed to laboratory rats, which are sacrificed about 1 month later. The larvae can be demonstrated in the muscles of such infected rats.
3. *Serodiagnosis*
4. *Radiological examination*
   Calcified cysts may be demonstrated on X-ray examination.
5. *Molecular diagnosis*
   PCR on clinical specimens.

Treatment

Supportive treatment consisting of bed rest, analgesics and antipyretics. Albendazole (400 mg twice/day orally for 8–14 days) or mebendazole (200–400 mg 3 times/day orally for 3 days, then 400–500 mg 3 times/day for 10 days) may also be useful for intestinal stage of the parasite. These drugs have not been shown to be effective against the encysted larva. Steroids are sometimes required in more severe cases.

Prevention and Control

1. Proper cooking of pork
2. Do not feed pigs with raw meat
3. Control of rats in pig farms

Filarial Worms

The filarial worms reside in the subcutaneous tissues, lymphatic system, or serous cavities of humans. The female worms are ovoviviparous and release larvae known as microfilariae. The microfilariae can be detected in the peripheral blood or cutaneous tissues, depending on the species. Presence of microfilariae in peripheral blood can exhibit nocturnal periodicity, diurnal periodicity or no periodicity at all. The basis of periodicity is unknown but it may be an adaptation to the biting habits of the vector. The life cycle of filarial nematodes is completed in 2 hosts: definitive host (human) and intermediate host (blood-sucking arthropods). The microfilariae complete their development in the arthropod host to produce the infective larval stage. Adult worms have a lifespan of many years in the human body whereas microfilariae survive for a few months.

Filarial Worms Causing Lymphatic Filariasis

Wuchereria bancrofti

Distribution

Wuchereria brancofti is distributed widely in the tropics and subtropics.



Fig. 10.14 *Wuchereria bancrofti* microfilaria

Habitat

The adult worms reside in the lymphatic system of human. The microfilariae are found in blood.

Morphology

The adults are whitish, thread-like worms with smooth cuticle and tapering ends. The female is larger (70–100 mm × 0.25 mm) than the male (25–40 mm × 0.1 mm).

Microfilariae measure 250–300 μm in length (Fig. 10.14). It has a body sheath. When stained with Giemsa, morphological details can be made out. Body nuclei are seen and they are discrete and countable. The sheath does not take up stain with Giemsa. At the cephalic end is a clear space called the cephalic space. The microfilaria of *W. bancrofti* has a cephalic space as long as it is broad (ratio is 1:1), while in *B. malayi*, it is longer than its breadth (ratio is 2:1). In *W. bancrofti* microfilaria, there are no terminal nuclei while in *B. malayi* microfilaria, there are presence of 2 terminal nuclei. Microfilariae do not multiply or undergo any further development in the human body. If they are not taken up by a female vector mosquito, they die. Their lifespan is about 2–3 months. The microfilariae show nocturnal periodicity in peripheral circulation and are present in peripheral blood only at night (between 10 pm and 2 am). This coincides with the night biting habit of the vector mosquito.

Life Cycle (Fig. 10.15)

(*1*) When vector mosquito takes a blood meal, the infective L3 larvae enter the human skin. (*2*) They enter the circulation and develop into adults in the lymphatics. (*3*) The female adult worm produces sheathed microfilariae that migrate into lymph and blood channels. (*4*) When vector mosquito takes a blood meal, it ingests microfilariae. (*5*) The microfilariae shed sheaths, penetrate the midgut of the mosquito, and migrate to the thoracic muscles. (*6*) It develops into L1 larva. (*7*) It moults twice and develops into L3 larva. (*8*) The L3 larvae migrate to the head and proboscis of the mosquito.

The vector or intermediate host of *W. bancrofti* is *Culex quinquefasciatus.*

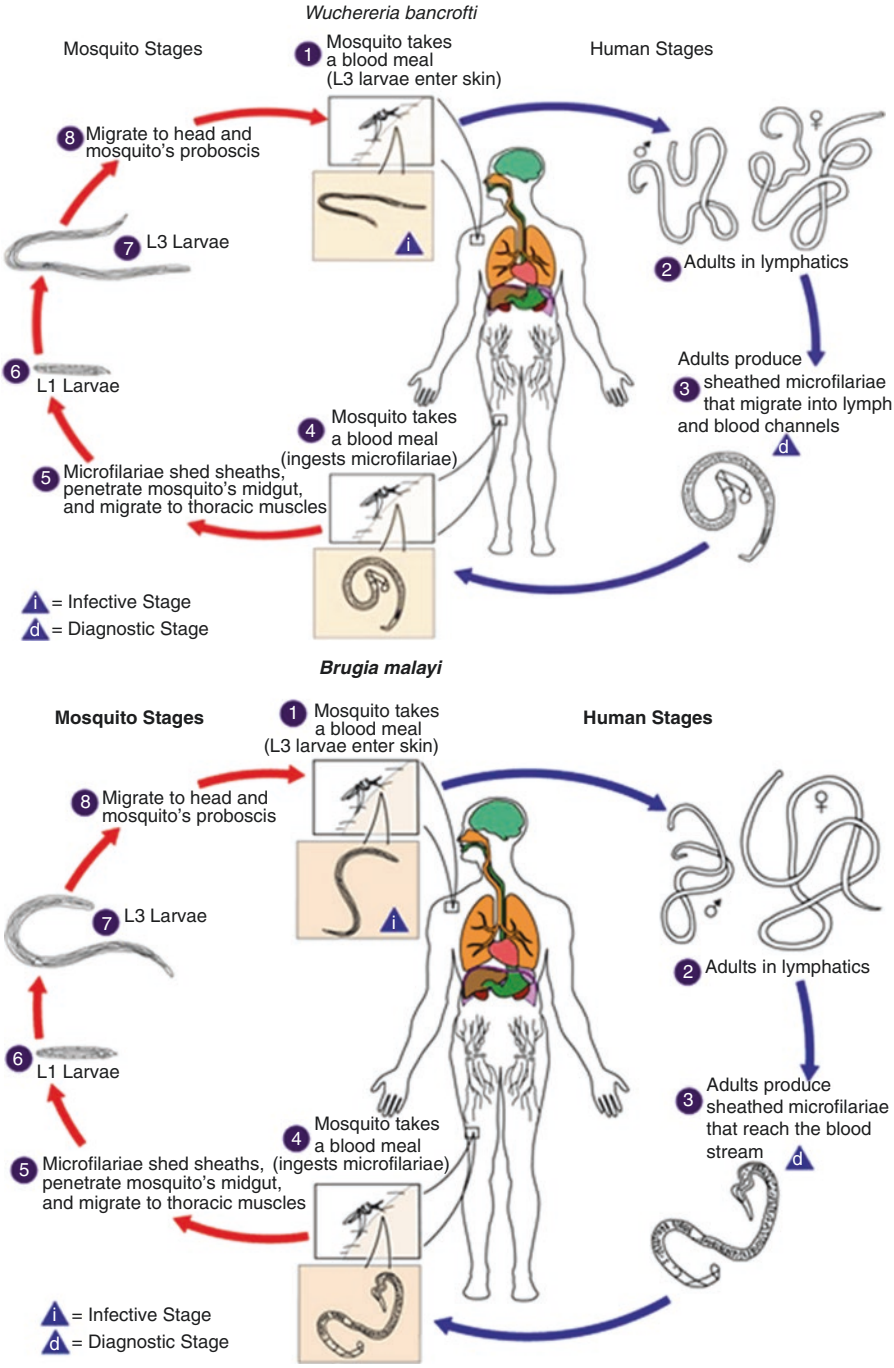


Fig. 10.15 Life cycle of *Wuchereria bancrofti* and *Brugia malayi* (Reproduced from https://www.cdc.gov/dpdx/lymphaticfilariasis/index.html)

Pathogenesis and Clinical Features

The pathogenesis of *W. bancrofti* infection is dependent on the immune system and inflammatory responses of the host. Infection may present as asymptomatic, inflammatory (in acute phase) and obstructive (in chronic phase). Asymptomatic phase may consist of high microfilaraemia. In the endemic regions, patients may show no overt symptoms of lymphatic filariasis. In the inflammatory (acute) phase, the antigens from the adult worms elicit inflammatory responses. It is characterized by high fever, lymphatic inflammation (lymphangitis and lymphadenitis) and lymphoedema. These symptoms subside after 5–7 days. Other symptoms that may occur include orchitis and epididymitis. The obstructive (chronic) phase is caused by blockage of lymph vessel and lymph nodes by the adult worms. The affected lymph nodes and vessels are infiltrated with macrophages, eosinophils, lymphocytes and plasma cells. The vessel walls become thickened and the lumen narrowed, causing lymph stasis and lymph vessel dilatation. It may cause granuloma formation, with subsequent scarring and even calcification. Inflammatory changes damage the valves in lymph vessels, further aggravating lymph stasis. Increased permeability of lymph vessel walls lead to leakage of protein-rich lymph into the tissues. This produces the typical hard pitting or brawny oedema of filariasis. Fibroblasts invade the oedematous tissues, laying down fibrous tissue, producing the non-pitting gross oedema of elephantiasis. Chronic lymphatic filariasis is also characterized by lymph varices, lymph scrotum, hydrocele and chyluria (lymph in urine). Involvement of the genitalia and chyluria are characteristics of *W. bancrofti* infection and not of *B. malayi* infection. Microfilariae are not normally present in the chronic phase. Elephantiasis affects men mainly in the legs, arms and scrotum. In women, the legs, arms and breasts are affected. Elephantiasis in *B. malayi* infection involves the leg below the knee. Incubation period is about 8–12 months.

Adult filarial worm contains endosymbiotic bacteria, *Wolbachia* spp. which has a role in the pathogenesis of its infection and is also essential for worm fertility. It has become a target for antifilarial chemotherapy.

In tropical pulmonary eosinophilia (TPE), there is a failure in the suppression of immune response to microfilarial antigens so that microfilariae are filtered out and destroyed in the lungs with allergic inflammatory reaction. TPE is a hypersensitivity reaction to filarial antigen. Patient may present with low-grade fever, loss of weight and pulmonary symptoms such as dry nocturnal cough, dyspnoea and wheezing. Children and young adults are more commonly affected in endemic areas. There is persistent eosinophilia. Chest X-ray shows changes similar to miliary tuberculosis. It is associated with a high level of serum IgE and filarial antibodies. Serological tests are usually strongly positive. Microfilariae are absent in peripheral blood. The condition responds to treatment with diethylcarbamazine (DEC), which acts on microfilariae. This condition may be caused by *W. bancrofti*, *B. malayi,* or by some animal filaria species.

Diagnosis

1. *Microscopic examination*

   Detection of microfilariae in thick blood film, chylous urine and hydrocele fluid stained with Giemsa. It is best to collect ‘night blood’ samples between 10 pm and 2 am. When the microfilariae density is low, concentration techniques

such as Knott's concentration technique and nucleopore filtration can be used. DEC provocation test is useful to bring out the microfilariae into peripheral circulation for blood collection during day time.

2. *Serodiagnosis*
   Immunochromatographic test (ICT). Blood samples can be collected at any time of the day.
3. *Molecular diagnosis*
   PCR on clinical samples.

Treatment

Diethylcarbamazine (DEC) (6 mg/kg/day orally either 1 day or 12 days. One day treatment is generally as effective as the 12-day regimen) is the drug of choice. Ivermectin (400 μg/kg single dose orally) can also be used. Tetracyclines have an effect in the treatment of filariasis by inhibiting endosymbiotic bacteria (*Wolbachia* species).

In elephantiasis, it requires elevation of the affected limb, use of elastic bandage and foot care to reduce symptoms. Surgery is required for hydrocele. Medical management of chyluria includes bed rest, high protein diet and treatment with DEC.

Prevention and Control

1. Control of the vector mosquito (anti-larval, anti-adult)
2. Using mosquito net and mosquito repellants
3. Detection and treatment of cases

Brugia malayi

Distribution

Brugia malayi occurs in India, Indonesia, Philippines, Malaysia, Thailand, Vietnam, China, South Korea and Japan. Besides *B. malayi*, another species of this genus includes *Brugia timori* which is found in Timor, Indonesia.

Habitat

The adult worms reside in the lymphatic system of human. The microfilariae are found in blood.

Morphology

The adult worms of *B. malayi* are generally similar to those of *W. bancrofti* though smaller in size.

The microfilaria of *B. malayi* is sheathed and it is stained with Giemsa. It is kinky, cephalic space is longer (ratio is 2:1), overlapping body nucleus with 2 terminal nuclei (terminal and subterminal) (Fig. 10.16).

Life Cycle

The life cycle of *B. malayi* is similar to that of *W. bancrofti*. However, the intermediate host of *Brugia* are vectors of genera *Mansonia*, *Anopheles* and *Aedes*. Pathogenesis, clinical features, laboratory diagnosis and treatment are similar to *W. bancrofti*.

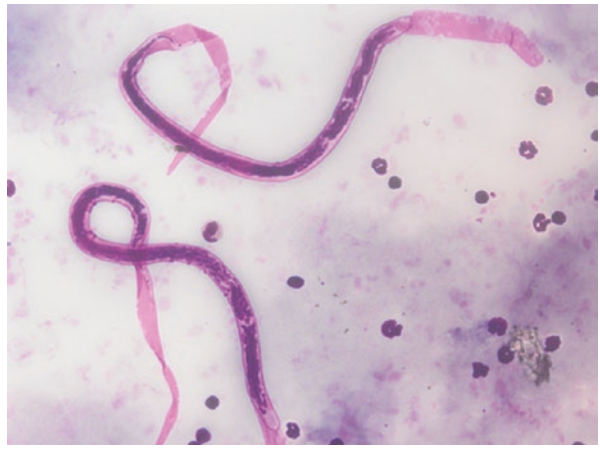


Fig. 10.16 *Brugia malayi* microfilariae

B. malayi shows nocturnal periodic (microfilariae are not detectable in the blood for the majority of the day, but the microfilarial density peaks between 10 pm and 2 am) and nocturnal subperiodic forms (microfilariae are present in the blood at all times, but appear at greatest density between noon and 8 pm). The nocturnal periodic form is transmitted by *Mansonia* and some *Anopheline* mosquitoes in open swamps and rice growing areas. Natural animal infections are rare. The nocturnal subperiodic form is transmitted by *Mansonia* in forest swamps. Natural zoonotic infections are common. Animals including cats, dogs and monkeys may serve as important reservoirs for human infection.

Prevention and Control

Prevention and control methods are similar to *W. bancrofti*. The breeding of *Mansonia* mosquito requires water plants, without which *Mansonia* mosquito cannot breed.

Brugia timori

Brugia timori is limited to Timor island of Eastern Indonesia. The vector of *B. timori* is *Anopheles barbirostris,* which breeds in rice fields and is a night feeder. Definitive host is human and no animal reservoir is known. Microfilariae of *B. timori* exhibit nocturnal periodicity. The microfilaria sheath of *B. timori* fails to take Giemsa stain. The cephalic space ratio is 3:1. The lesions produced by *B. timori* are milder than those of bancroftian or *B. malayi* filariasis. DEC and albendazole are used in the treatment of *Brugia timori* filariasis.

Filarial Worms Causing Subcutaneous Filariasis

Loa loa

Common name	African eye worm

Distribution
It is limited to West and Central Africa.

Habitat
In human, the adults are found in subcutaneous tissues and the microfilariae are found in the blood.

Morphology
Adult worm measures about 30–70 mm in length. They live in subcutaneous tissues, through which they migrate. They may also occur in the subconjunctival tissue. Adults live for 10–15 years.

The microfilariae are sheathed with column of nuclei extending completely to the tip of the tail. They appear in peripheral circulation only during the day from 12 noon to 2 pm (diurnal periodicity).

Life Cycle (Fig. 10.17)
(*1*) The *Chrysops* takes a blood meal and infective L3 larvae enter the bite wound. (*2*) The larvae are carried in the circulation to the subcutaneous tissue where they moult and develop into mature adult worms over 6–12 months. (*3*) Adult females produce sheathed microfilariae. (*4*) The microfilariae are ingested by *Chrysops* during its blood meal. (*5–7*) They cast off their sheaths, penetrate the stomach wall and reach thoracic muscles where they develop into infective larvae. (*8*) The infective larvae migrate to the head and proboscis of the fly.

Life cycle is completed in 2 hosts. Human is the definitive host. The intermediate host or vector is the day biting flies (mango flies) of the genus *Chrysops* in which the microfilariae develop into the infective third-stage larvae.

Pathogenesis and Clinical Features
The adult migration through subcutaneous tissues causes temporary inflammation, which appear as swellings, of up to 3 cm in size, usually seen on the extremities. These are the calabar swellings or fugitive swellings. Swellings disappear in a few days, only to reappear elsewhere. Ocular manifestations occur when the worm reaches the subconjunctival tissues during its migration.

Diagnosis
Diagnosis can be made on the appearance of fugitive swelling and the appearance of worm in the eye in persons exposed to infection in endemic area.

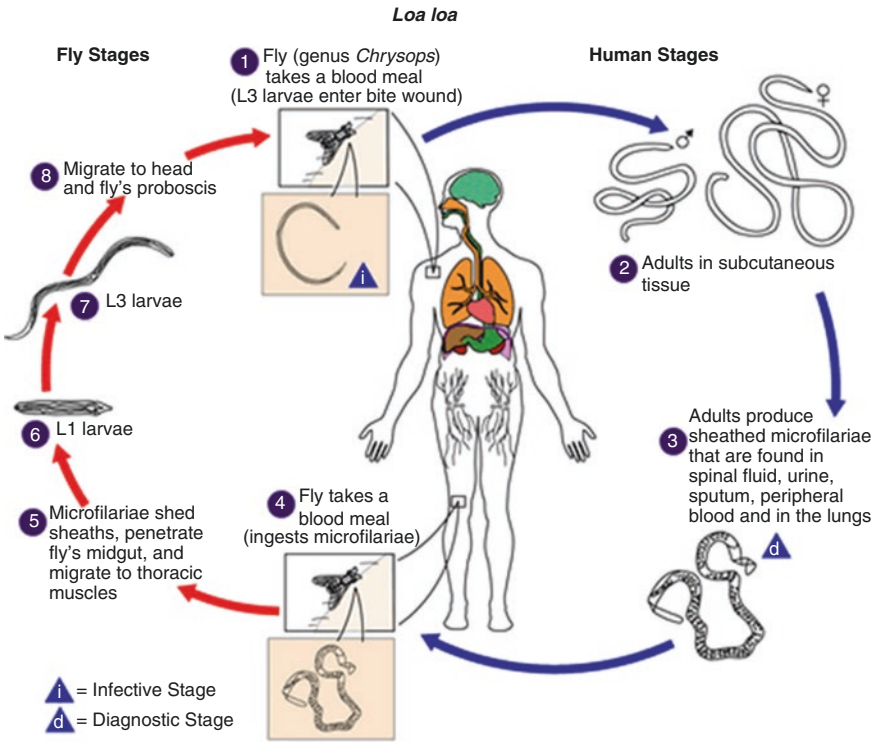


Fig. 10.17 Life cycle of *Loa loa* (Reproduced from https://www.cdc.gov/dpdx/loiasis/index.html)

1. *Microscopic examination*
   Detection of microfilariae stained with Giemsa in peripheral blood at daytime.
2. *Biopsy*
   Isolation of the adult worm from the eye or from a subcutaneous biopsy specimen.

Treatment

DEC (8–10 mg/kg orally in 3 divided doses daily for 21 days) is effective against both the adult and the microfilarial forms of *L. loa*. Severe adverse reactions may develop following the sudden death of large numbers of microfilariae after giving DEC. Administration of corticosteroids at the same time minimizes such reaction.

Surgical removal of the migrating adult worms that are found in the conjunctiva or under the skin.

Prevention and Control

1. Avoiding areas where *Chrysops* are found
2. Avoid vector bites by using insect repellents and protective clothings
3. Treatment of positive cases

Onchocerca volvulus

Distribution
Mainly in tropical Africa, Central and South America. A small focus of infection exists in Yemen and south Arabia.

Habitat
The adult worms are in nodules in subcutaneous connective tissue of infected persons.

Morphology
The adult male worm measures not more than 5 cm in length and the female measures 50 cm.

The microfilariae are unsheathed and non-periodic. They measure about 300 μm in length. The microfilariae are found in the skin and subcutaneous lymphatics in the vicinity of parent worms. They may also be found in the eye and not in peripheral blood.

Life Cycle (Fig. 10.18)
(*1*) The vector, black fly, takes a blood meal and L3 larvae enter the bite wound. (*2–3*) The larvae travel to the subcutaneous tissue and develop into adults which are

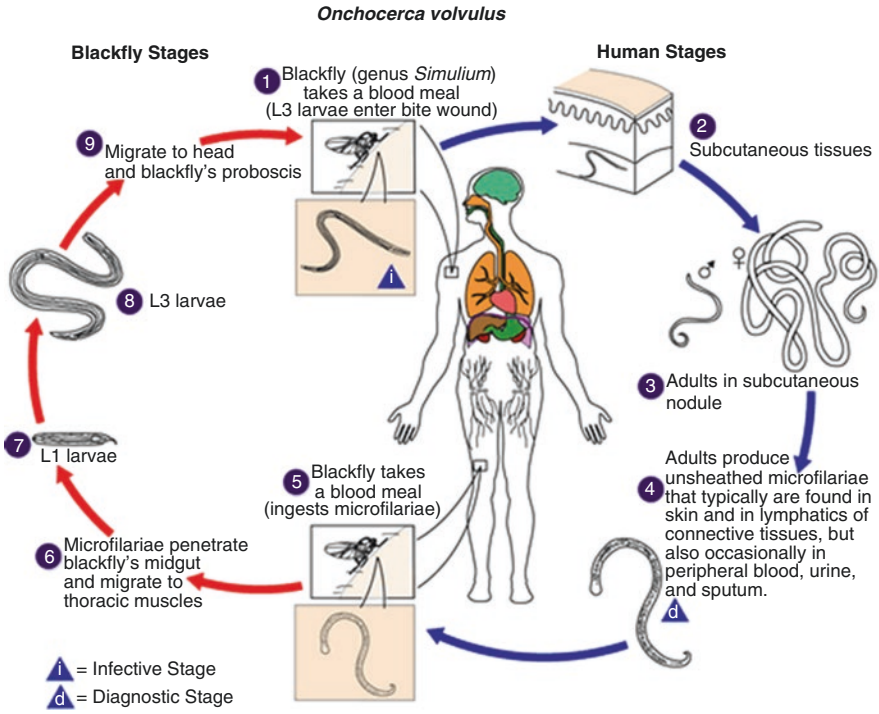


Fig. 10.18 Life cycle of *Onchocerca volvulus* (Reproduced from https://www.cdc.gov/dpdx/onchocerciasis/index.html)

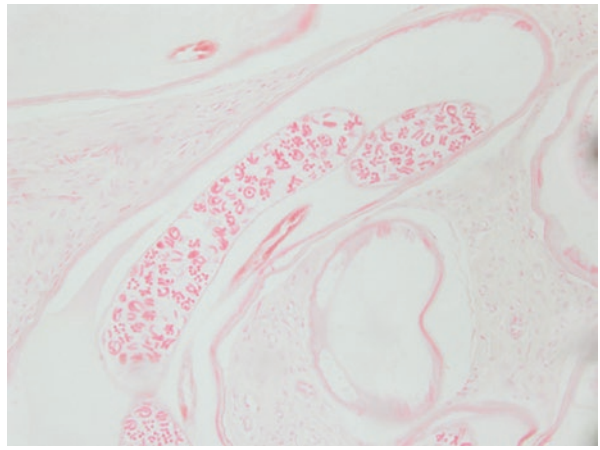


Fig. 10.19 Cross section of subcutaneous nodule of *Onchocerca volvulus*

found in the subcutaneous nodule. (*4*) Adult females produce unsheathed microfilariae that are found in skin and in lymphatics of connective tissue. (*5–9*) The female black flies are 'pool feeders' and suck blood and tissue fluids. Microfilariae from the skin and lymphatics are ingested and develop within the vector, becoming the infective third-stage larvae, which migrate to its mouth parts.

Life cycle is completed in 2 hosts. Humans are the only definitive host. Day-biting female black fly of the genus *Simulium* is the intermediate host. The vector *Simulium* species breed in fast-flowing rivers, hence, the disease is most common along the course of rivers and it is also known as 'river blindness'. The adult worm lives in the human host for about 15 years and the microfilariae for about 1 year.

Pathogenesis and Clinical Features

Pathogenesis depends on the host's allergic and inflammatory reactions to the adult worms and microfilariae.

The subcutaneous nodule or onchocercoma containing adult worms is a circumscribed, firm, non-tender and it is formed as a result of fibroblastic reaction around the worms. Nodules measure from a few mm to about 10 cm. They tend to occur over anatomical sites where the bones are superficial, such as the scalp, scapulae, ribs, elbows, iliac crest, sacrum and knees. The nodules are painless. Microfilariae cause lesions in the skin and eyes. Cross section of the subcutaneous nodule with adult worms is as shown in Fig. 10.19.

The skin lesion is a dermatitis with pruritus, pigmentation, atrophy and fibrosis. Ocular manifestations range from photophobia to gradual blurring of vision, progressing to blindness. Lesions may develop in all parts of the eye. The most common early finding is conjunctivitis with photophobia. Other ocular lesions include

punctate or sclerozing keratitis, iridocyclitis, secondary glaucoma, chorioretinitis and optic atrophy.

Diagnosis

1. *Microscopic examination*
   Detection of microfilariae from skin snip. The specimen is best collected around midday.
2. *Biopsy*
   In patients with ocular manifestations, microfilariae may be found in conjunctival biopsies. Adult worms can be detected in the biopsy material of the subcutaneous nodule.
3. *Molecular diagnosis*
   PCR of skin snips.

Treatment

Ivermectin (150 mg/kg once) is the main stay of treatment. DEC and suramin have also been used. A 6-week course of doxycycline is given to target *Wolbachia*. Surgical excision is recommended when nodules are located on the head due to the proximity of the worm to the eyes.

Prevention and Control

1. Vector control (larvicides)
2. Insect repellents and protective clothings
3. Treatment of patients

Other Species That Can Cause Subcutaneous Filariasis

Mansonella streptocerca

Species That Can Cause Serous Cavity Filariasis

1. *Mansonella ozzardi*
2. *Mansonella perstans*

Species That Can Cause Zoonotic Filariasis

1. *Brugia pahangi* (filarial nematode of cats and dogs)
2. *Dirofilaria immitis* (dog heartworm)
3. *Dirofilaria repens* (filarial nematode of dogs and cats)

Other Types of Nematodes Infecting Humans

Angiostrongylus cantonensis

Common name	Rat lungworm

Distribution

Angiostrongylus cantonensis causes eosinophilic meningoencephalitis (cerebral angiostrongyliasis) in humans. Cases have been reported in Taiwan, Thailand, Indonesia, the Pacific islands, India, Egypt, Cuba and the USA

Habitat

In human, larvae cause infection in the brain. The adult worm is present in the branches of pulmonary artery in rats.

Morphology

Adult worm is about 20 mm long. Eggs of *Angiostrongylus* resemble those of hookworms.

Life Cycle

Rats are its natural host. Intermediate hosts are mollusks, slugs and snails. The infective form is the third-stage larvae. Adults in the branches of pulmonary artery of rats produce eggs which hatch in the lungs of rats and the larvae which migrate up the trachea are swallowed and expelled in the faeces. The larvae infect mollusks, slugs and snails. Crabs and freshwater prawns have been found to be carrier hosts. The larva undergoes 2 moults in the intermediate host. In about 2 weeks, the infective third stage larvae develop, which can survive in the body of the intermediate host for about a year. Rats become infected when they eat the mollusks. In the rat, the larvae penetrate the gut wall to enter the venules and are carried in circulation to the brain, where they develop into young adults in about a month. These penetrate the cerebral venules and reach the pulmonary artery, where they lodge, mature and start laying eggs. Human infection is acquired by eating infected mollusks and other intermediate hosts containing the third stage larvae. Infection may also occur through ingestion of raw vegetables contaminated by the mucus of infected mollusks. The larvae penetrate the gut and are carried to the brain, but in human, they are unable to develop further. They die and induce an inflammatory reaction in the brain and meninges to produce meningoencephalitis. The incubation period is about 2–3 weeks.

Pathogenesis and Clinical Features

Angiostrongylus is the most common cause of eosinophilic meningitis in humans. Patients present with intense headache, fever, neck stiffness, convulsions and pareses. The worm may also cause eye invasion. In severe infection, it can cause damage to the CNS.

Diagnosis

Peripheral eosinophilia, high cerebrospinal fluid (CSF) eosinophilia. Larvae and immature worms may be seen in CSF.

History of exposure to snail hosts helps in diagnosis.

Treatment
Frequently, most cases will resolve and recover spontaneously without treatment and some may develop residual pareses. There is no specific treatment. Supportive treatment may relieve the severity of headache and the duration of symptoms.

Prevention and Control
1. Avoid consumption of raw snails and freshwater prawns
2. Avoid drinking water from open sources contaminated by mollusks, slugs and snails
3. Prevent children from playing with snails

Capillaria philippinensis

Distribution
It was first reported in the Philippines in 1963. Rare cases have also been reported in Thailand, Japan, Iran and Egypt. The parasite causes intestinal capillariasis.

Habitat
In human, the adult worm inhabits the small intestine.

Morphology
Adult worms are very small, males measure 1.5–3.9 mm long, females measure 2.5–5.3 mm long. Eggs measure 36–45 μm × 20 μm, peanut shaped.

Life Cycle (Fig. 10.20)
(*1*) Unembryonated eggs are passed by birds or humans in their faeces. (*2*) They develop into embryonated eggs and are infective to fish (fresh or brackish-water fish). (*3*) Infective larvae develop in the fish. (*4*) Human acquires infection by ingestion of raw or undercooked infected fish. (*5*) The larvae develop into adult worms in the mucosa of the small intestine and produce eggs which are passed out in faeces. (*6*) Larviparous female worms may produce larvae that can reinvade the intestinal mucosa causing internal autoinfection.

Birds (fish-eating birds) are definitive host. Freshwater fish is the intermediate host.

Pathogenesis and Clinical Features
Worms are found in the mucosa of the small intestine. They cause degeneration of the mucosa and submucosa. The clinical disease consists of malabsorption syndrome with severe diarrhoea, borborygmi (stomach growling), abdominal pain, oedema, weight loss and severe hypoalbuminaemia. Serious cases may be fatal in 2 weeks to 2 months. The clinical features resemble that of strongyloidiasis. If left untreated, it may become severe because of autoinfection. Protein-losing enteropathy may develop which can result in cachexia and death.

Diagnosis
Diagnosis is made by detection of the eggs, larvae and adults in stools. The egg resembles that of *Trichuris trichiura*, but the bipolar plugs are nonprotruding and its shell is striated (Fig. 10.21).

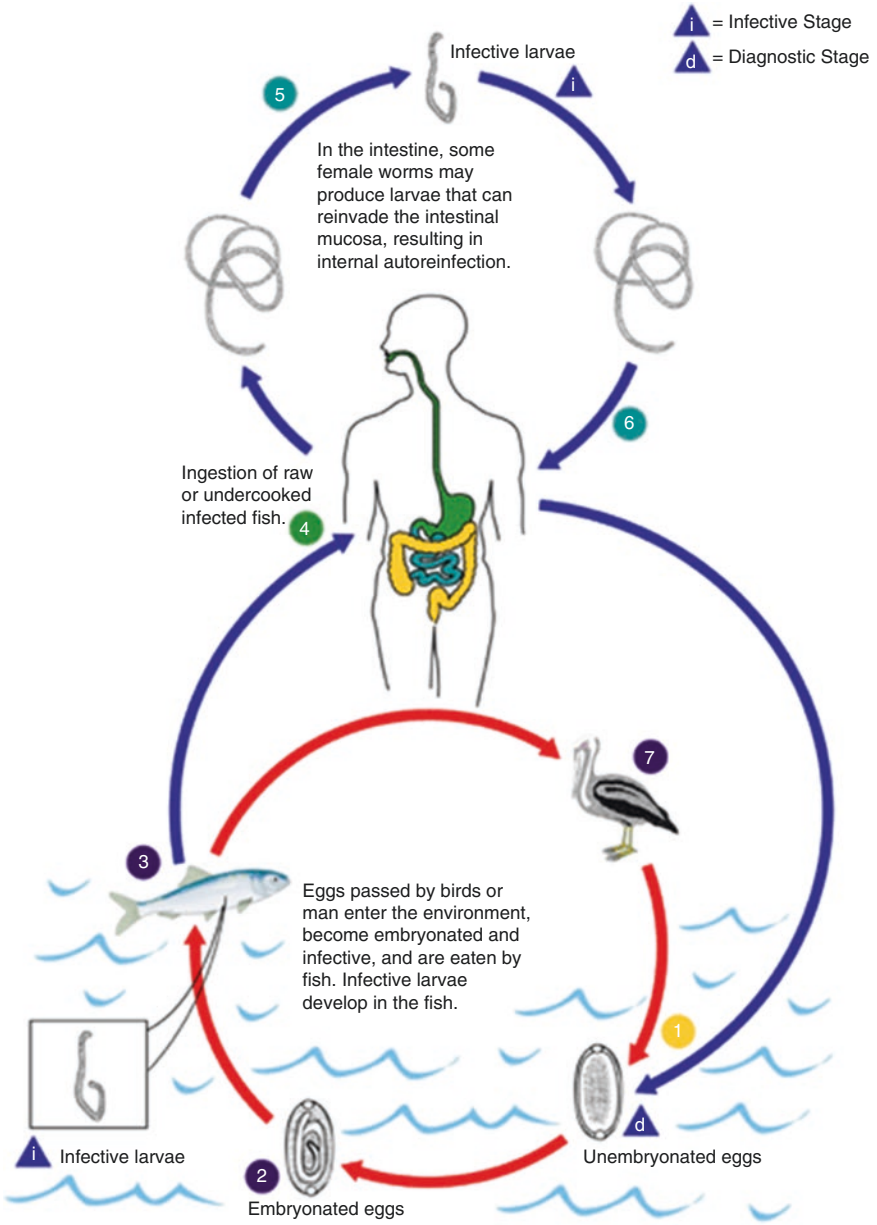


Fig. 10.20 Life cycle of *Capillaria philippinensis* (Reproduced from https://www.cdc.gov/dpdx/intestinalcapillariasis/index.html)

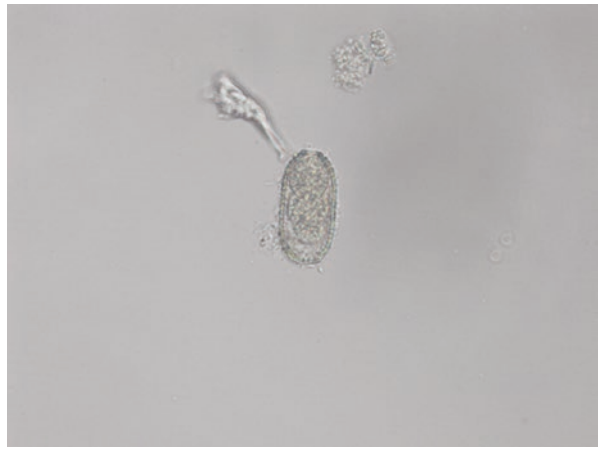


Fig. 10.21 *Capillaria philippinensis* egg

Treatment
Mebendazole (200 mg twice/day for 20 days) and albendazole (400 mg/day for 10 days). In acute illness, fluid and electrolyte replacement and a high protein diet are recommended.

Prevention and Control
1. Avoid eating small, whole, uncooked fish
2. Proper sanitation

Gnathostoma spinigerum

Distribution
Gnathostoma spinigerum, originally described from gastric tumours of a tiger, parasitizes dogs, cats and other vertebrates. Gnathostomiasis is a zoonotic infection of human. Human infections have been reported from Thailand and other countries in the Far East.

Habitat
In human, the larva stage migrates throughout the body.

Morphology
It is a small nematode. The female (25–55 mm) is longer than the male (10–25 mm). The eggs are oval, brown, unsegmented with a knob at one end. The larva is about 4 mm long with numerous spines on the head and body.

Life Cycle
The definitive hosts are dog, cat and other carnivorous animals. Cyclop is the first intermediate host. Second intermediate host are freshwater fish and frog. Birds and humans are paratenic hosts.

Adult worm resides in the tumours or granulomatous lesions in the stomach wall of cat and dog. Eggs are laid in the tumours. Eggs pass into gastric lumen and are discharged in faeces into water, where they hatch into first stage larva (L1). L1 larvae are ingested by cyclops (first intermediate host) where the second-stage larvae develop. Cyclops are eaten by the second intermediate host: fish frogs and snakes, where the third-stage larvae develop (L3). When the L3 larvae are eaten by cats, dogs, or other suitable hosts, the larvae develop into adults inside their body. When other paratenic hosts (reptiles, birds, or mammals) get infected, the larva does not undergo any further development. Humans acquire infection by eating undercooked fish containing third-stage larvae. They are unable to complete their development as human is a paratenic host and they migrate in the skin, subcutaneous tissue or other organs.

Pathogenesis and Clinical Features

After ingestion of the larva, its migration may produce epigastric pain, fever and vomiting. The migration of larvae in the tissues may lead to visceral gnathostomiasis and cutaneous lesion. Superficial nodules can be incised and the larvae removed. The migrating larvae may reach the brain causing eosinophilic meningoencephalitis or reach the eyes causing severe damage.

Diagnosis

The lesion can be biopsied. Presence of larva confirms the diagnosis.

Treatment

Removal of larva via surgery. Albendazole (400 mg daily for 21 days) or mebendazole is recommended.

Prevention and Control

1. Avoid eating uncooked fish, frogs, or snakes

Anisakis

Distribution

Anisakis species are nematode parasites of marine mammals like dolphins, seals and whales. Anisakiasis is common in Japan and other places where fresh or undercooked infected marine fish is eaten containing larvae of the nematode *Anisakis simplex*.

Habitat

In human, the parasite is found in the gastrointestinal tract.

Morphology

Anisakis are free-living, non-segmented, cylindrical worms. The third-stage larvae may reach a length of 50 mm and a diameter of 1–2 mm. It has a boring tooth ventral to the mouth.

Life Cycle (Fig. 10.22)

(*1*) Marine mammals excrete unembryonated eggs. (*2*) Eggs become embryonated in water and hatch releasing L2 larvae. (*3*) The larvae are ingested by crustaceans and mature into L3 larvae (Fig. 10.23a). (*4–5*) Infected crustaceans are eaten by fish and squid where the L3 larvae are maintained. (*6*) When the fish or squid containing the L3 larvae are ingested by marine mammals, the larvae moult twice and develop into adult worms. Adult worms produce eggs that are shed by marine mammals. (*7*) Humans are incidental hosts. They acquire infection via ingesting infected raw or undercooked seafood containing L3 larvae.

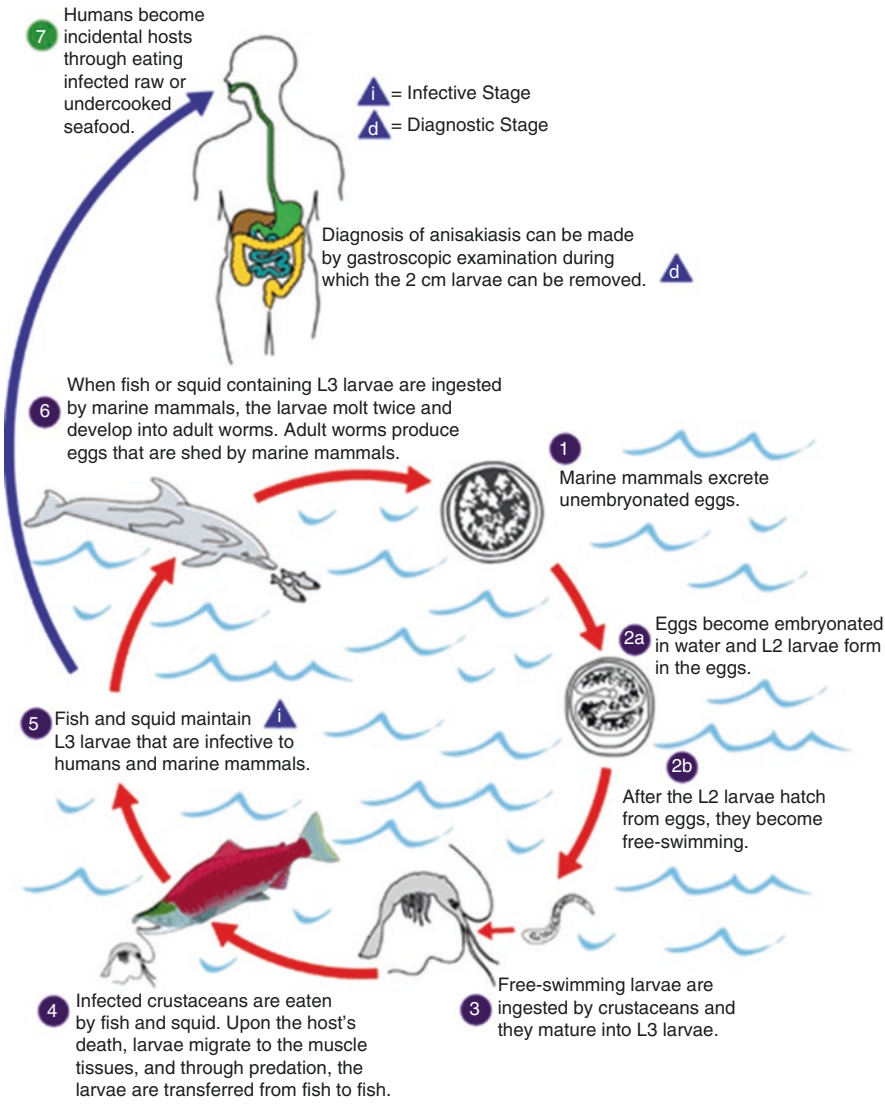


Fig. 10.22 Life-cycle of *Anisakis* (Reproduced from https://www.cdc.gov/dpdx/anisakiasis/index.html)

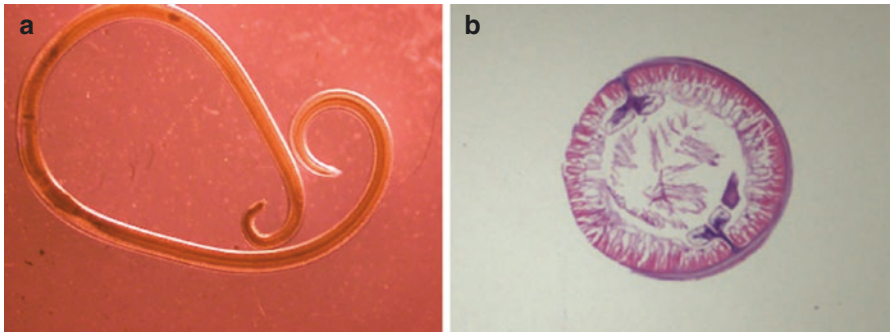


Fig. 10.23 *Anisakis*, (**a**) L3 larva, (**b**) Cross section of L3 larva

Pathogenesis and Clinical Features

When humans consume uncooked or improperly preserved fish containing the infective larvae, they penetrate the gut wall leading to local inflammation and granuloma formation. Clinical manifestations vary depending on the site of penetration of the intestinal wall, such as throat irritation, acute gastric (abdominal pain, nausea, vomiting) or bowel symptoms (lower abdominal pain, diarrhoea, dysentery). Symptoms can occur within 1 h to 2 weeks after consumption of raw or undercooked infected seafood.

Diagnosis

History of consuming raw marine fish shortly before the onset of symptoms should suggest the possibility of anisakiasis.

1. *Endoscopic examination*
   May provide visual evidence and removal of the worm for identification.
2. *Molecular diagnosis*
   PCR on the worm specimen obtained after removal.
3. Serodiagnosis
   To detect *Anisakis*-induced IgE. This antibody, however, lacks specificity as a result of cross-reactivity with other nematode antigens. The serological test is not generally available and it is of limited benefit in early diagnosis.
4. *Histological examination*
   To demonstrate the Y-shaped lateral epidermal cords on cross section of the worm (Fig. 10.23b).

Treatment

The preferred treatment is the extraction of the worm via endoscopy. Larvae do not respond to anthelmintics. In cases of surgical complications, laparotomy or bowel resection may have to be performed.

Prevention and Control

1. Proper cooking of marine fish
2. Freezing of marine fish
   (Salting and marinating will not kill the parasites)

Cestodes: Tapeworms

11

General Characteristics

Tapeworms can be classified into 2 orders—Pseudophyllidea and Cyclophyllidea.

The adult worm consists of 3 parts:

1. Head (Scolex)

   It is the organ of attachment to the intestinal mucosa of the definitive host. In parasites of the order Cyclophyllidea, the scolex possesses 4 suckers. In some Cyclophyllidea like *Taenia solium*, scolex has an apical protrusion called rostellum. The rostellum may or may not be armed with hooks. In parasites of the order Pseudophyllidea, the scolex does not possess suckers but possesses a pair of longitudinal grooves called bothria, by which it attaches to the intestine of the host.
2. Neck

   It is the part, immediately behind the head and is the region of growth from where the new proglottids are being formed.
3. Proglottids (strobila)

   The proglottids consist of immature followed by mature and gravid proglottids. Tapeworms are hermaphrodites and every mature segment contains both male and female reproductive organs. In the immature segments, the reproductive organs are not well developed. The gravid segments have uterus filled with eggs. Tapeworms do not have a body cavity or alimentary canal. Nutrients are absorbed via the cuticle. Rudimentary excretory and nervous systems are present.

   The eggs of Cyclophyllidea and Pseudophyllidea are different from each other. In Cyclophyllidea, the embryo inside the egg is called the oncosphere (hexacanth embryo). It is spherical and has 3 pairs of hooklets. In Pseudophyllidea, the egg is operculated.

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Table 11.1 Classification of cestodes of medical importance based on order and habitat

Order	Genus/Species	Habitat of adult worm in human	Habitat of larval stage in human
Pseudophyllidea	*Diphyllobothrium latum*	Small intestine	—
	Spirometra	—	Plerocercoid larva in subcutaneous tissues and other organs
Cyclophyllidea	*Taenia saginata*	Small intestine	—
	Taenia solium	Small intestine	Larva in subcutaneous tissues and other organs
	Echinococcus granulosus	—	Hydatid cyst is most commonly found in the liver followed by lungs and other organs
	Hymenolepis nana	Ileum	Cysticercoid larva in the intestinal villus

Clinical disease can be caused by the adult worm or the larval form. In general, adult worm causes mild disease or are asymptomatic, while the larvae can produce serious illness and complications, particularly when they lodge in the CNS or eyes. Classification of cestodes of medical importance based on order and habitat is shown in Table 11.1.

Pseudophyllidean Tapeworms

Diphyllobothrium latum

Common name	Fish tapeworm/Broad tapeworm

Distribution

Its infection occurs in central and northern Europe, particularly in the Scandinavian countries. It is also found in Siberia, Japan, North America and Central Africa. Dogs, cats and many wild animals may be naturally infected.

Habitat

The adult worm is found in the small intestine of human, usually in the ileum.

Morphology

Adult measures up to 10 m or more. It is the largest tapeworm inhabiting the small intestine of human. Scolex is spatulate or spoon shaped, about 2–3 mm long and 1 mm broad (Fig. 11.1a). It has 2 slitlike longitudinal dorsoventral sucking grooves (bothria). Neck is thin and unsegmented. Strobila consists of 3000–4000 proglottids (Fig. 11.1b). Proglottids are wider than they are long. The genital pores open midventrally.

Egg is broadly ovoid, about 65 µm by 45 µm, with a thick, light brown shell. It has an operculum at one end (Fig. 11.1c). It is passed in faeces and completes development in freshwater. The egg is not infective to humans.

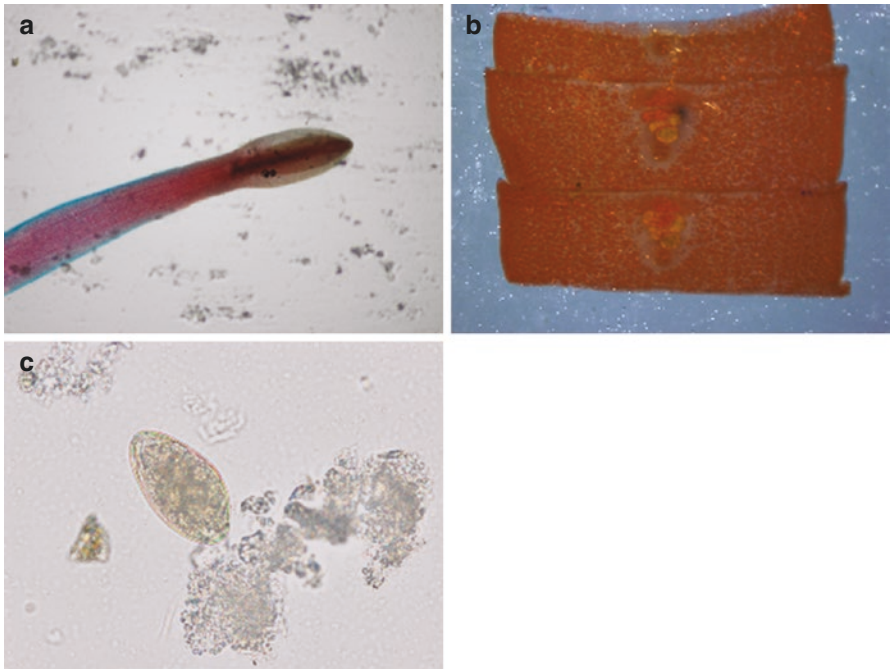


Fig. 11.1 *Diphyllobothrium latum.* (**a**) Scolex, (**b**) Gravid proglottids, (**c**) Egg

There are 3 stages of larval development:

1. First stage larva (coracidium)
2. Second stage larva (procercoid)
3. Third stage larva (plerocercoid)

Life Cycle (Fig. 11.2)

(*1*) Unembryonated eggs are passed in faeces of infected human. (*2*) Eggs embryonate in water. (*3*) Coracidia hatch from eggs and are ingested by crustaceans. (*4*) Procercoid larvae develop in body cavity of crustaceans. (*5*) The infected crustaceans are ingested by small freshwater fish and the procercoid larvae develop into plerocercoid larvae. (*6*) Predator fish eats the infected small fish. (*7*) Human acquires infection via ingesting raw or undercooked infected fish containing plerocercoid larvae. (*8*) Adults develop in the small intestine. (*9*) Proglottids release immature eggs which are passed in the faeces.

Pathogenesis and Clinical Features

Infection may be asymptomatic, while some patients may present with intestinal obstruction. Abdominal discomfort, diarrhoea, nausea, weakness, weight loss and anaemia are the usual manifestations. The worm lives in the ileum where vitamin B_{12} absorption takes place. It competes with the host for vitamin B_{12} and may cause vitamin B_{12} deficiency anaemia.

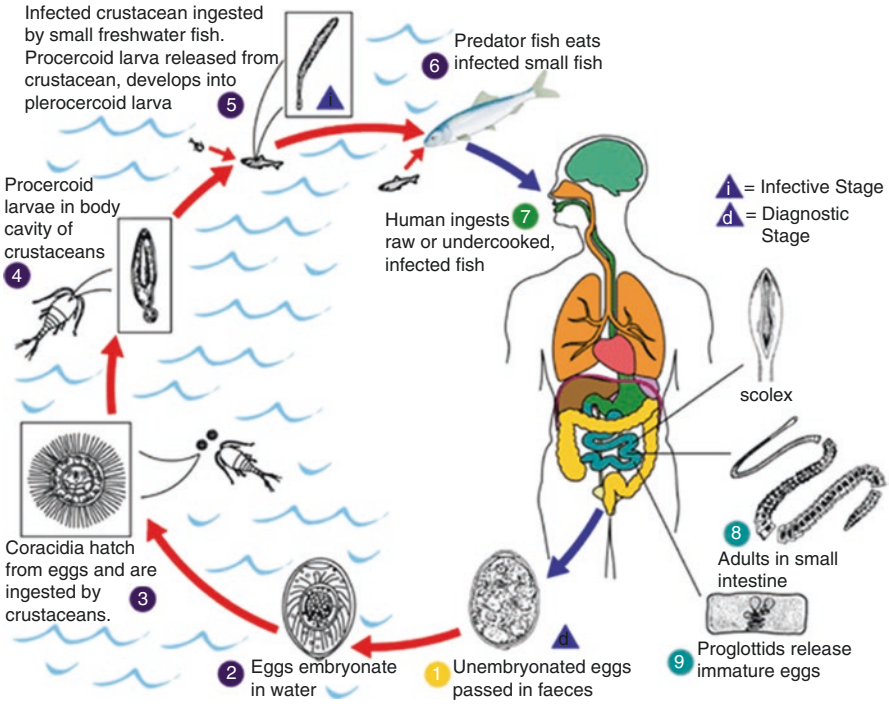


Fig. 11.2 Life cycle of *Diphyllobothrium latum* (Reproduced from https://www.cdc.gov/dpdx/diphyllobothriasis/index.html)

Diagnosis

1. Microscopic examination

   Detection of operculated eggs or gravid proglottids in faeces. The arrangement of the uterus in gravid proglottid at its center is frequently likened to a rosette.
2. Molecular diagnosis

   PCR on clinical specimens.

Treatment

Praziquantel (5–10 mg/kg orally in a single-dose therapy). Parenteral vitamin B_{12} should be given in vitamin B_{12} deficiency anaemia.

Prevention and Control

1. Proper cooking of fish
2. Deep freezing of fish (–10 °C for 24–48 h)
3. Proper sanitation
4. Periodical deworming of pet dogs and cats as they can be infected by eating contaminated raw fish
5. Treatment of cases

Spirometra

Distribution

Spirometra can accidentally infect human and cause sparganosis. Sparganosis has been reported mostly from Japan and Southeast Asia. The disease is caused by sparganum (plerocercoid larva) of the parasite.

Habitat

In human, plerocercoid larva is found in subcutaneous tissue and other organs. It does not grow into adult in human. Adult worms live in the intestinal tract of definitive host (cats and dogs).

Morphology

The sparganum larvae are white, wrinkled and ribbon shaped. They measure from a few millimetres to several centimetres in length. The anterior end can invaginate and appears like sucking grooves as seen in the scolex of the mature worm.

The eggs of *Spirometra* resemble the eggs of *Diphyllobothrium latum* but smaller.

Life Cycle (Fig. 11.3)

(*1*) Unembryonated eggs are passed in faeces of cats and dogs. (*2*) Eggs embryonate in water. (*3*) Coracidia hatch from eggs and are ingested by crustaceans. (*4*)

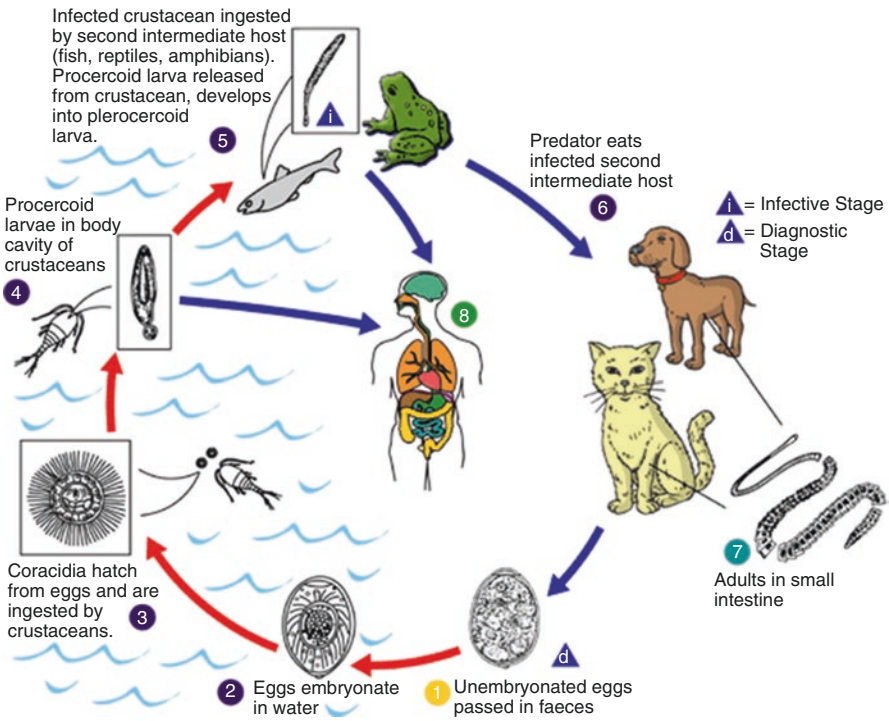


Fig. 11.3 Life cycle of *Spirometra*. (Reproduced from https://www.cdc.gov/dpdx/sparganosis/index.html)

Procercoid larvae develop in body cavity of crustaceans. (*5*) Infected crustaceans are ingested by second intermediate host (e.g. fish, reptiles, amphibians) and procercoid larvae develop into plerocercoid larvae. (*6*) Predator (dogs and cats) eats infected second intermediate host. (*7*) The plerocercoid larvae develop into adults in the small intestine of dogs and cats. (*8*) Human acquires infection by ingesting procercoid larvae in crustaceans or by ingesting plerocercoid larvae in second intermediate hosts or by applying raw poultices of the second intermediate hosts containing plerocercoid larvae on open wounds, lesions or the eyes for medicinal reasons.

Pathogenesis and Clinical Features

The sparganum (plerocercoid larva) are liberated from the second intermediate host (fish, reptiles, amphibians) in the human intestine. Humans can also acquire infection by ingesting cyclops containing procercoid larvae in contaminated water. The procercoid larvae will develop to the plerocercoid larvae and they will penetrate the intestinal wall and migrate to subcutaneous tissue and other organs. The early migratory stages are asymptomatic. When it reaches its final site, it begins to grow, causing painful inflammatory reaction in the surrounding tissues. The larvae do not encyst.

Clinical features of sparganosis depend on the organs or tissues affected which include subcutaneous nodules, periorbital oedema and in the CNS may cause seizures, parasthesias and hemiparesis.

Diagnosis

1. Surgical removal of the nodules and demonstration of the plerocercoid larva.
2. Antisparganum ELISA test.
3. CT and MRI scans are useful for diagnosis of cerebral sparganosis.

Treatment

Surgical removal is the treatment of choice. Antihelminthic drugs are not effective to treat infection with these larvae.

Prevention and Control

1. Filter and boil drinking water to remove and kill cyclops
2. Eating properly cooked fish or meat of reptiles and amphibians
3. Avoid applying raw meat of frogs and snakes as poultices on wounds

Cyclophyllidean Tapeworms

Taenia saginata and *Taenia solium*

Common name	
Taenia saginata	Beef tapeworm
Taenia solium	Pork tapeworm

Distribution

Taenia saginata and *Taenia solium* have a worldwide distribution.

Habitat

The adult worms of both *T. saginata* and *T. solium* live in the small intestine of human.

Morphology

The adult *T. saginata* is dorsoventrally flattened and segmented, measuring 5–10 m in length. The scolex of *T. saginata* is about 1–2 mm in diameter, bearing 4 suckers for attachment. The scolex has no rostellum or hooklets (Fig. 11.4a). The neck is long and narrow. The strobila consists of 1000–2000 proglottids. They are hermaphrodites. The gravid segments are about 20 mm long and 5 mm broad and each gravid segment has 15–30 lateral uterine branches (Fig. 11.4b). The gravid segments break away and are expelled singly out through the host's anus. The gravid segment can be seen moving actively.

Eggs of *T. solium* and *T. saginata* are identical. They are brown and spherical, measuring 31–43 μm in diameter. The shell is radially striated (Fig. 11.5). The embryo (oncosphere) has 6 hooklets.

Cysticercus bovis is the larva of *T. saginata*. The larva is the infective stage to humans. It is ovoid, milkywhite opalescent fluidfilled vesicle measuring about 5 mm × 10 mm in diameter and contains a single invaginated scolex (bladder worm). The cysticerci are found in the muscles of infected cattle. They can be seen grossly as white dots in the infected beef (measly beef). Cysticercus bovis infection is not reported in humans.

The adult *T. solium* is dorsoventrally flattened and segmented, measuring 2–3 m in length. The scolex of *T. solium* is about 1 mm in diameter, bearing 4 suckers for attachment. The scolex has rostellum and hooklets (Fig. 11.6a). The neck is short.

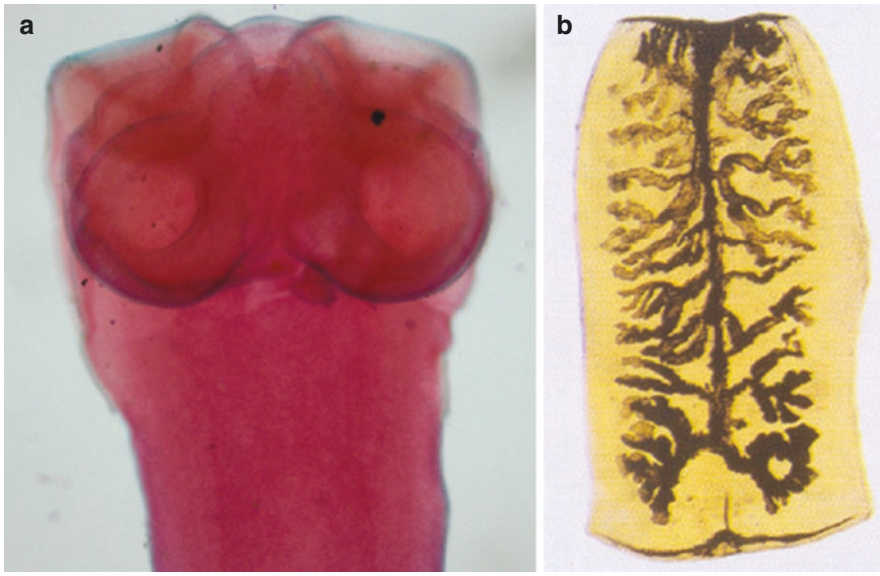


Fig. 11.4 *Taenia saginata.* (**a**) Scolex, (**b**) Gravid proglottid

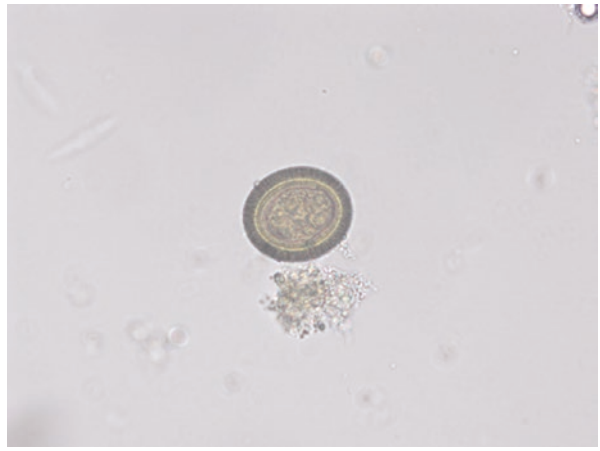


Fig. 11.5 Egg of *Taenia*

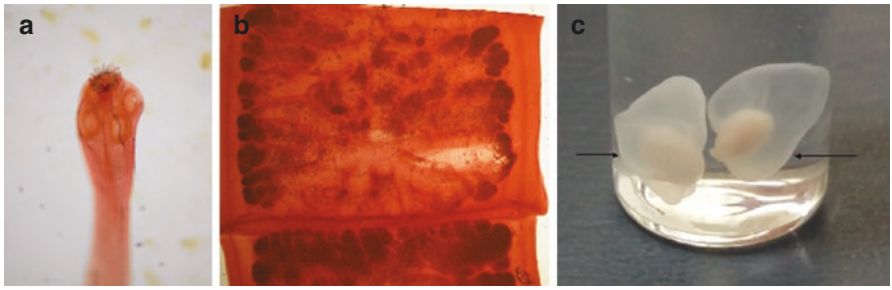


Fig. 11.6 *Taenia solium.* (**a**) Scolex, (**b**) Gravid proglottid, (**c**) Larvae (cysticercus cellulosae)

The strobila consists of less than 1000 proglottids. The gravid segments are about 12 mm long and 6 mm broad and each gravid segment has 7–13 lateral uterine branches (Fig. 11.6b). They are hermaphrodites. The gravid segments are expelled in chains through the host's anus.

Cysticercus cellulosae is the larval form of *T. solium* (Fig. 11.6c) and also the infective form of the parasite to humans. It can develop in various organs of pig as well as in human. Its morphology is similar to cysticercus bovis. The morphology of the invaginated scolex of cysticercus cellulosae is similar to the adult scolex of *Taenia solium*.

Life Cycle (Fig. 11.7)

(*1*) Eggs or gravid proglottids in faeces of infected humans are passed out. (*2*) Cattle (*T. saginata*) and pigs (*T. solium*) become infected by ingesting vegetation contaminated by eggs or gravid proglottids. (*3*) Oncospheres hatch, penetrate intestinal wall and circulate to muscles to develop into cysticerci. (*4*) Humans acquire infection by ingesting raw or undercooked infected meat containing the larvae. (*5–6*) Adults develop in the small intestine of human and scolex attaches to the mucosa of the small intestine.

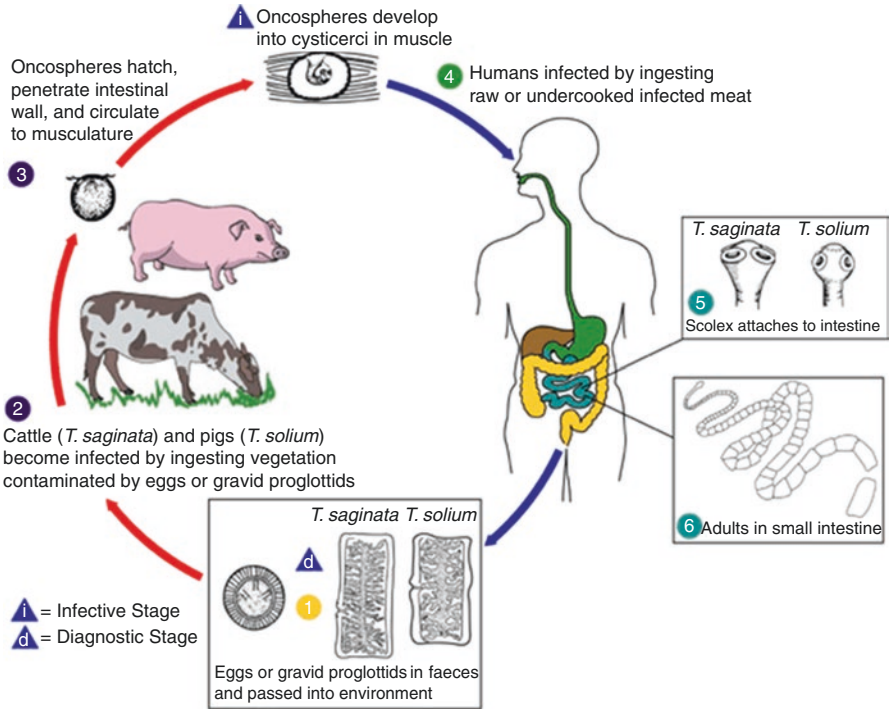


Fig. 11.7 Life cycle of *Taenia saginata* and *T. solium* (Reproduced from https://www.cdc.gov/dpdx/taeniasis/index.html)

Pathogenesis and Clinical Features

Intestinal taeniasis can be caused by both *T. saginata* and *T. solium.* It is mostly asymptomatic. In symptomatic infection, patient presents with vague abdominal discomfort, indigestion, nausea, diarrhoea and weight loss. Cases of acute intestinal obstruction and acute appendicitis have been reported.

Cysticercosis is caused by larval stage (cysticecus cellulosae) of *T. solium*. Humans acquire infection after ingesting eggs of *T. solium* in contaminated food or water. Any organ or tissue may be involved, the most common being subcutaneous tissues, brain and eye. The cysticercus is surrounded by a fibrous capsule except in the eye and ventricles of the brain. The degenerating larvae evoke a cellular reaction with infiltration of neutrophils, eosinophils, lymphocytes and plasma cells. This is followed by fibrosis and death of the larva which eventually calcify. The clinical features depend on the site affected. Subcutaneous nodules are mostly asymptomatic. Muscular cysticercosis may cause acute myositis. Neurocysticercosis (cysticercosis of the brain) is the most common and most serious form of cysticercosis. Majority of adult onset epilepsy is due to neurocysticercosis. Headache is also a common manifestation of neurocysticercosis. In ocular cysticercosis, patients may present with blurred vision or loss of vision.

Diagnosis of Taeniasis

1. *Microscopic examination*

   Detection of characteristic eggs, scolex or gravid proglottids of *Taenia* in faeces. Species identification cannot be made from the eggs since the eggs of *T. saginata* and *T. solium* look alike. Eggs can also be detected around the perianal region by cellophane swab technique.
2. *Molecular diagnosis*

   PCR on faecal sample.

Diagnosis of Cysticercosis

1. *Serodiagnosis*
2. *Biopsy*

   HPE examination of biopsied lesion to show the invaginated scolex with suckers and hooks.
3. *Imaging*

   Calcified cysticerci can be detected by radiography of subcutaneous tissue and muscles. X-ray of the skull may demonstrate calcified cyst in the brain. CT scan of brain is the best method for detecting dead calcified cysts. MRI scan of the brain is more helpful in detection of non-calcified cysts and ventricular cysts.

Treatment

1. Intestinal taeniasis

   Praziquantel (5–10 mg/kg orally in a single-dose therapy) is the drug of choice. Niclosamide (2 g orally in a single-dose therapy) is an alternative drug.
2. Cysticercosis

   Excision is the best method, where the cysts are accessible. For cerebral cysticercosis, praziquantel (50 mg/kg in 3 divided doses daily for 15 days) and albendazole (15 mg/kg daily (maximum 800 mg/day) for 8 days) may be administered. Corticosteroids may be given along with praziquantel or albendazole to reduce the inflammatory reactions caused by the dead cysticerci. Antiepileptic drugs should be given. Surgical intervention is indicated for hydrocephalus.

Prevention and control

1. Proper cooking of beef and pork
2. Proper sanitation
3. Personal hygiene
4. Avoid eating raw vegetables grown in polluted soil to prevent from acquiring cysticercosis
5. Treatment of cases with taeniasis solium as they can develop cysticercosis due to autoinfection

Taenia saginata asiatica

Taenia saginata asiatica is closely related to *T. saginata* and is found mainly in Asia. It is morphologically similar to *T. saginata* except it is smaller in size. Pig is its intermediate host and its cysticerci are located primarily in liver of pig. Clinical features, diagnosis and treatment are similar to that of *T. saginata*.

Echinococcus granulosus

Common name	Dog tapeworm

Distribution

The hydatid disease caused by *E. granulosus* is prevalent in most parts of the world and is most extensive in the sheep and cattle rearing countries (Australia, Africa and South America).

Habitat

The adult worm lives in the small intestine of dogs and other canine. The larval stage (hydatid cyst) is found in humans and herbivorous animals (sheep, goat, cattle and horse).

Morphology

Adult worm measures 3–6 mm in length. It consists of a scolex, neck and strobila. The scolex is pyriform, with 4 suckers and a rostellum bearing 2 circular rows of hooklets. The strobila is composed of 3 proglottids; immature, mature and gravid proglottids. The gravid proglottid contains branched uterus filled with eggs. The lifespan of the adult worm is 6–30 months.

The eggs of *Echinococcus* are indistinguishable from those of *Taenia* species.

The larval form (hydatid cyst) develops in various organs of the intermediate host (Fig. 11.8). At the site of deposition, the embryo slowly develops into a hollow bladder or cyst filled with fluid. This becomes the hydatid cyst. It enlarges slowly and reaches a diameter of 0.5–1 cm in about 6 months. The growing cyst evokes host tissue reaction leading to the formation of fibrous capsule around it. The cyst wall secreted by the embryo consists of 3 layers; pericyst, ectocyst and endocyst. The cyst is filled with fluid which is antigenic and its release into circulation may cause anaphylaxis.

From the germinal layer of the endocyst, small knobs protrude into the lumen of the cyst. These enlarge, become vacuolated and are filled with fluid. These are brood capsules which are initially attached to the germinal layer by stalks, but later are detached and released into the fluidfilled cyst cavity. From the inner wall of the brood capsules, protoscolices develop. Inside mature hydatid cysts, further

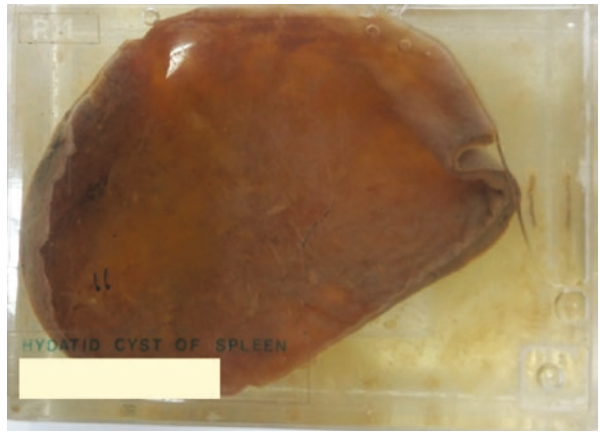


Fig. 11.8 Hydatid cyst of spleen

generation of cyst, daughter cysts and grand-daughter cysts may develop. Cyst contains hydatid sand which is made of protoscolices and hooklets. The cyst takes many years to grow into a large cyst, causing clinical illness.

Life Cycle (Fig. 11.9)

(*1*) Adult worm is found in the small intestine of definitive host (dogs and other canidae). (*2*) Embryonated eggs are passed out in the faeces of the definitive host. Intermediate hosts (human, sheep, goats, etc.) acquire infection by ingesting embryonated eggs. (*3–4*) The egg hatches releasing oncosphere which penetrates the intestinal wall and is carried by the blood circulation to various organs (liver, lungs, heart, spleen and bones) where it develops into hydatid cyst. (*5–6*) When the definitive host ingests hydatid cyst in organs of intermediate host, the protoscolices from the cyst are released and the scolex attaches to the intestine to develop into adults.

Pathogenesis and Clinical Features

Hydatid cyst infection is often asymptomatic. Clinical illness develops when the hydatid cyst causes obstruction or pressure effect. In majority of cases, the primary hydatid cyst occurs in liver, mostly in the right lobe. Clinical manifestations are hepatomegaly, pain and obstructive jaundice. The next common site is the lower lobe of the right lung. Cough, haemoptysis, chest pain, pneumothorax and dyspnoea are the usual presentation. In the kidney, hydatid cyst causes pain and haematuria. Other sites affected include spleen, brain, pelvic organs, orbit and bones. Cerebral hydatid cysts may present as focal epilepsy. Hydatid cyst in bones may cause pathological fractures. Hypersensitivity to hydatid fluid seeping through the capsule may cause urticaria. Massive release of hydatid fluid from spontaneous rupture or surgical procedure may cause anaphylactic shock.

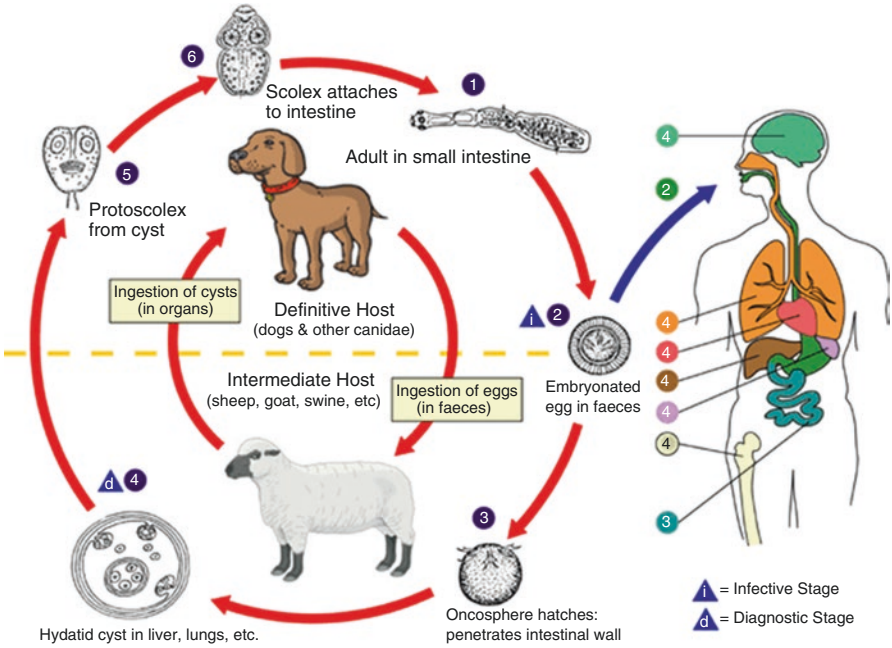


Fig. 11.9 Life cycle of *Echinococcus granulosus* (Reproduced from https://www.cdc.gov/dpdx/echinococcosis/index.html)

Diagnosis

1. *Serodiagnosis*
2. *Molecular diagnosis*
   PCR on clinical specimens.
3. *Microscopic examination*
   Detection of scolices and hooklets from aspirated cyst fluid.
4. *Imaging*
   Radiological examinations and other imaging techniques such as ultrasonography (USG), CT scan and MRI.

Treatment

Puncture, aspiration, injection and reaspiration (PAIR) is carried out in early stages of the disease. Surgical treatment in cases where the cysts are accessible. Patients with small or multiple cysts can be treated with albendazole (400 mg twice/day for 1–6 months). Praziquantel may be useful prior to surgery or in cases of spillage of cyst contents during surgery.

Prevention and Control

1. Prevent dogs from eating animal carcass or offal
2. Periodical deworming of dogs
3. Personal hygiene

Echinococcus multilocularis

This parasite causes rare but serious condition of alveolar or multilocular hydatid disease in humans. Its distribution is from Siberia to Canada. The adult worm of *Echinococcus multilocularis* is smaller than *E. granulosus* and lives in the intestines of foxes, dogs and cats which are the definitive hosts. Rodents are the main intermediate hosts. Human acquires infection from ingesting eggs of *E. multilocularis* from faeces of definitive host. The multilocular infiltrating lesion appears like an invasive growth, without any fluid or brood capsules and can be mistaken for a malignant tumour. The liver is the most commonly affected organ. Patients present with right upper quadrant and epigastric pain, hepatomegaly and obstructive jaundice. It may metastasize to other organs. The prognosis is poor and can be fatal if not treated. Treatment is by surgical resection when possible. Albendazole is recommended after surgery or in cases where surgery is not an option.

Hymenolepis nana

Common name	Dwarf tapeworm

Distribution
It is cosmopolitan in distribution but is more common in tropical countries. Infection is most common in children.

Habitat
The adult worm lives in the ileum of human.

Morphology
Hymenolopis nana is the smallest intestinal cestode that infects human. The adult worm is 5–45 mm in length and less than 1 mm thick. The scolex has 4 suckers and a retractile rostellum with a single row of hooklets. It has a long slender neck and a strobila consisting of 200 or more proglottids, which are much broader than long. The uterus is lobulated with 3 round testes. Eggs are released in the intestine by disintegration of the gravid segments.

The egg is roughly spherical or ovoid, 30–40 μm in size (Fig. 11.10). It has a thin outer membrane and an inner embryophore enclosing the hexacanth oncosphere. The space between the 2 membranes contains 4–8 thread-like polar filaments arising from 2 knobs on the embryophore. Eggs are immediately infective when passed in faeces.

Life Cycle (Fig. 11.11)
(*1*) Embryonated eggs are passed out in faeces of infected human. (*2*) The eggs are ingested by insects (flea, beetle) and develop into cysticercoid larvae. (*3*) Humans and rodents are infected when they ingest cysticercoid infected arthropods.

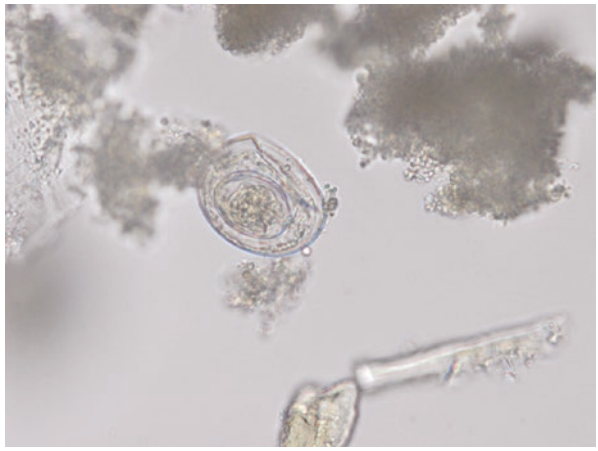


Fig. 11.10 *Hymenolepis nana* egg

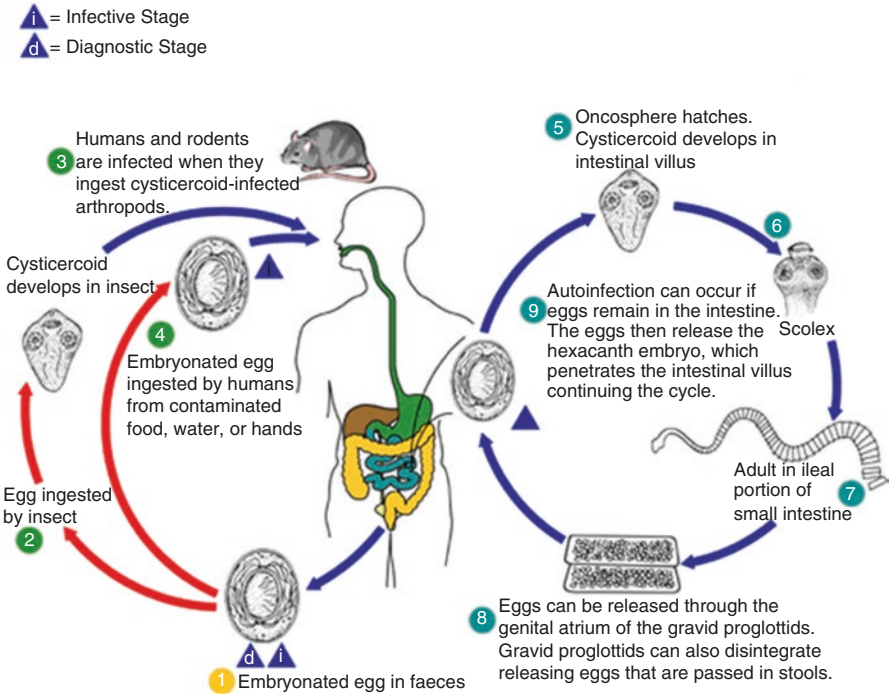


Fig. 11.11 Life cycle of *Hymenolepis nana* (Reproduced from https://www.cdc.gov/dpdx/hymenolepiasis/index.html)

(*4*) Human can also acquire infection by ingesting embryonated eggs from contaminated food, water, or via contaminated hands. (*5*) The egg hatches and releases oncosphere which develops into cysticercoid in the intestinal villus. (*6–7*) The larva breaks out of the villus in the lumen of the small intestine and grows into an adult worm. The scolex of the adult worm attaches to the ileal portion of the small intestine. (*8*) Eggs are released by the gravid proglottids and are passed out in faeces.

Pathogenesis and Clinical Features

Hymenolepiasis is usually asymptomatic but in heavy infections, patients may present with nausea, anorexia, abdominal pain, diarrhoea and irritability. Anal pruritus may be due to an allergic response.

Diagnosis

1. *Microscopic examination*
   Detection of characteristic eggs in faeces.

Treatment

Praziquantel (25 mg/kg in a single-dose therapy) is the drug of choice. It acts both against the adult worms and the cysticercoids in the intestinal villi. Alternative drug is nitazoxanide.

Prevention and Control

1. Personal hygiene
2. Proper sanitation
3. Avoid consumption of contaminated food and water by flea or beetles
4. Rodent control

Hymenolepis diminuta

Its common name is rat tapeworm and is a common parasite of rats and mice. It measures 10–60 cm in length. Its eggs are bigger than that of *H. nana* and it has no polar filaments. Its life cycle is similar to that of the murine strain of *H. nana.* Human infection follows accidental ingestion of infected rat fleas. Most infections are asymptomatic. Occasionally, patients may complain of mild gastrointestinal symptoms.

Dipylidium caninum

Distribution

This common double-pore tapeworm of dogs and cats may cause human infection, mainly in children. It is distributed globally.

Habitat

The adult tapeworm resides in the small intestine of the host.

Morphology

The adult worm in the intestine is about 10–70 cm long. The scolex has 4 prominent suckers and a retractile rostellum with up to 7 rows of spines. It has 60–175 melon seed-like proglottids. The mature proglottid has 2 genital pores, one on either side. Gravid proglottids which contain packets of eggs enclosed by capsules are passed out of the anus of the host singly or in groups.

Life Cycle (Fig. 11.12)

(*1–2*) The eggs or proglottids passed out in faeces of dogs and cats are eaten by larval stages of dog flea (*Ctenocephalides canis*) and cat flea (*C. felis*). (*3*) The oncospheres hatch and penetrate the intestinal wall to develop into cysticercoid in the body cavity of the flea larva. (*4*) Adult fleas harbour the infective cysticercoid. (*5–7*) Definitive hosts including humans are infected by ingesting fleas containing cysticercoid. (*8*) Adult worm develops with scolex attached to the small intestine.

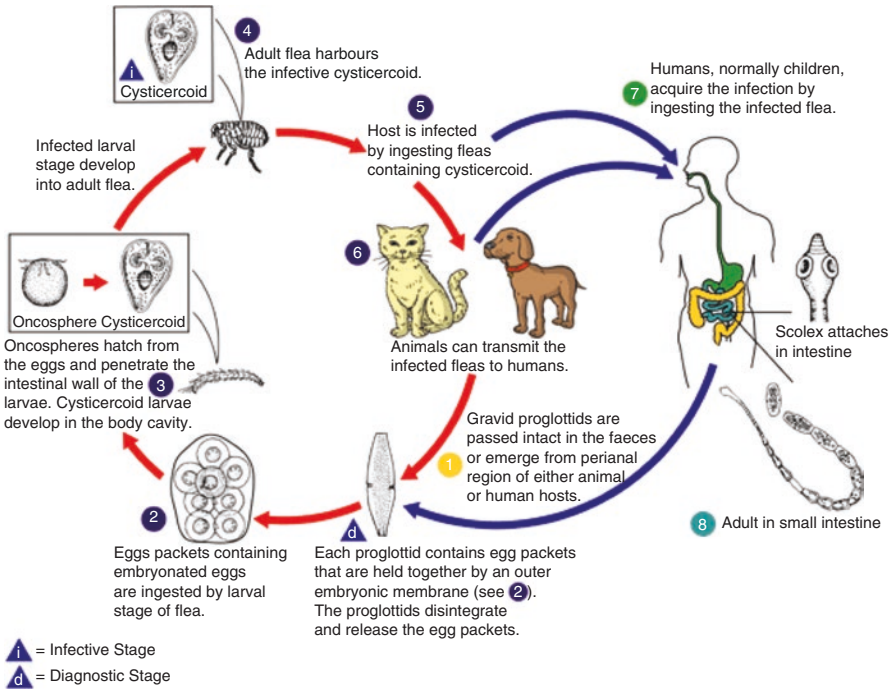


Fig. 11.12 Life cycle of *Dipylidium caninum* (Reproduced from https://www.cdc.gov/dpdx/dipylidium/index.html)

Pathogenesis and Clinical Features

Gravid proglottids may migrate actively from the anus. Human infection is generally asymptomatic. Abdominal pain, diarrhoea, and anal pruritus may occur in some patients.

Diagnosis

The diagnosis is made by identification of proglottids or egg packets in stool via microscopy.

Treatment

The drug of choice is praziquantel (5–10 mg/kg orally in a single-dose therapy).

Prevention and Control

1. Periodic deworming of infected dogs and cats
2. Control of fleas so that the animals do not become reinfected
3. Treatment of cases

Trematodes: Flukes

12

General Characteristics

Trematodes are unsegmented helminths, flat, broad and leaf shaped. They have large prominent suckers. Trematodes are hermaphrodites except for schistosomes. Their eggs are operculated except for schistosome eggs. Snails are the only intermediate host for schistosomes and are the first intermediate host for other trematodes. Metacercaria is the infective stage for trematodes except for schistosomes whereby cercariae is the infective stage. Trematodes are classified as in Table 12.1.

Table 12.1 Classification of trematodes of medical importance based on habitat

Habitat	Trematode
Blood	**Blood fluke** 1. *Schistosoma haematobium* (In the vesical and pelvic venous plexuses) 2. *Schistosoma mansoni* (In the inferior mesenteric vein) 3. *Schistosoma japonicum* (In the superior mesenteric vein)
Biliary tract	**Liver fluke** 1. *Clonorchis sinensis* 2. *Opisthorchis viverrini* 3. *Fasciola hepatica*
Intestine	**Intestinal fluke** 1. *Fasciolopsis buski* 2. *Heterophyes heterophyes* 3. *Metagonimus yokogawai*
Respiratory tract	**Lung fluke** 1. *Paragonimus westermani*

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Blood Flukes

Schistosoma haematobium

Distribution
Schistosoma haematobium is endemic in most parts of Africa and West Asia.

Habitat
The adult worms live in the vesical and pelvic venous plexuses of humans.

Morphology
The adult male worm is 10–15 mm long by 1 mm thick and is covered by a finely tuberculated cuticle. It has 2 muscular suckers: a small oral sucker and a large prominent ventral sucker. Immediately behind the ventral sucker and extending to the caudal end is the gynecophoric canal, where the female worm is found. The adult female is 20 mm by 0.25 mm with the cuticular tubercles confined to the 2 ends. The gravid female worm contains 20–30 eggs in its uterus at one time and may pass up to 300 eggs a day.

The eggs are ovoid, about 150 μm by 50 μm, non-operculated, with a terminal spine (Fig. 12.1). The eggs contain ciliated miracidium and are laid in the venules of the vesical and pelvic plexuses. From the venules, the eggs penetrate the vesical wall by the action of the spine, assisted by a lytic substance released by the eggs. The eggs pass into the lumen of the urinary bladder together with some extravasated blood. They are excreted in the urine, more during midday, particularly towards the end of micturition. The eggs may be found in ectopic sites such as rectum where they generally die and evoke local tissue reactions.

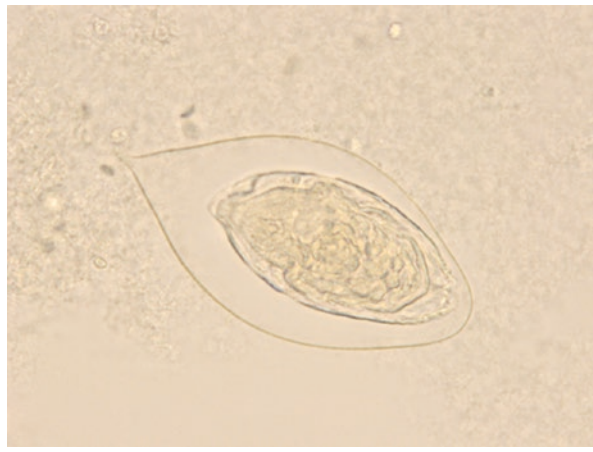


Fig. 12.1 *Schistosoma haematobium* egg

Life Cycle (Fig. 12.2)

(*1*) The eggs are passed in urine (*S. haematobium*) and in faeces (*S. mansoni* and *S. japonicum*) from infected humans. (*2*) Eggs hatch in water releasing miracidia. (*3*) Miracidia penetrate tissue of freshwater snail (intermediate host). (*4*) Sporocysts develop in snail. (*5*) Free swimming cercariae are released by snail into water. (*6*) Cercariae penetrate skin of human. (*7*) Cercariae lose their tails during penetration and become schistosomulae. (*8–9*) The schistosomulae are carried in blood circulation and migrate to portal blood in liver and mature into adults. (*10*) Paired adult worms migrate to venous plexus of bladder (*S. haematobium*) or mesenteric venules (*S. mansoni* and *S. japonicum*) where the female lay their eggs.

Pathogenesis and Clinical Features

Cercarial dermatitis presents with transient itching and petechial lesions at the site of entry of the cercariae, more often seen in visitors to endemic areas than among locals who may be immune due to repeated exposure. Acute systemic schistosomiasis may cause Katayama fever which presents with leucocytosis, eosinophilia and hepatosplenomegaly. Clinical features during oviposition include painless terminal

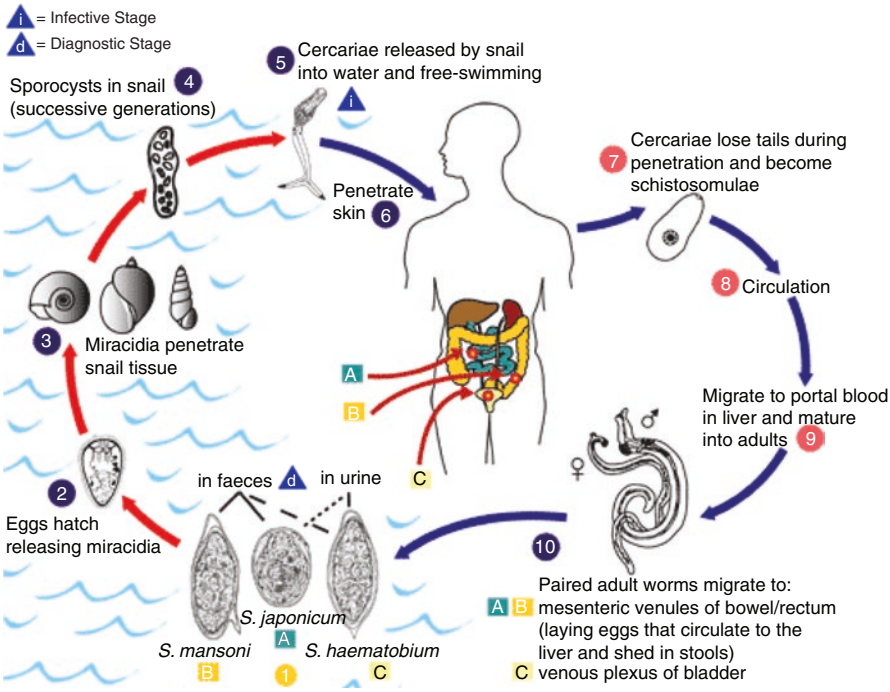


Fig. 12.2 Life cycle of blood flukes (Reproduced from https://www.cdc.gov/dpdx/schistosomiasis/index.html)

haematuria. Haematuria is initially microscopic, but become gross in heavy infection. Patients develop frequency of micturition with burning sensation. Cystoscopy shows hyperplasia and inflammation of bladder mucosa. In the chronic stage, there is generalized hyperplasia and fibrosis of the bladder mucosa with a granular appearance (sandy patch). At the sites of deposition of the eggs, there is dense infiltration with lymphocytes, plasma cells and eosinophils. Initially, the trigone is involved, but as it progresses, the entire mucosa becomes inflamed, thickened and ulcerated. Calculi form in the bladder around the eggs and blood clots. There may be obstructive hyperplasia of the ureters and urethra. Chronic urinary schistosomiasis has been associated with squamous cell carcinoma of the bladder.

Diagnosis

1. *Microscopic examination*
   Detection of eggs with characteristic terminal spines in centrifuged urine sample. Eggs which are deposited in rectum may be occasionally found in faeces.
2. *Biopsy*
   Bladder mucosa or rectal biopsies to demonstrate eggs.
3. *Serodiagnosis*
4. *Molecular diagnosis*
   PCR on clinical samples.

Treatment

Praziquantel (40 mg/kg/day orally in 2 divided doses for 1 day) is the drug of choice. Metrifonate is the alternative drug.

Prevention and Control

1. Proper disposal of urine and faeces
2. Treatment of infected persons
3. Avoid swimming, bathing and washing in snail-infested water
4. Control of snails

Schistosoma mansoni

Distribution

It is widely distributed in Africa, South America and the Caribbean islands.

Habitat

Adult worm lives in the inferior mesenteric vein.

Morphology

Schistosoma mansoni resembles *S. haematobium* in morphology and life cycles, except the adult worms are smaller and their integuments are covered with coarse

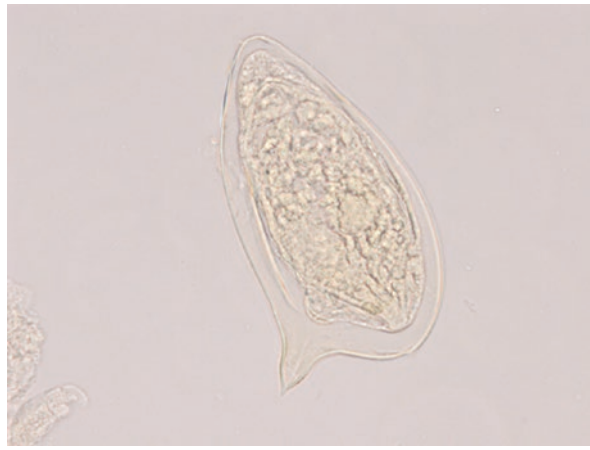


Fig. 12.3 *Schistosoma mansoni* egg

tubercles. The uterus of the gravid female contains very few eggs (1–3 only). The egg has a lateral spine (Fig. 12.3).

Life Cycle

Similar to *S. haematobium*

Pathogenesis and Clinical Features

Cercarial dermatitis may develop after skin penetration by the cercariae. It is self-limiting. Katayama fever may develop in acute infection. Symptoms of schistosomiasis mansoni are mainly intestinal. Patients develop colicky abdominal pain and dysentery, which may persist intermittently for many years. The eggs deposited in the intestinal wall of colon and rectum, cause inflammatory reactions causing granulomas, hyperplasia and followed by fibrosis. Eggs that are carried through portal circulation to the liver may cause hepatosplenomegaly, periportal fibrosis and portal hypertension.

Diagnosis

1. *Microscopic examination*
   Detection of eggs with lateral spines in stool sample. Stool concentration methods may be used in light infection.
2. *Biopsy*
   Biopsy of rectal mucosa to demonstrate eggs.
3. *Serodiagnosis*
4. *Molecular diagnosis*
   PCR on stool sample.

Treatment

Praziquantel (40 mg/kg/day orally in 2 divided doses for 1 day) is the drug of choice. Oxamniquine is also effective.

Prevention and Control
Same as *S. haematobium*

Schistosoma japonicum

Common name	Oriental blood fluke

Distribution
Schistosoma japonicum is found in the Far East, Japan, China, Taiwan, Philippines and Sulawesi.

Habitat
The adult worms are seen in the venules of the superior mesenteric vein.

Morphology
Morphologically, they are similar to *S. haematobium* and *S. mansoni* except the adult male is comparatively slender with smooth cuticle. The uterus of gravid female contains as many as 100 eggs at one time and may pass out 3500 eggs daily. The egg has a small lateral knob (Fig. 12.4).

Life Cycle
Similar to *S. haematobium*

Pathogenesis and Clinical Features
Its pathogenesis is similar to that of *S. mansoni*, but because of its higher egg output, the clinical manifestations are more severe. During the acute phase,

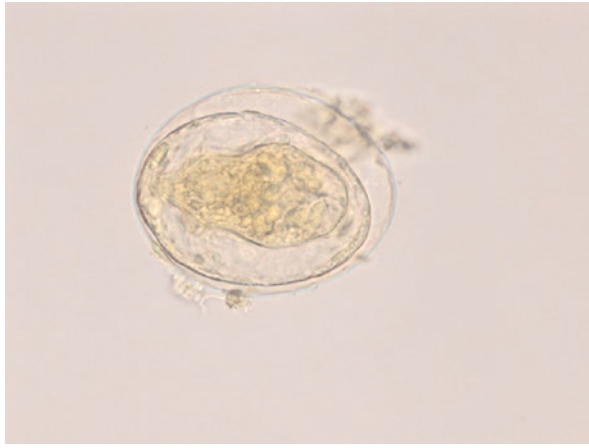


Fig. 12.4 *Schistosoma japonicum* egg

Katayama fever is similar to that seen in *S. mansoni.* Intestinal manifestations are colicky abdominal pain and dysentery. Patient may also develop anaemia. There is hepatomegaly with periportal fibrosis and portal hypertension.

Diagnosis
Similar to that of *S. mansoni*

Treatment
Praziquantel (60 mg/kg/day orally in 3 divided doses for 1 day) is the drug of choice.

Prevention and Control
Similar to that of *S. haematobium*

Schistosoma intercalatum

This species, first recognized in 1934 is found in West and Central Africa. The fully embryonated eggs with terminal spines are passed in stool. Human acquires infection through penetration of skin by cercariae. The adults are found in the mesenteric venules of the colon. The disease produced in human is relatively benign. Diagnosis is made by the detection of eggs in faeces and rectal biopsy. Praziquantel (40 mg/kg/day orally in 2 divided doses for 1 day) is the drug of choice.

Schistosoma mekongi

This species was first recognized in 1978 and is found in Thailand, Laos and Cambodia. It is closely related to *S. japonicum* but *S. mekongi* eggs are smaller and have a small lateral spine. The adult worms are found in the mesenteric venules. Human and dog are the definitive hosts. Human acquires infection through penetration of skin by cercariae. It produces a mild disease in humans. Praziquantel (60 mg/kg/day orally in 3 divided doses for 1 day) is the drug of choice.

Schistosomal Dermatitis

Schistosomes of birds and semiaquatic mammals produce cercariae that are capable of penetrating human skin but cannot develop into adults. Humans may present with dermatitis which is frequently more severe than the dermatitis produced by human schistosomes.

Liver Flukes

Clonorchis sinensis

Common name	The Chinese liver fluke, oriental liver fluke

Distribution
Human clonorchiasis occurs in Japan, Korea, Taiwan, China and Vietnam.

Habitat
Adult worm lives in the biliary tract.

Morphology
The adult worm has a flat, transparent, spatulate body; pointed anteriorly and rounded posteriorly (Fig. 12.5a). It is 10–25 mm long and 3–5 mm broad. The adult worm can survive many years in the biliary tract. The worm is hermaphrodite and passes eggs into the bile duct. The testes of the adult worm are branched.

Its eggs are broadly ovoid, 30 µm by 15 µm with a yellowish brown (bile-stained) shell. It is jug shaped and operculated with characteristic shoulders (Fig. 12.5b). At the terminal end of the egg, a small knob is sometimes visible. The eggs passed in faeces contain ciliated miracidia.

Life Cycle (Fig. 12.6)
(*1*) Embryonated eggs are passed out in faeces of infected human. (*2*) The eggs in water are ingested by freshwater snail. (*3*) Free swimming cercariae released by the snail encyst in the skin or flesh of freshwater fish. (*4*) The metacercariae in flesh or skin of freshwater fish are ingested by human host. (*5–6*) The metacercariae excyst in the duodenum and adults develop in the biliary duct.

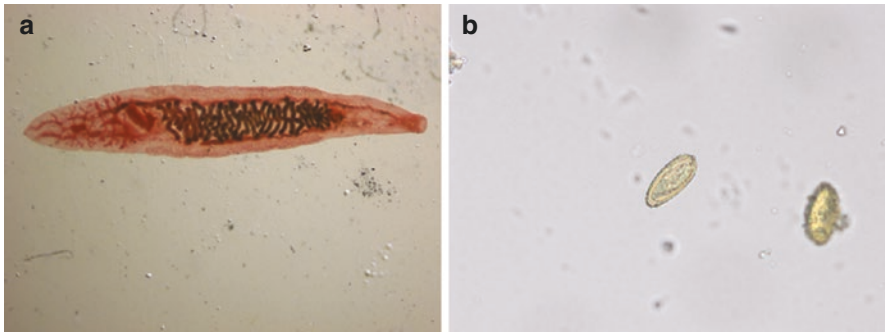


Fig. 12.5 *Clonorchis sinensis.* (**a**) Adult, (**b**) Egg

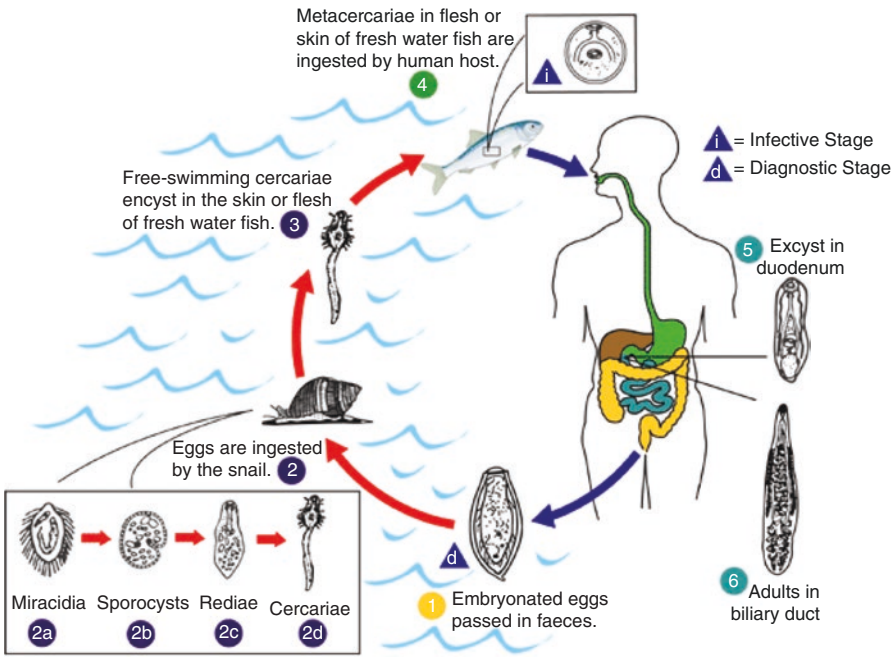


Fig. 12.6 Life cycle of *Clonorchis sinensis* (Reproduced from https://www.cdc.gov/dpdx/clonorchiasis/index.html)

Pathogenesis and Clinical Features

In endemic areas, most infected persons are asymptomatic. The migration of the larva up the bile duct induces desquamation, followed by hyperplasia and adenomatous changes. The adult worm may cause obstruction of the common bile duct causing cholangitis. Acute presentations are fever, epigastric pain, diarrhoea and hepatomegaly. Chronic infection may result in calculus formation. Some patients may progress to biliary cirrhosis and portal hypertension. Clonorchiasis has been associated with cholangiocarcinoma.

Diagnosis

1. *Microscopic examination*

   Detection of eggs in faeces or aspirated bile. Identification of adult worm extracted during surgical treatment.
2. *Serodiagnosis*

   Not very useful because of cross reaction against other trematodes.

Treatment

Drug of choice is praziquantel (75 mg/kg/day orally, 3 doses per day for 2 days). Surgical intervention in cases of obstructive jaundice.

Prevention and Control

1. Proper cooking of freshwater fish
2. Proper disposal of faeces
3. Control of snails
4. Treatment of cases

Opisthorchis viverrini

Its infection is usually asymptomatic but may sometimes resemble clonorchiasis. *Opisthorchis viverrini* is common in Thailand and is associated with cholangiocarcinoma. The life cycle and other features of *Opisthorchis* are similar to *Clonorchis*. Adult worm of *Opisthorchis* has lobe-shaped testes. The egg is similar in morphology to that of *Clonorchis*. Praziquantel (75 mg/kg/day orally, 3 doses per day for 2 days) is the drug of choice.

Fasciola hepatica

Common name	Sheep liver fluke

Distribution

It is worldwide in distribution, being found mainly in sheep-rearing countries.

Habitat

The parasite resides in the liver and biliary passages of the definitive host.

Morphology

The adult worm is large, leaf-shaped fleshy fluke, measuring 30 mm long and 15 mm broad. It has a conical projection anteriorly with an oral sucker and is rounded posteriorly. It is a hermaphrodite.

Its eggs are large, ovoid, operculated, measuring 140 μm by 80 μm in size (Fig. 12.7). Eggs are unembryonated when passed in faeces. Eggs of *Fasciola hepatica* and *Fasciolopsis buski* (intestinal fluke) cannot be differentiated.

Life Cycle (Fig. 12.8)

(*1*) Unembryonated eggs are passed in faeces of infected human, sheep or cattle. (*2*) The eggs embryonate in water. (*3*) Miracidia hatch and penetrate freshwater snail. (*4*) In the snail, they undergo development to the cercarial stage. (*5*) The free swimming cercariae encyst on water plants. (*6*) The metacercariae on water plants are ingested by human, sheep or cattle. (*7–8*) The metacercariae excyst in the duodenum and develop into adults in hepatic biliary ducts.

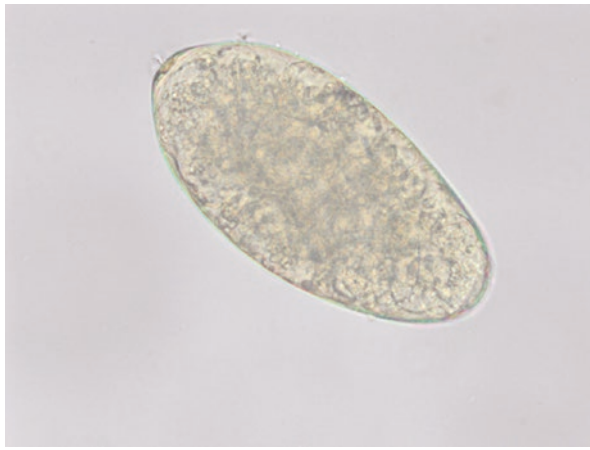


Fig. 12.7 *Fasciola hepatica* egg

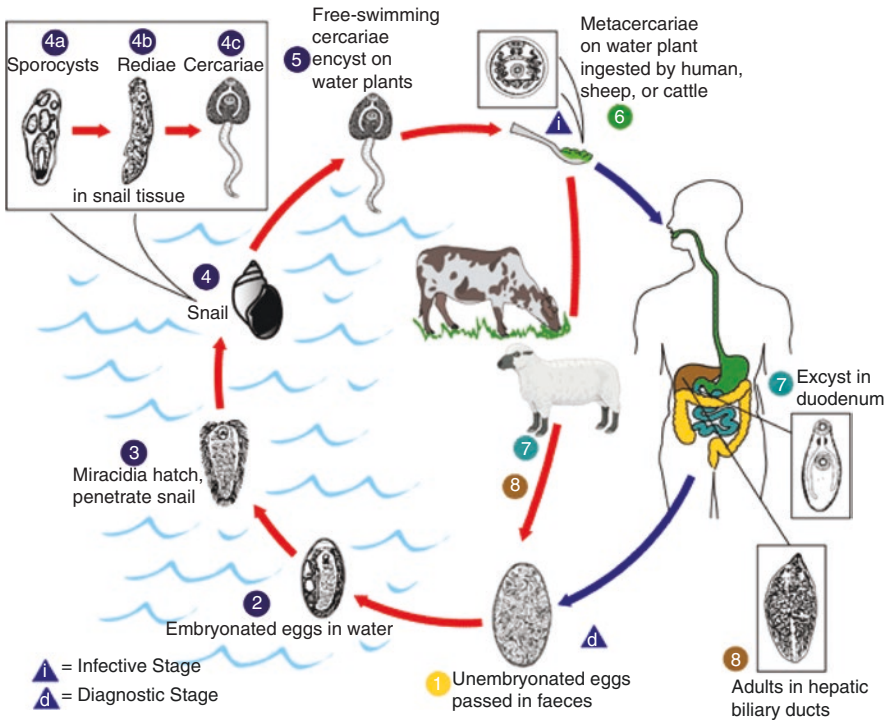


Fig. 12.8 Life cycle of *Fasciola hepatica* (Reproduced from https://www.cdc.gov/dpdx/fasciliasis/index.html)

Pathogenesis and Clinical Features

Fasciola hepatica causes mechanical damage due to its large size. It causes parenchymal injury while passing through the liver tissues. Humans develop severe inflammatory response as they are not its primary host. During larval migration, patients may present with fever, right upper quadrant pain, eosinophilia and hepatomegaly. The symptoms subside as parasites reach the liver. In chronic infection, patients may present with biliary obstruction, cholelithiasis, obstructive jaundice, biliary cirrhosis and anaemia. Its larvae may undergo ectopic migration and penetrate through the diaphragm to reach the lung. Other ectopic sites include subcutaneous tissue, genitourinary tract and brain.

Diagnosis

1. *Microscopic examination*
   Demonstration of eggs in faeces or aspirated bile.
2. *Serodiagnosis*
3. *Imaging*
   Ultrasound and CT abdomen.

Treatment

Triclabendazole (single oral dose of 10 mg/kg) is the treatment of choice. Bithionol is an alternative drug.

Prevention and Control

1. Prevent pollution of water courses with sheep and cattle faeces
2. Proper sanitation
3. Wash watercresses and other water vegetations, preferably in hot water or cook well before consumption

Intestinal Flukes

Fasciolopsis buski

Common name	Giant intestinal fluke

Distribution

It is a common parasite of humans and pigs in China and in Southeast Asian countries.

Habitat

The adult worm lives in the duodenum or jejunum of pigs and humans.

Morphology

The adult is a large fleshy worm, 20–75 mm long, 8–20 mm broad and 0.5–3 mm in thickness. It is elongated, ovoid in shape, with a small oral sucker and a large acetabulum. The adult worm has a lifespan of about 6 months.

The operculated eggs are similar to those of *Fasciola hepatica.* Eggs are laid in the lumen of the intestine.

Life Cycle (Fig. 12.9)

(*1*) Unembryonated eggs are passed in faeces of humans or pigs. (*2*) The eggs embryonate in water. (*3*) Miracidia hatch and penetrate freshwater snail. (*4*) In the snail, the miracidia develop to the cercarial stage. (*5–6*) The snail releases free swimming cercariae. The cercariae develop into metacercariae on water plants and are ingested by humans or pigs causing infection. (*7–8*) The metacercariae excyst in the duodenum and develop into adults in the small intestine.

Pathogenesis and Clinical Features

Adults that attach to the duodenal and jejunal mucosa cause inflammation and local ulceration. In heavy infections, the adult worms may cause partial obstruction of the bowel, malabsorption and protein-losing enteropathy. Clinical manifestations of fasciolopsiasis are diarrhoea and abdominal pain.

Diagnosis

1. *Microscopic examination*

Detection of eggs in faeces. Adult worms are rarely found in faecal specimen.

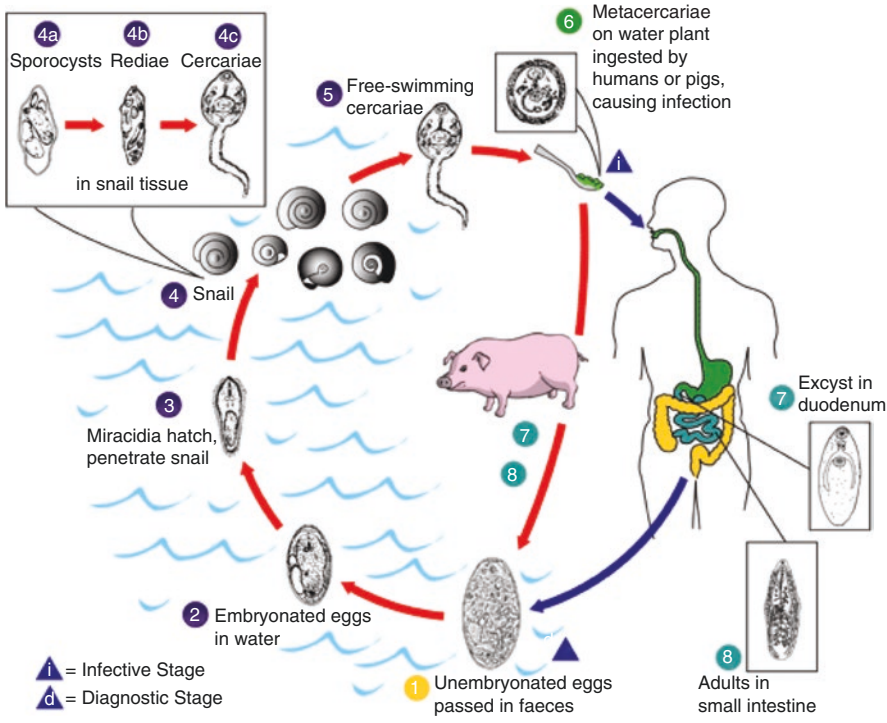


Fig. 12.9 Life cycle of *Fasciolopsis buski* (Reproduced from https://www.cdc.gov/dpdx/fasciolopsiasis/index.html)

Treatment
Drug of choice is praziquantel (75 mg/kg/day orally in 3 divided doses for 1 day). Hexylresorcinol and tetrachlorethylene have also been found useful.

Prevention and Control
1. Treatment of infected cases
2. Wash water vegetations, preferably in hot water or cook well before consumption
3. Prevent contamination of ponds and other water sources with pig or human excreta
4. Control of snails

Heterophyes heterophyes

This is the smallest intestinal trematode of human. The infection is prevalent in the Nile delta, Turkey and in the Far East. The adult worm lives in the small intestine and has a lifespan of about 2 months. Its definitive hosts are humans, cats, dogs, foxes and other fish eating mammals. Freshwater snail is its first intermediate host, and freshwater fish is its second intermediate host. Humans acquire infection through ingestion of infected freshwater fish. Praziquantel is the drug of choice.

Metagonimus yokogawai

It is found in the Far East, northern Siberia, Balkan states and Spain. Its definitive hosts are humans, pigs, dogs, cats and pelicans. The first intermediate host is the freshwater snail and second intermediate host is the freshwater fish. Humans acquire infection through ingestion of infected freshwater fish. Praziquantel is the drug of choice.

Lung Fluke

Paragonimus westermani

Common name	Oriental lung fluke

Distribution
The parasite is endemic in Japan, Korea, Taiwan, China and Southeast Asian countries.

Habitat
Adult worms live in the lungs, usually in pairs in cystic spaces that communicate with bronchi.

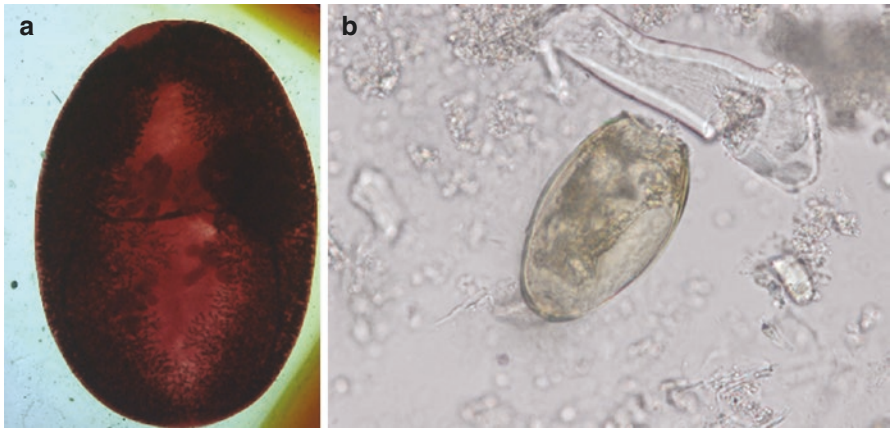


Fig. 12.10 *Paragonimus westermani.* (**a**) Adult, (**b**) Egg

Morphology

The adult worm is coffee bean shaped about 10 mm long, 5 mm broad and 4 mm thick. It is reddish brown in colour (Fig. 12.10a). It has an oral sucker and a ventral sucker. It has a lifespan of up to 20 years in humans.

The eggs are operculated, golden brown in colour and about 100 μm by 50 μm in size (Fig. 12.10b). Eggs are unembryonated when freshly laid.

Life Cycle (Fig. 12.11)

(*1*) Unembryonated eggs are passed out in sputum of infected human. (*2–3*) Embryonated eggs hatch in water to release miracidia which penetrate freshwater snail. (*4*) In the snail, the miracidia develop to the cercarial stage. (*5*) Cercariae released by the snail invade the crustacean and encyst into metacercariae. (*6*) Human ingests inadequately cooked or pickled crustaceans containing metacercariae. (*7–8*) The metacercariae excyst in the duodenum and the larvae penetrate the intestinal wall and migrate to the abdominal cavity, diaphragm and pleural cavity to the lungs. The larvae mature in the lungs to adults. Adults in cystic cavities in lungs lay eggs which are excreted in sputum. Eggs may be swallowed and are passed out in stool.

Pathogenesis and Clinical Features

In the lungs, the worms live in cystic spaces surrounded by fibrous capsule formed by the host tissues. Inflammatory reaction to the worms and eggs causes peribronchial granulomatous lesions, cystic dilatation of the bronchi, abscesses and pneumonitis. Patients present with cough, chest pain, dyspnoea and haemoptysis. The rusty sputum contains golden brown eggs. Chronic cases may mimic symptoms of pulmonary tuberculosis.

Paragonimiasis may also be extrapulmonary. Ectopic sites include abdomen and CNS. In the abdomen, it may cause abdominal pain and diarrhoea. In the CNS, it may cause Jacksonian epilepsy. Some children may present with mental retardation.

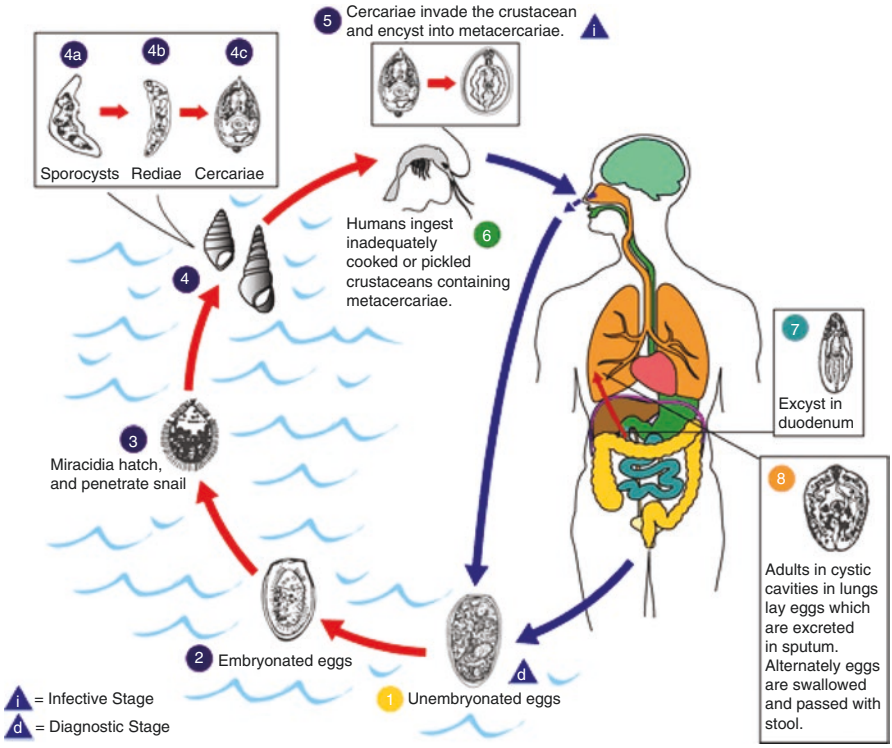


Fig. 12.11 Life cycle of *Paragonimus westermani* (Reproduced from https://www.cdc.gov/dpdx/paragonimiasis/index.html)

Diagnosis

1. *Microscopic examination*
   Detection of the eggs in sputum or faeces (if the patient swallows the eggs).
2. *Serodiagnosis*
3. *Molecular diagnosis*
   PCR on clinical specimens.
4. *Biopsy*
   Identification of species is made when adult or egg is recovered from the lesion in the lungs.

Treatment

Praziquantel (25 mg/kg orally 3 times per day for 2 days) is the drug of choice. Bithinol and niclofolan are also effective.

Prevention and Control

1. Adequate cooking of crabs and crayfish
2. Treatment of infected cases
3. Control of snails

Ectoparasites of Medical Importance

13

General Characteristics of Mites and Lice

The parasitic mites and lice are mainly ectoparasites. Mite is of the order Acarina. Louse is of the order Anoplura (sucking louse).

Sarcoptes scabiei

Distribution

This mite has a cosmopolitan distribution especially in crowded environment. It causes scabies and its infestation is more common in slumps, jails and orphanages.

Habitat

Skin of human.

Morphology

Sarcoptes scabiei is a small, oval, dorsally convex, ventrally flattened mite. The male measures 200–250 μm and the female measures 330–450 μm. It has 4 pairs of legs. The first 2 pairs of legs terminate in long tubular processes, each with a bell-shaped sucker (Fig. 13.1). The posterior 2 pairs of legs end in long bristles, but in males, the fourth pair have suckers. The dorsal surface bears spines, scales and bristles.

Life Cycle

The mites live in serpiginous cutaneous burrows. Both male and female mites burrow into the corneous layer of the skin. The female deposits up to 40–50 eggs in the burrow during its lifespan of 4–5 weeks. Hexapod larvae emerge from the eggs in 3–10 days. The larva develops into an eight-legged nymph which later matures into adult stage. The life cycle is completed in 8–15 days.

Scabies is transmitted by close personal contact with an infected person.

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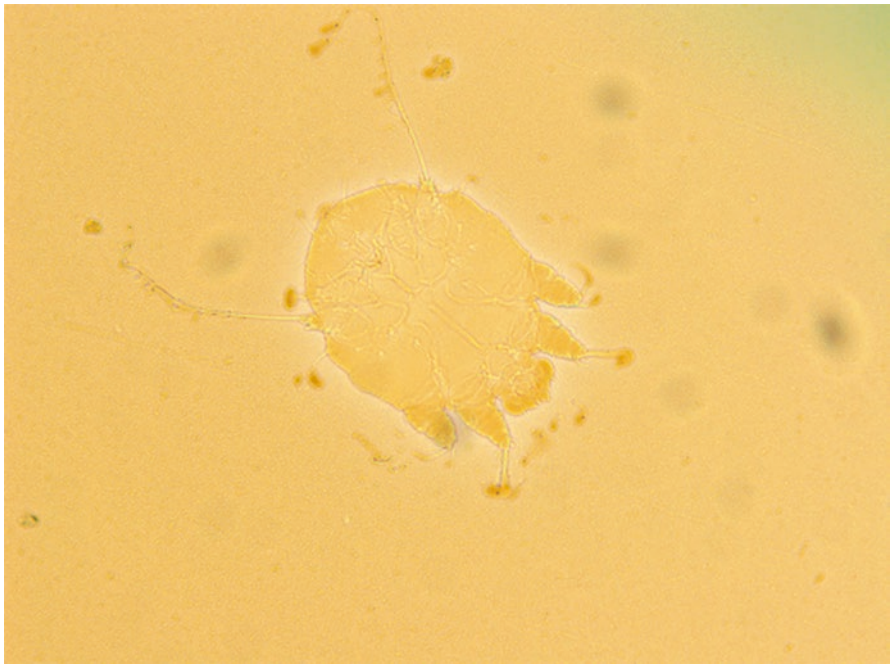


Fig. 13.1 Adult of *Sarcoptes scabiei*

Pathogenesis and Clinical Features

The common sites for cutaneous lesions are the interdigital spaces, flexor surfaces of the wrists and forearms, elbows, axillae, inguinal region and genitalia. The main symptom is itch. The lesions appear as slightly reddish elevated tracks in the skin. Intense itching, aggravated by sweat causes scratching which spread the infestation and causes secondary bacterial infection. As a result, multiple papular, vesicular and pustular lesions may be produced.

Crusted or Norwegian scabies is seen in patients with AIDS.

It is highly contagious with huge numbers of mites. Pruritus may be minimal or absent.

Diagnosis

The types of lesion, itching and rash are suggestive of scabies.

1. *Microscopic Examination*

Demonstration of the mite, eggs, or faecal material after scraping or teasing the lesion with the tip of a scalpel blade or a sterile needle.

Treatment

1. Permethrin 5%, cream/lotion
2. Lindane 1%, lotion/cream
3. Crotamiton 10%, ointment

4. Ivermectin, oral drug is used for patients with altered immune systems, crusted scabies, or those who do not respond to the prescription lotions and creams (not for children below 5 years old).

The cream/lotion should be applied to all skin surfaces for 8–12 h and then washed off. Treatment should be repeated in a week if infestation is still present. Secondary bacterial infection in scabies has to be treated with antibiotics.

Prevention and Control

1. Treatment of infected individuals
2. Sterilization of garments and beddings
3. Personal cleanliness

Lice

Distribution

Lice are exclusively human parasites and have a worldwide distribution.

Habitat

The parasitic lice of humans include 3 species:

1. *Pediculus humanus capitis* (head louse)
2. *Pediculus humanus humanus* (body louse)
3. *Phthirus pubis* (crab louse/pubic louse)

Morphology

Lice are small, dorsoventrally flattened, wingless insects. The insect has a head, thorax and abdomen. The thorax has 3 segments and each segment bears a pair of strong legs that terminate in a single hook-like claw. Both body and head lice are identical, and they measure 2–3 mm in length (Fig. 13.2). The body louse is more robust.

The crab louse is small, measuring 0.8–1.2 mm, oblong with rectangular head, short-segmented abdomen and 3 pairs of legs with big claws arising from the thorax (Fig. 13.3).

The eggs (nits) are operculated, white in colour, measuring 0.6–0.8 mm and are deposited and firmly attached to the hairs (head louse and crab louse) or to the fibres of clothing (body louse).

Life Cycle

After eggs are deposited by the female louse, they hatch in 5–11 days. The nymph develops within the egg case and emerges through the opened operculum. It undergoes 3 moults within 2 weeks. The life cycle of body/head louse takes 18 days and that of crab louse 15 days. The lifespan of the adult is about 1 month.

The lice are readily transmitted from host to host through close contact. The head louse is easily transmitted by brushes, combs and hats. It is most prevalent in school



Fig. 13.2 Adult of *Pediculus humanus capitis/P. h. humanus*

children. The body louse is transmitted by contact or by clothing infested with nits. The crab louse is usually transmitted during sexual intercourse and less frequently through toilet seats, clothing or bedding.

Pathogenesis and Clinical Features

Both sexes take a blood meal. The head louse sucks most frequently on the back of the head and neck. The body louse sucks on the parts of the body in contact with clothing. The crab louse sucks blood mainly in the pubic region. The irritating saliva injected during feeding causes itching. Scratching increases inflammation and secondary bacterial infection resulting in pustules and crusts. The body louse is the vector of epidemic typhus, relapsing fever and trench fever. The head louse and crab louse are not known to be vectors of disease.

Diagnosis

Diagnosis is suspected from itching and scratching. Detection of the adult louse or the nits of the head and crab lice confirms the diagnosis. The eggs of body louse are usually hidden in the seams of clothing.

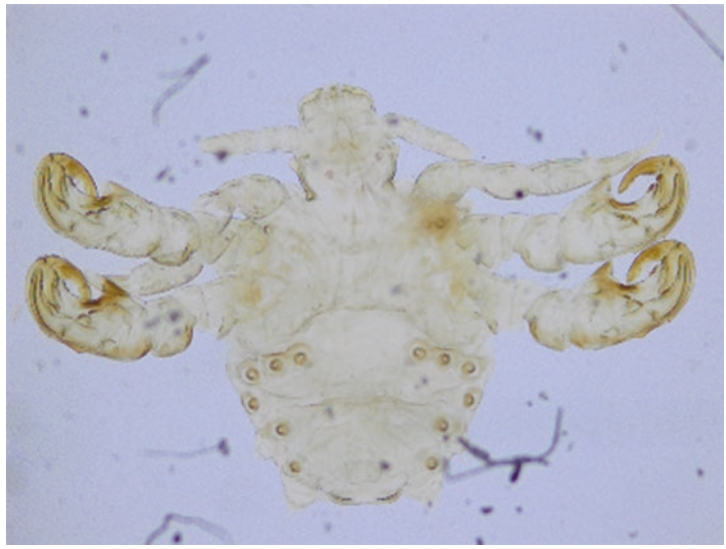


Fig. 13.3 Adult of *Phthirus pubis*

Treatment

1. Head lice

Any of the following pediculicides can be used:

(a) Pyrethrins combined with piperonyl butoxide
(b) Permethrin lotion, 1%
(c) Benzyl alcohol lotion, 5%
(d) Ivermectin lotion, 0.5%
(e) Malathion lotion, 0.5%
(f) Spinosad, 0.9% topical suspension
(g) Lindane shampoo, 1%

2. Body lice

Conservative management such as improving personal hygiene is adequate. Pediculicide (as for head lice) can also be used.

3. Crab lice

On pubic area, treat as for head lice. For infestation on the eye lashes, nits and lice can be removed with forceps.

Prevention and Control

1. Head louse
   (a) Treat infested persons
   (b) Avoid hair-to-hair contact
   (c) Do not share clothing, hats, scarves, combs, brushes or towels
   (d) Do not lie in beds or use pillows that have recently been in contact with an infested person
2. Body louse
   (a) Treat infested persons
   (b) Improve the personal hygiene of the infested persons
   (c) Regular changing of clothes
   (d) Wash clothing and bed linens used by infested person using hot water
3. Crab louse
   (a) Treat infested persons
   (b) Avoid sexual promiscuity

Case Reports

14

Case 1: Amoebic Liver Abscess

Case report: A 6-year-old boy presented with fever for 4 days duration associated with right hypochondriac pain, non-bloody diarrhoea, and vomiting (last 3 days). At presentation, he was lethargic with reduced oral intake and urine output. There was a history of swimming in a water park 1 month prior to presentation. On physical examination, the child was dehydrated but fully conscious, tachypnoeic (respiratory rate 40 breaths/minute), febrile (temperature 38.5 °C), tachycardic (heart rate 134 beats/minute) but blood pressure was normal (104/62 mmHg) and oxygen saturation was 98%. The abdomen was distended, tensed and guarded. There was a palpable vague mass and tenderness in the right upper quadrant. Respiratory examination was normal.

On admission, total white cell count was 27.3 × 10^9/L (neutrophils 84.3%, 23 × 10^9/L), haemoglobin 11.0 g/L, platelets 617 × 10^9/L, urea 1.1 mmol/L, sodium 126 mmol/L, potassium 2.8 mmol/L, chloride 92 mmol/L, creatinine 33 mmol/L, albumin 20 g/L, and C-reactive protein 291.5 mg/L. Alkaline phosphatase, hepatic transaminases, bilirubin level, and blood gas were normal. CT thorax and abdomen subsequently confirmed two loculated hepatic abscesses in the right lobe (one measuring 6.9 cm × 8.3 cm × 9.3 cm and another 5.5 cm × 6.5 cm × 7.2 cm), ascites, bilateral pleural effusion and collapsed consolidation of both lungs (right more than left). Ultrasound guided percutaneous liver abscesses drainage was done and thick anchovy paste-like pus was aspirated.

Microscopy examination and staining of the pus for *Entamoeba histolytica* trophozoites was negative. *E. histolytica* was positive in the aspirated material by PCR technique. Serological test for *E. histolytica* was not done. There was no *E. histolytica* cyst or trophozoites found in the stool sample and PCR test on the stool for *E. histolytica* was also negative. Unfortunately, despite treatment, the patient continued to deteriorate and became hypotensive requiring 4 inotropes. Patient passed away on day 7 of admission.

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R. Mahmud et al., *Medical Parasitology*,
https://doi.org/10.1007/978-3-319-68795-7_14

Source: Ng, Khuen Foong, Kah Kee Tan, Romano Ngui, Yvonne AL Lim, Amirah Amir, Yamuna Rajoo, Hamimah Hassan, and Rohela Mahmud. "Fatal case of amoebic liver abscess in a child." Asian Pacific Journal of Tropical Medicine 8, no. 10 (2015): 878–80.

Learning Points

1. Lack of suspicion of an amoebic liver abscess leads to a delay in treatment which can be fatal.
2. Aspirated 'anchovy sauce' coloured pus is strongly suggestive of amoebic liver abscess which should prompt the attending clinician to start treatment with metronidazole.

Case 2: Gigantic Amoebic Liver Abscess in Pregnancy

Case report: A 29-year-old pregnant woman gravida 6 para 4 + 1 at 30-weeks gestation came to the hospital complaining of 4 days of fever, lethargy and flu like symptoms. There were no known comorbidities. She was initially given a course of amoxicillin by her General Practitioner but to no avail and was subsequently admitted to the hospital where she was suspected to have pneumonia. She appeared pale, mildly tachypneic with a blood pressure of 107/63 mmHg, heart rate of 120–140 bpm, temperature of 37.5 °C and a SpO_2 of 98% on nasal prong 2 L/min. Examination of her cardiovascular system was unremarkable. Respiratory examination revealed mild bibasal fine inspiratory crepitations which were attributed to over-hydration. Abdominal examination revealed mild upper abdominal tenderness. Organomegaly was difficult to appreciate in view of the gravid uterus. Laboratory investigations showed an elevated ESR at 140 mm/h, total white count of 30–40 × 10^9/L, elevated alkaline phosphatase at 346 IU/L with borderline increment in alanine transaminase at 40–50 IU/L, raised lactate dehydrogenase at 1200–1300 IU/L with persistently low albumin at 18 g/L. Bilirubin was normal. Her blood cultures, tuberculosis workup and viral hepatitis were negative. Likewise, her transthoracic echocardiography was normal while her chest X-ray revealed interstitial edema in keeping with the clinical findings of over-hydration. An abdominal ultrasonography revealed a huge nonliquefied abscess at the right lobe of liver measuring 13.6 cm × 15.9 cm × 20.2 cm in dimension. Antibiotics were changed to intravenous meropenem 500 mg 8 hourly alongside intravenous metronidazole 500 mg 8 hourly to cover for potential pyogenic and amoebic liver abscess. Further history revealed factors of poor personal hygiene and sanitation coupled with overcrowded living conditions. There was no history of dysentery, no suggestion of immunosuppression and her HIV screen was negative. Her travel history was insignificant. Ultrasound guided percutaneous liver abscess drainage was done upon transfer to a subspecialized tertiary centre in which 2.3 L of odourless brownish pus (anchovy sauce pus) was drained over time. This was tested to be positive for *Entamoeba histolytica* by PCR. She completed 2 weeks of intravenous metronidazole with no untoward complications and the pregnancy progressed normally to term, when she delivered a healthy baby girl. Repeated ultrasonography showed progressive size reduction of the liver abscess cavity.

Source: Chiam, K. H., Yvonne AL Lim, Rohela Mahmud, Romano Ngui, and Lee Lee Low. "Gigantic amoebic liver abscess in pregnancy: A case report." Tropical Biomedicine 32, no. 4 (2015): 699–703.

Learning Points

1. Amoebic liver abscess in pregnancy is rare and is associated with high risk of mortality.
2. It poses diagnostic challenge/dilemma especially when symptoms are vague and subtle.
3. A combination of a detailed epidemiological history, biochemical, radiographic and molecular investigations aid in the diagnosis.
4. Elevated alkaline phosphatase alongside leukocytosis guide clinicians towards the diagnosis of liver abscess.

Case 3: Child Infected with *Plasmodium vivax* via Blood Transfusion

Case report: A 12-year-old Chinese male child who was diagnosed with intracranial malignant germ cell tumour received packed red cell transfusions for chemotherapy-induced anaemia. He received blood from 3 donors: a Myanmarese male and 2 Malaysian donors. A week later, upon returning home, the patient developed fever with rigors. He was admitted to the hospital and blood film malaria parasite (BFMP) was carried out.

Giemsa-stained blood smear from the patient was prepared and examined under light microscope. Examination of the blood smear showed *Plasmodium vivax* infection with 0.03% parasitaemia. PCR was carried out on the blood samples of the patient and the 3 donors to confirm the species of the malaria parasite.

Based on the PCR results, it was confirmed that the Myanmarese male donor was infected with *P. vivax* and the other 2 donors were found to be negative for malaria. The 26-year-old donor from Sagaing Region, Myanmar came to Malaysia and worked in Semenyih, Selangor for 3 years. He then returned to Myanmar for 4 months and returned to resume work in Semenyih. Medical history of the donor did not suggest prior malaria infection nor was there any other significant medical or surgical history. There was no prior history of receiving blood transfusion either.

Source: Anthony, Claudia N., Yee-Ling Lau, Jia-Siang Sum, Mun-Yik Fong, Hany Ariffin, Wai-Linn Zaw, Indra Jeyajothi, and Rohela Mahmud. "Malaysian child infected with *Plasmodium vivax* via blood transfusion: a case report." Malaria Journal 12, no. 1 (2013): 308.

Learning Points

1. Blood used for transfusion should be free of malarial parasites.
2. Clinicians investigating fever in a patient need to ask about history of recent transfusion.

Case 4: Hyperparasitaemia of *Plasmodium knowlesi* Infection in Human

Case report: A 56-year-old Chinese man was admitted to the hospital with a history of 5 days of high-grade fever, 2 days of yellowish discolouration of the skin and extreme tiredness. He worked as a sawmill supervisor in Kluang, Johor. He had no history of travelling overseas or trekking into deep jungles. However, he often visited a recreational park at the foothill of Gunung Lambak, Kluang, Johor.

Upon admission, he was alert, conscious but appeared lethargic. There was neither neck stiffness nor papilloedema. He was febrile with temperature of 38 °C. He had mild pallor, deep jaundice but no petechiae. He was haemodynamically stable, with well-perfused peripherals, no signs of tachypnea and good oxygenation. Physical examinations of cardiovascular and respiratory systems were normal. He had hepatomegaly, but no splenomegaly.

The initial haematological investigations revealed mild anaemia (Hb level 10.0 g/dL), thrombocytopaenia (48,000 platelets/μL) with normal total white count and haematocrit. Dengue tests were negative. Serology tests for Hepatitis B, Anti-HCV and HIV tests were negative. Renal function was abnormal as evidenced by high urea and creatinine levels. Liver enzymes were elevated with hyperbilirubinaemia of a mixed picture. Lactate dehydrogenase (LDH) level was elevated but reticulocyte count was normal and Coombs test was negative. The initial chest radiography revealed normal lung field and no pulmonary congestion.

Rapid diagnostic test for malaria showed infection caused by non-*Plasmodium falciparum*. Thick and thin Giemsa-stained blood smears examination unravelled abundant parasitized erythrocytes. Presence of numerous golden brown pigments with no enlargement of infected erythrocytes was indicative of *P. knowlesi* infection. The parasitemia level was 27%. Nested PCR of the blood sample was positive for *P. knowlesi* infection.

The patient was treated with 4 doses of intravenous (IV) artesunate at 2.4 mg/kg at 0, 12, 24, and 48 h in combination with oral doxycycline 100 mg BD for 1-week duration. Packed cell transfusions were given to the patient for the anaemia. Unfortunately, the patient went into the oliguric phase of acute kidney injury. He needed 7 sessions of hemodialysis before his renal function recovered. On the second day, a repeat blood smear showed dead and unhealthy parasites. The parasite count declined by 4 to 5 fold for every 24 h after treatment. No malaria parasite was noted in the peripheral blood film from day 5 onwards.

Source: Lee, Wenn-Chyau, Pek-Woon Chin, Yee-Ling Lau, Lit-Chein Chin, Mun-Yik Fong, Chee-Jiek Yap, Raymond Raj Supramaniam, and Rohela Mahmud. "Hyperparasitaemic human *Plasmodium knowlesi* infection with atypical morphology in peninsular Malaysia." Malaria Journal 12, no. 1 (2013): 88.

Learning Points

1. In a patient with a febrile illness, a history of trekking into jungle/recreational park is important to help in the diagnosis of *P. knowlesi* infection.
2. The presence of fever, anaemia, thrombocytopaenia and acute renal failure should prompt the attending clinician to include malaria as a differential diagnosis.
3. When malaria is suspected, its confirmation needs to be pursued to minimize delay in treatment.

Case 5: *Plasmodium knowlesi* Reinfection in Human

Case report: A 41-year-old Chinese man from Peninsular Malaysia was first admitted to the hospital in October 2009 with a 4-day history of fever, chills and headache. His symptoms started 2 weeks after a camping trip in the jungle in Raub, Pahang. Initial examination showed thrombocytopaenia and hepatitis, and *Plasmodium knowlesi* malaria was subsequently confirmed with nested PCR. He recovered fully after a treatment course of oral quinine plus doxycycline.

The patient was readmitted to the hospital on June 11, 2010, with a 5-day history of fever, chills and rigors, followed by epigastric pain, nausea and vomiting. His symptoms began 15 days after another camping trip in a jungle in Tanjung Malim, Perak. Laboratory investigations showed severe thrombocytopaenia. Falciparum malaria was diagnosed initially on the basis of blood film microscopic examination with 1% parasitaemia. The patient was administered oral mefloquine (750 mg) followed by 500 mg and 250 mg at 6 h and 12 h, respectively. His parasitaemia level increased from 1.0 to 2.5% despite treatment. Oral quinine and doxycycline were initiated. However, renal function deteriorated and acute haemolysis was evident. Oral quinine was changed to intravenous quinine and oral riamet was added. Haemodialysis was initiated, and 1 unit each of packed erythrocyte cells and whole blood were transfused. Parasitaemia eventually cleared on June 16, 2010. PCR done later on patient's blood sample confirmed *P. knowlesi* infection. PCR genotyping indicates reinfection rather than recrudescence.

Source: Lau, Yee Ling, Lian Huat Tan, Lit Chein Chin, Mun Yik Fong, Mydin Abdul-Aziz Noraishah, and Mahmud Rohela. "*Plasmodium knowlesi* reinfection in human." Emerging Infectious Diseases 17, no. 7 (2011): 1314.

Learning Points

1. In the early stage of *P. knowlesi* infection, the parasite morphology cannot be distinguished from that of *P. falciparum*.
2. In knowlesi malaria, patients can rapidly progress to severe malaria due to the quotidian (24 h) erythrocytic cycle of the parasite.
3. Early diagnosis and treatment of severe malaria with IV anti-malarial therapy is important to prevent complications and death.
4. *Plasmodium knowlesi* infection does not cause relapse because the parasite has no liver hypnozoite stage.

Case 6: Severe *Plasmodium knowlesi* Infection

Case report 1: A 50-year-old gentleman with no known medical history presented to a district hospital with fever and rigors and a 3-day history of cough. On examination, he was alert and orientated but hypotensive (blood pressure 83/51 mmHg) and hypoxic (oxygen saturation 70% on 10 L oxygen via high flow mask), rhonchi was noted on chest auscultation. Otherwise, other systems were unremarkable. Blood film for malaria parasite (BFMP) done was reported as *Plasmodium malariae '4+'*. The patient was commenced on intravenous fluids, antibiotics and oral chloroquine, and transferred to a general hospital. He deteriorated rapidly needing intubation and ventilation and was commenced on inotropic support. Chest radiograph showed

diffuse infiltrates. The patient had renal failure (creatinine 330 μmol/L). Haemodialysis was commenced with other supportive ICU care. Intravenous artesunate was commenced; however, the patient remained on maximum inotropic and ventilator support. He died 9 h later with multiple organ failure. Blood cultures and dengue serology were negative, and PCR performed on a blood sample taken on day 3 confirmed *P. knowlesi* mono-infection. Cause of death was reported as severe malaria.

Learning Points

1. *Plasmodium malariae* infection does not usually cause high parasitaemia and symptoms are usually mild. If atypical *P. malariae* infection is encountered, it should alert the clinician of the possibility of *P. knowlesi* infection to guide them in treatment since *P. knowlesi* is known to cause severe infection.
2. Although blood film for malaria parasites (BFMP) is a gold standard diagnostic test, it cannot differentiate morphologically *P. knowlesi* from *P. malariae*.
3. Clinicians must be vigilant in picking up the signs and symptoms of severe malaria.
4. Clinicians must be aware of non-falciparum *Plasmodium* species as potential cause of severe and fatal malaria. Patients who present with severe malaria should be commenced with intravenous anti-malarial treatment.

Source: Rajahram GS, Barber BE, William T, Menon J, Anstey NM, Yeo TW. Deaths due to Plasmodium knowlesi malaria in Sabah, Malaysia: association with reporting as Plasmodium malariae and delayed parenteral artesunate. Malaria Journal 2012, 11:284.

Case report 2: A 71-year-old female with a history of hypertension was admitted to a district hospital for fever associated with chills and rigors, myalgia and arthralgia. She had stayed overnight at her palm oil and rubber plantation in the forest fringe 10 days prior to becoming unwell. On admission, she was alert but jaundiced and tachypnoeic with a respiratory rate of 38 breaths per minute, and the oxygen saturation was 98% on room air. The blood pressure was 127/87 mmHg, pulse rate was 111 bpm and temperature was 37.8 °C. She had hepatomegaly and bilateral lower zone crepitations were heard on respiratory examination. Chest radiograph was normal. Blood film for malaria parasites (BFMP) was reported as *Plasmodium malariae* with a parasite count of 120,000 parasites/μL. The patient was commenced on intravenous artesunate, oral doxycycline and intravenous ceftriaxone within 2 h of presentation. However, her condition deteriorated rapidly, with oxygen saturation decreasing to 70% on 15 L of oxygen, and blood pressure dropping to 80/50 mmHg. She was intubated, transferred to the intensive care unit and commenced on dopamine, dobutamine and noradrenaline. Chest radiograph post intubation showed bilateral diffuse heterogenous opacities, and she died 18 h after presentation from severe malaria with acute respiratory distress syndrome (ARDS). PCR performed on the extract

of her blood film confirmed *P. knowlesi* mono-infection, and blood cultures done on admission were negative.

Learning Points

1. The case highlights the need for close monitoring of the respiratory status of patient even after the institution of anti-malarial treatment. ARDS with hypoxemia can develop even with a decreasing parasite count. This may be more important in severe knowlesi malaria where pulmonary complications are common.
2. Clinicians must be alert to the possibility of knowlesi malaria, particularly if a history reveals recent activities in or near forested areas in Southeast Asia.

Source: Rajahram GS, Barber BE, Yeo TW, Tan WW, William T. Case report: fatal Plasmodium knowlesi malaria following an atypical clinical presentation and delayed diagnosis. Medical Journal of Malaysia 2013, 68(1):71–2.

Acknowledgement

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Case 7: Imported Case of *Plasmodium ovale* Infection in Malaysia

Case report: A 20-year-old Nigerian male student who has been in Malaysia for the last 6 months presented with a history of fever associated with chills and rigors for the last 4 days. Other physical examination findings were unremarkable. Laboratory findings on admission revealed anaemia (haemoglobin of 10.8 g/dL), platelet count of 117,000/μL and eosinophils of 2%. Microscopy examination of thin blood smear stained with Giemsa showed parasites resembling *Plasmodium vivax* with enlarged infected red blood cells. However, PCR followed by sequencing confirmed the species to be *Plasmodium ovale*. He was treated with quinine 600 mg tds and doxycycline 100 mg bd. One week after admission, the patient was discharged well.

Source: Lim, Yvonne AL, Rohela Mahmud, Ching Hoong Chew, T. Thiruventhiran, and Kek Heng Chua. "*Plasmodium ovale* infection in Malaysia: first imported case." Malaria Journal 9, no. 1 (2010): 272.

Learning Points

1. *Plasmodium ovale* should be considered as a differential diagnosis in febrile patients from endemic regions (West Africa).
2. Although microscopy is the gold standard diagnostic test for malaria, molecular techniques such as PCR is useful to confirm the causative *Plasmodium* species.
3. Primaquine should be added into the treatment regime in ovale malaria to prevent relapse.

Case 8: *Plasmodium ovale* Infection with Fatal Outcome

Case report: Two Malaysian acquaintances (patients A and B) went to Victoria Island, Nigeria together for a two-week working trip. Mefloquine was used as malaria prophylaxis for the trip. They fell sick after returning to Malaysia and were admitted to different hospitals. Their cases are presented as follows:

Patient A: Two months after the trip to Nigeria, patient A (52-year-old Chinese male) was admitted due to fever, chills and rigors for 5 days. He was jaundiced, anorexic and febrile with body temperature of 37.7 °C upon admission. He had mild cough, blood pressure of 110/66 mmHg, pulse rate of 98 bpm with peak bilirubin level of 45 μmol/L and hepatosplenomegaly. Lung examination was normal. His urine was tea coloured. Ultrasound confirmed the findings of hepatosplenomegaly with signs of chronic cholecystitis and cholelithiasis. Initial haematological investigation showed that he was thrombocytopaenic (37,000/μL) with normal WBC count (5800 cells/μL) and haemoglobin level of 13.9 g/dL. He had not travelled to any other places after the trip to Nigeria. The patient had a history of malaria 3 times in the past. The last episode of malaria was 6 months prior to present admission. However, the species of malaria parasites for the previous malaria episodes was not known. The patient also had an underlying hypertension and was a heavy alcohol consumer.

Patient A was treated immediately for cholecystitis with IV ceftriaxone 2 g daily and IV metronidazole 500 mg thrice daily by the attending gastroenterologist. However, his fever and thrombocytopaenia persisted, and WBC count dropped progressively. On day 5 of admission, blood smears were prepared and examined under the microscope. '*Plasmodium vivax*-like' parasites were found with parasitaemia of 0.1%. Further microscopic examination by a referral diagnostic centre subsequently indicated that this was a mono-infection of *P. ovale*. This was confirmed with nested PCR. Meanwhile, bacteriological culture of patient's blood samples were negative.

He was treated with a course of 6 doses of riamet (artemether and lumefantrine), 4 tablets per dose, and primaquine for 2 weeks. He responded well to the antimalarial treatment clinically and biochemically. Patient's parasitaemia dropped to 0.06% the following day. Malaria parasites were cleared in less than 48 h after initiation of riamet. He was discharged well on day 8 of hospitalization. He remained well without relapse throughout his medical follow-up.

Patient B: Six months after the trip to Nigeria, patient B (59-year-old Chinese male) fell sick and was referred to a hospital. He gave a history of intermittent fever with rigors, myalgia and nausea for 10 days. His blood pressure upon admission was 102/55 mmHg, with pulse rate of 60 bpm. Plasma glucose level was 9.5 mmol/L. Jaundice and hepatosplenomegaly were not detected. He was alert and conscious. Lung examination was normal. He made a 1-day trip to Kota Kinabalu, Sabah, 3 months before the admission. He had no known medical illness and no known history of acquiring malaria. Initial haematological investigation revealed that he was thrombocytopaenic (65,000/μL) with low WBC count (3100/μL) and haemoglobin level of 12.4 g/dL. Malaria parasites were detected in his blood, with parasitaemia of 0.18%. The species was identified as *Plasmodium ovale*, which was confirmed by nested PCR.

Chloroquine phosphate 150 mg base and primaquine (30 mg) was started. However, he remained febrile (38.4 °C) 24 h later. On day 3 of the admission, he developed loose stools and lung examination revealed fine basal crepitations. Blood smear examination showed that the malaria parasites were still present. On the morning of day 4, he complained of breathlessness and lethargy. His body temperature surged to 39.2 °C.

Later that day, his dyspnoea worsen with haemoptysis and subsequent epistaxis. Chest X-ray showed bilateral haziness up to the upper zone. Haematological investigation showed that his platelet count was 120,000/μL and the malaria parasite load was reduced to 0.03%. Despite the lowering of parasitaemia, he progressed into respiratory failure. He was intubated and ventilated. His anti-malarial treatment was changed to IV quinine 850 mg (1 dose) and subsequently to IV artesunate 160 mg (for 7 days).

On day 5 of admission, malaria parasites were completely cleared. However, patient was still febrile with temperature of 40.8 °C. Patient subsequently developed acute kidney injury, ARDS, and nosocomial sepsis and succumbed to his illness.

Source: Lau, Yee-Ling, Wenn-Chyau Lee, Lian-Huat Tan, Adeeba Kamarulzaman, Sharifah Faridah Syed Omar, Mun-Yik Fong, Fei-Wen Cheong, and Rohela Mahmud. "Acute respiratory distress syndrome and acute renal failure from *Plasmodium ovale* infection with fatal outcome." Malaria Journal 12, no. 1 (2013): 389.

Learning Points

1. Clinicians must advice travellers going to malaria endemic areas to be compliant with malaria prophylaxis and to seek immediate treatment if they develop fever during or after returning from the trip.
2. Travel history is essential in patients with febrile illness.
3. Early diagnosis and treatment of severe malaria with IV anti-malarial therapy is important to prevent complications and death.

Case 9: Unusual Manifestation of Cutaneous Toxoplasmosis in a HIV-Positive Patient

Case report: The patient was a 49-year-old HIV-positive Chinese male who was diagnosed as having HIV infection many years ago. Despite treatment with highly active anti-retroviral therapy with undetectable HIV RNA levels, he failed to fully respond immunologically with CD4 cell level persistently below 100 cells/mm^3. He presented with multiple hard and painful nodular lesions on both arms, hands and a few on the chest. The nodules were non-tender and variable in size (0.5–3 cm in diameter). Other parts of the body were not affected and no skin ulcers were observed. Serological tests for anti-*Toxoplasma* IgG and IgM were negative. Histopathology examination of the lesions showed numerous foci of macrophages with intra- and extracellular organisms in the underlying dermis. These organisms were crescent shaped, resembling the zoites of *Toxoplasma gondii*. The skin biopsy

also showed granulomatous inflammation. The histology slide was examined under electron microscopy, and *T. gondii* was identified on the basis of ultrastructural features of the zoites. The organism was confirmed when the skin biopsy was subjected to a nested PCR which successfully amplified a 96-base pair region of the *T. gondii* B1 gene. The origin of the *T. gondii* infection was uncertain. It is likely that the patient might have a previous latent infection that was reactivated during the HIV infection. Another possibility is that the patient might have acquired *T. gondii* infection following HIV infection. Humoral immunity of the patient might have been affected as evidenced by the absence of anti-*Toxoplasma* antibody response. Despite treatment with standard anti-*Toxoplasma* drugs which included sulphadiazine and pyrimethamine, the lesions failed to resolve. The patient continues to develop new lesions while on therapy.

Source: Fong, M. Y., K. T. Wong, M. Rohela, L. H. Tan, K. Adeeba, Y. Y. Lee, and Y. L. Lau. "Unusual manifestation of cutaneous toxoplasmosis in a HIV-positive patient." Tropical Biomedicine 27, no. 3 (2010): 447–50.

Learning Points

1. Clinicians have to be aware of opportunistic parasitic infections in immunocompromised patients.
2. When faced with difficulty in diagnosing skin lesions, skin biopsy provides samples that can be used for HPE and PCR which can aid in the diagnosis.

Case 10: Zoonotic *Ancylostoma ceylanicum* Infection Detected by Endoscopy

Case report: A 58-year-old Chinese woman who presented with upper gastrointestinal (GI) bleeding was admitted to a private hospital for management. She was passing out black-coloured stool (melaena) 1 to 2 times per day for 1 week. She was admitted to a local hospital for a similar problem before this admission. She had a few episodes of dizziness, tightness of chest and cold sweats. There was no history of fever or weight loss. Laboratory investigations showed a haemoglobin concentration of 11.4 g/dL, a platelet count of 169,000/μL, a total white blood cell count of 8000/μL, neutrophils of 68%, lymphocytes of 24%, monocytes of 6% , eosinophils of 1% and basophils of 1%. Liver and renal functions were normal. The patient underwent oesophagogastroduodenoscopy (OGDS) and colonoscopy. Colonoscopy showed 3 polyps that were removed by polypectomy. Histopathological examination (HPE) showed them to be malignant. OGDS showed a gastric ulcer with signs of bleeding. Biopsy of the ulcer edge proved it to be malignant. Incidentally, a single adult blood-filled worm that measured 8–10 mm in size was seen moving on the duodenal mucosa. The worm was removed and sent to the Parasitology Diagnostic Laboratory, Department of Parasitology, Faculty of Medicine, University of Malaya for species identification. Microscopic examination of the worm, including its buccal capsule or mouthpart, showed it to be an adult female hookworm. In addition, ova that were characteristic of hookworm species were seen in the ruptured uterus.

Microscopic examination of the mouthpart was not clear and detailed enough to allow specific species identification. For specific species characterization, the worm was therefore, subjected to PCR which confirmed the hookworm species as *Ancylostoma ceylanicum*.

Source: Ngui, Romano, Yvonne AL Lim, Wan Hafiz Wan Ismail, Kie Nyok Lim, and Rohela Mahmud. "Zoonotic *Ancylostoma ceylanicum* infection detected by endoscopy." The American Journal of Tropical Medicine and Hygiene 91, no. 1 (2014): 86–8.

Learning Points

1. This report calls attention to the fact that, in areas where *A. ceylanicum* (cat and dog hookworm) occurs, this worm can infect and reach maturity in human and in heavy infections, may produce hookworm disease (in this case, the bleeding is unlikely due to *A. ceylanicum* since only 1 worm was found on OGDS). Often, this information is forgotten by practitioners who assume that all adult hookworms reported from humans are either *Necator americanus* or *Ancylostoma duodenale*.
2. PCR aids in confirmation of the hookworm species.

Case 11: *Enterobius vermicularis* Salpingitis Seen in the Setting of Ectopic Pregnancy

Case report: A 23-year-old woman in her second pregnancy at 8 weeks gestation, presented to the Emergency Department, complaining of vaginal bleeding for 3 days associated with pricking, nonradiating and progressively increasing suprapubic pain. She did not have any vaginal discharge or fever. The urine pregnancy test was positive. On physical examination, she was pale, tachycardic, and hypotensive. Her abdomen was mildly distended with tenderness at the lower abdomen and guarding. Vaginal examination revealed a positive cervical excitation test with fullness in the Pouch of Douglas. Adnexal tenderness was elicited bilaterally. Transabdominal pelvic sonography revealed an empty uterus with a right irregular adnexal mass measuring 9 mm and a free fluid. She had a haemoglobin of 6.7 g/dL and a normal white blood cell count and platelet level. Preoperative diagnosis of a ruptured right ectopic pregnancy with hypovolemia was made. She underwent laparotomy and a ruptured right ovarian ectopic pregnancy was discovered and removed. She was transfused with 4U of packed cells and had an uneventful postoperative recovery. The histopathological examination of the ectopic pregnancy revealed a fibrotic nodule attached to the wall of the right fallopian which contained rounded structures reminiscent of eggs and adult remnants of pinworms (*Enterobius vermicularis*). Clinicopathological and molecular findings confirmed the final diagnosis of *E. vermicularis* salpingitis complicated with intra-abdominal bleeding secondary to perforation of vessels of mesosalpinx and complete miscarriage. Upon review later, she was pain free and ambulating well. She was started on albendazole for a week.

Source: Ngui, Romano, Sarala Ravindran, Diana Bee Lan Ong, Tak Kuan Chow, Kah Pin Low, Zaidi Syeda Nureena, Yamuna Rajoo et al. "*Enterobius vermicularis* salpingitis seen in the setting of ectopic pregnancy in a Malaysian patient." Journal of Clinical Microbiology 52, no. 9 (2014): 3468–70.

Learning Points

1. Ectopic migration of *Enterobius vermicularis* can cause lesions with symptoms in the female reproductive tract.

Case 12: Case Report on Anisakiasis

Case report: Patient is a 64-year-old man from Sarawak. He complained of abdominal discomfort and passing of blood in his stool after eating sushi 2 days before.

On examination, the patient was afebrile, blood pressure of 124/88 mmHg, and a pulse rate of 82 bpm. Abdominal examination was unremarkable with no tenderness or guarding upon palpation. Blood test showed haemoglobin of 10.1 g/dL, total white cell count of 4.3 k/μL (neutrophils 47%, lymphocytes 40%, monocytes 9%, eosinophils 3%, and basophils 1%), platelet count of 162,000/μL, and ESR of 7 mm/h. A colonoscopy was performed on the patient on the same day. A worm was observed burrowing into the mucosa of the ascending colon. There was blood oozing from the penetration site with blood clots forming around the worm. The whole worm was pulled out for identification. The specimen was examined under a stereomicroscope, and it showed a nematode larva measuring approximately 25 mm long, off-white in colour, and moving actively. Histological examination of the cross sections of the worm showed the characteristic Y-shaped lateral epidermal cords which is diagnostic of *Anisakis* which was confirmed with PCR and sequencing.

Source: Amir, Amirah, Romano Ngui, Wan Hafiz Wan Ismail, Kum T. Wong, Jaxinthe SK Ong, Yvonne AL Lim, Yee-Ling Lau, and Rohela Mahmud. "Anisakiasis Causing Acute Dysentery in Malaysia." The American Journal of Tropical Medicine and Hygiene 95, no. 2 (2016): 410–2.

Learning Points

1. Detailed history including dietary history has to be taken from patients with gastrointestinal symptoms. Thorough physical examination and investigation cannot be overemphasized.

Case 13: Zoonotic *Brugia pahangi* Filariasis

Case report: Five patients (P1–P5) were referred to a medical centre between October 2003 and September 2006. All patients except P4 lived near a hill in Petaling Jaya, a residential suburbia located 10 km southwest of Kuala Lumpur, the capital city of Malaysia. The hill and its surroundings are a popular place for recreational activities. However, there is no history or record of *Brugia malayi* infection in this suburbia. Although P4 did not reside in this residential area, he frequently

visited the area for regular jogs. P1 and P2 had together climbed Mount Kinabalu in Sabah (on Borneo Island) years before the illness. P3 had history of travel to India as well as other Southeast Asian countries due to his job requirements. P4 and P5 did not report any history of travel in the past.

All 5 patients were referred by various private physicians after having been treated for unusual and unresolved lower limb cellulitis. The first four patients presented with lymphangitis and cellulitis of the lower limb, whereas P5 presented with recurrent cellulitis of his right foot without a history of lymphangitis. Apart from P3 and P5, who presented relatively early following the acute onset of their first episode of lymphangitis and cellulitis, respectively, the other patients were referred after recurrent episodes of symptoms. Fever was a transient symptom associated with the acute presentation of lymphangitis or cellulitis in all the patients.

All the patients were seropositive by Brugia Rapid test at the time of diagnosis, but became seronegative following treatment. All of them were negative for microfilariae (mf) on nocturnal peripheral blood smear. None of them had eosinophilia on full blood picture. Family members of the patients (including their housemaids, all of whom were migrant workers) also had their blood screened for mf and Brugia Rapid test at the time of diagnosis. None of them were positive for any of these tests.

The first 4 patients were treated with diethylcarbamazine (DEC, single dose of 50 mg on day 1, 50 mg 3×/day on day 2, 100 mg 3×/day on day 3, 150 mg 3×/day on days 4–14) and albendazole (single dose of 400 mg) with complete resolution of lymphangitis and cellulitis. P5 was treated with an 8-week course of doxycycline (100 mg 2×/day for 8 weeks). His symptoms also resolved completely. No recurrence of symptoms was recorded.

PCR was only available in Parasitology Diagnostic Laboratory, University Malaya in 2006, hence the first four patients did not have PCR test done on their fresh blood samples at the time of diagnosis.

Patient P5 was found to be PCR positive for *B. pahangi* COXI when the test was performed on his fresh nocturnal blood sample. Following this, the previously stored blood samples were retrieved for PCR testing, but only patient P4 was found to be positive for *B. pahangi* COXI. The nucleotide sequence of the PCR product showed 99% similarity with that of a *B. pahangi* COXI sequence.

A repeat screening using nocturnal blood mf examination, Brugia Rapid test and PCR was carried out in October 2006 on the first 3 patients and their family members including their maids, but all were found to be negative. Repeat screening tests were not carried out for P4 and his family members as they were not living in the suburbia.

Our survey of mosquitoes within a 2 km radius of the suburbia revealed that mosquitoes of the genera *Armigeres, Aedes* and *Culex* were present. Mosquitoes of *Mansonia* spp., the principal vectors of *B. malayi* in Peninsular Malaysia, were not found. Only adult female mosquitoes of the species *Armigeres subalbatus* were infected with filarial larvae. Of the 801 adult females *A. subalbatus* collected and dissected, 54 (7%) harboured larvae. PCR on the larvae DNA, and subsequent DNA sequencing of the PCR product showed that the COXI nucleotide sequence of the *B. pahangi* larvae was identical to that of the COXI of *B. pahangi* in patient P4, thus, suggesting that *Ar. subalbatus* was most likely the vector of the parasite.

In order to determine the reservoir animal host of the *B. pahangi*, blood samples were taken from wild monkeys and domestic cats in the suburbia for microscopy examination and PCR. None of the 15 monkeys caught were positive for *B. pahangi* mf or COXI. Of the 12 domestic cat blood samples, 5 were positive for *B. pahangi* mf based on their morphology and length. These mf-positive blood samples were also positive for *B. pahangi* COXI but negative for *B. malayi* COXI. The sequence of the PCR product was found to be identical to that of patient 4 and of the larvae in the *Ar. subalbatus* mosquitoes. These findings thus suggest that infected domestic cats might be the source of the zoonotic infection in the suburbia.

Source: Tan, Lian Huat, Mun Yik Fong, Rohela Mahmud, Azdayanti Muslim, Yee Ling Lau, and Adeeba Kamarulzaman. "Zoonotic *Brugia pahangi* filariasis in a suburbia of Kuala Lumpur City, Malaysia." Parasitology International 60, no. 1 (2011): 111–3.

Learning Points

1. These cases highlight the importance of clinicians to be aware of zoonotic parasitic infections in pursuing diagnoses.
2. The use of PCR helps to confirm diagnosis. The diagnosis would have been missed if only conventional diagnostic standards (blood smears) were applied.

Case 14: Eye Lesion Caused by Filarial Worm

Case report 1: The patient is a 3-year-old Chinese boy from the East coast of Peninsular Malaysia. He presented with a 1-week history of redness and palpebral swelling of his right eye. He had no history of travelling overseas and the family kept dogs at home. On physical examination, the attending physician only found enlarged axillary and inguinal lymph nodes. The patient was later seen by an ophthalmologist, who found a subconjunctival worm in his right eye. Two days after being warded, 4 worm fragments, each about 1 cm long were removed from his right eye under general anaesthesia. Unfortunately, no attempts were made to identify the worm.

A full blood count revealed eosinophilia (10%). A peripheral blood film examination revealed microfilariae. A thick blood smear was done and stained with Giemsa. The microfilariae detected were diagnosed to be that of *Brugia malayi*. The microfilaria is kinky and has a sheath which stained pink with Giemsa. It has overlapping nuclei with two terminal nuclei at the tail end. The cephalic space is 2:1 (length:breadth). His serum tested positive with a Brugia Rapid test kit. Since there was no attempt to identify the adult worm recovered, we assumed that the adult worm belongs to *B. malayi* from the findings of its microfilariae in the blood. The patient was treated with diethylcarbamazine.

Source: Rohela, M., I. Jamaiah, and C. C. Yaw. "Eye lesion caused by adult *Brugia malayi*: a first case reported in a child from Malaysia." Southeast Asian Journal of Tropical Medicine and Public Health (2006): 37(4):652–5.

Case report 2: The patient is a 42-year-old Chinese male, from Kuching, Sarawak. He worked as a contractor and his only trip out of Malaysia was to China. His hobby is hunting and he likes eating meat from wild game. He has only one pet dog.

He seeked treatment for a 1-day history of redness and itchiness over the temporal aspect of his left eye. His eyes were normal except for congestion of the left temporal bulbar conjunctiva. Slit lamp examination showed a live mobile worm just beneath the conjunctiva. It was removed immediately under local anaesthesia. The worm was put in formalin and sent for identification to the Department of Parasitology, Faculty of Medicine, University of Malaya. On examination, the specimen was found to be an immature female nematode worm measuring 11.5 cm long, with a maximum width of 400 μm. The worm was rounded at both ends, the anterior end being wider than the posterior. The head was rounded with evidence of papillae arranged in two circles. The vulva opening was 2400 μm from the anterior end. The width of the vulva opening was 260 μm. The tail length was 110 μm and the width at the anus was 120 μm. The cuticle had longitudinal ridges and circular annulations. Based on the morphological characteristics, the worm was identified as an immature *Dirofilaria repens*.

Physical examination showed no skin rash. Examination of both eyes showed a normal retina and vitreous fluid bilaterally. His vision was 6/6 in both eyes. There were no other positive findings except for the laboratory test which showed that he was hepatitis B positive.

Source: Rohela, M., I. Jamaiah, T. T. Hui, J. W. Mak, I. Ithoi, and A. Amirah. "*Dirofilaria* causing eye infection in a patient from Malaysia." Southeast Asian Journal of Tropical Medicine and Public Health 40, no. 5 (2009): 914–8.

Learning Points

1. Exposure to animals and pets is a relevant history in arriving at a diagnosis.
2. Clinicians have to consult parasitologist when a worm is detected in a patient for further lab test to confirm the species and determine the diagnosis.

Case 15: Taeniasis saginata and Neurocysticercosis

Case report 1: The patient is a 57-year-old French businessman. He was seen for abdominal discomfort for the past 1 year. He claimed to have expelled worms in his stools. He had seen several doctors and was given albendazole but the symptom and passing of worms persisted. Patient gave a history of travelling to countries in Southeast Asia in the course of his work. During his travelling, he consumed many types of local delicacies including raw meat. Physical examination showed a healthy man weighing 100 kg. He was afebrile and his vital signs were all normal. Abdominal examination showed no mass. There was absence of subcutaneous nodules and no history of headache, seizures, or visual impairment. Patient has a history of recurrent lower limb deep vein thrombosis (DVT) over the past few years and is still on Warfarin. There was no other significant medical history. A full blood count, renal and liver functions and chest X-ray were normal. Stool examination was negative for ova and cyst.

He brought along a single worm specimen that was expelled in his stool to the clinic. The specimen was identified to be that of a proglottid gravid of *Taenia* spp. It was whitish in colour measuring 1.7 × 0.5 cm. From the size of the gravid proglottid, the species was identified as *Taenia saginata*. The proglottid was active and was still motile. It was observed to be stretching and contracting its body. *Taenia* spp. eggs were recovered from the gravid proglottid. The egg measured 33 × 42 μm. The larva (oncosphere) was enclosed in a thick, radially striated coat, dark brown in colour. The 6 hooked larva was easily observed.

Upon diagnosis, the patient was treated with 1 dose of praziquantel, 600 mg.

Source: Rohela Mahmud, Jamaiah Ibrahim, Romano Ngui, Yvonne AL Lim, Matvinder Singh, Khadijah Othman, Mohd Redzuan AN and Amirah Amir. Taeniasis Saginata*:* A case report from Malaysia after 4 decades (unpublished report).

Case report 2: A 23-year-old Malaysian man presented with a history of passing out worms in his stools. He had a history of travelling to Madagascar to visit his father. His last visit was for a total duration of 3 weeks, 4 months prior. During his stay, he consumed undercooked beef. He claimed to have expelled worms in his stools for 2 weeks. He took 3 doses of albendazole 400 mg in 10 days. Since the passing out of worms persisted, he sought treatment at a private clinic and was given 3 tablets of ivermectin. On the day of presentation, he brought along a flat whitish object which looked like proglottids of a tapeworm. His full blood count was normal without eosinophilia. The specimen was whitish in colour and identified as the proglottids of *Taenia* spp. From the size of the gravid proglottid, the species was identified as *Taenia saginata*. *Taenia* eggs recovered from the gravid proglottid measured 20–40 μm and had 6 hooked larva (oncosphere) enclosed in a thick dark brown radially striated shell. As the proglottid was kept in formalin, molecular approach for species determination was not done on the specimen. The patient's father who was residing in Madagascar was asymptomatic while the patient's mother who did not travel to Madagascar, did not show any symptoms. The patient received 600 mg Praziquantel and has been asymptomatic since then.

Case report 3: Taeniasis was diagnosed in a 56-year-old male native Sabahan who was a veterinarian assistant. He presented with complaints of abdominal discomfort, loss of appetite, and weight. For the past 6 years, he was passing loose stools intermittently which contained worms. His stool was greyish in colour, mixed with mucus. He lost a total of 6 kg over 3 years. He had been given a total of 13 courses of albendazole from various GPs which provided only a brief relief for his symptoms each time. He was subsequently referred to a medical centre. An interesting facet of his dietary history included the consumption of raw beef, the timing of which coincided with the onset of his symptoms. His job scope over the years had been to examine cow dung daily for worms. On examination, his vitals were stable and he was afebrile. His blood serum biochemical and haematological parameters were within the normal range. Oesophagogastroduodenoscopy (OGDS) and colonoscopy performed revealed pangastritis and an adenomatous rectal polyp,

respectively. There were no worms noted endoscopically. However, a few gravid proglottids were recovered from the stool measuring an average of 1.5 × 0.5 cm each. The proglottid was subjected to PCR-based molecular diagnosis and confirmed to be *Taenia saginata*. He was given praziquantel (400 mg stat dose) and has been asymptomatic since.

Case report 4: A 43-year-old, previously healthy ethnic Malay Muslim man presented with an episode of generalized tonic-clonic seizure. There were no associated constitutional symptoms. He worked as a project director and travelled frequently all these years, mostly to Southeast Asia and South Asia as per his job requirements. He was admitted to a teaching hospital and brain MRI showed a partially calcified enhancing lesion in the posterior occipital region with surrounding oedema. CT scan of thorax and abdomen were unremarkable. He underwent stereotactic right craniotomy excision of the brain lesion. Frozen section showed granulomatous inflammatory mass with parasitic parts. Further histopathological examination showed changes in keeping with neurocysticercosis.. He was treated with 1 month course of albendazole 400 mg bid and dexamethasone. He has been well and seizure free since. A repeat MRI brain showed complete resolution of previous lesion.

Source: Chua, T. H., J. Emmanuel, K. T. Lee, F. K. Kan, K. S. Tee, Z. Abidin, R. Ganeswrie et al. "Taeniasis and neurocysticercosis among Malaysians." Tropical Biomedicine 34, no. 1 (2017): 7–13.

Learning Points

1. Travellers to countries where hygiene and food preperation practices are not optimal need to take precautions to reduce the risks of contracting infections.
2. Travel and occupational history should be obtained during history taking.
3. History of consuming undercooked/raw beef or pork should raise a suspicion of taeniasis.
4. The first episode of seizure in an adult requires radiological imaging to rule out space occupying lesions (in this case, lesion was due to neurocysticercosis).
5. Space occupying lesions in the brain often require biopsies to ascertain the aetiology.
6. Radiologists can identify features of neurocysticercosis on MRI.

Case 16: *Hymenolepis diminuta* Infection in a Child

Case report: A 2-year-old Malay girl living in a semi-rural area of Selangor, Malaysia was seen for abdominal discomfort and itchiness over the abdomen especially at night. She has been experiencing these symptoms for the last 3 months. There was no history of fits, anuresis, vomiting, passing of worm or fever. The main complaint was that the mother observed the intermittent passing of a 'small white paste-like structure' from the anal region for the last 3 months which was never resolved with deworming medication. The child is the youngest of 3 siblings. Other family members and surrounding neighbours were healthy, showing no signs of

similar illness. The specimen passed out by the child was brought along to the clinic. The attending physician sent it to a private laboratory and the result was reported as 'normal'. Six weeks later, the child returned with the same complaints and again another specimen sent for examination came back as 'normal'. On her third visit, a similar specimen retrieved from the faeces of the child was sent to a diagnostic laboratory for a second opinion. When the specimen, which looked like proglottids reached the laboratory, it was ruptured and microscopic examination demonstrated numerous spherical eggs measuring approximately 76 μm in diameter. The egg had thick shell with striated outer membrane and thin inner membrane containing 6 hooklets which is distinctive of tapeworm egg with absence of polar filaments. Although the eggs of *Hymenolepis diminuta* are similar to *H. nana*, they can be easily differentiated as *H. nana* eggs are smaller (40–60 μm × 30–50 μm) and have 2 evident polar thickenings, from each of which arise 4 to 8 polar filaments. Based on the bigger egg size and absence of polar filaments, they were identified as *H. diminuta* eggs. The infected child was prescribed with a single-dose praziquantel (20 mg/kg of body weight) and a stool examination carried out 2 weeks after treatment was negative for *H. diminuta* eggs and at the same time, her symptoms subsided.

Source: Rohela, M. T., Rl Ngui, Y. A. Lim, B. Kalaichelvan, W. I. Wan Hafiz, and A. N. Mohd Redzuan. "A case report of *Hymenolepis diminuta* infection in a Malaysian child." Tropical Biomedicine 29, no. 2 (2012): 224–30.

Learning Points

1. Helminthic infections are common among children in rural communities.
2. History of pica should be sought in a child suspected of having helminthic infection.
3. When there is a high index of suspicion, repeat samples should be sent to the diagnostic laboratory for species identification so that patient can be given proper treatment.

Case 17: Diphyllobothriasis

Case report 1: A 62-year-old Chinese male presented with a 4-day history of passing loose stools with no mucus or blood. The patient had slight abdominal discomfort and no fever. Clinical examination was normal. Charcoal and imodium tablet were prescribed. Two days later, the patient passed off white proglottids in his stool which was sent to the diagnostic laboratory for identification. A diagnosis of *Diphyllobothrium latum* was confirmed by examination of the gravid proglottids that had been expelled with typical operculated eggs seen after rupturing the gravid proglottids. The patient was given 750 mg praziquantel as a single dose. The patient has been well since his treatment. The patient admitted a fondness for *sashimi* (Japanese raw fish) which he ate regularly; none of his dining companions had been unwell.

Even though most cases of *D. latum* infection are asymptomatic, manifestations may include transient abdominal discomfort, diarrhoea, vomiting, weakness, and

weight loss. Occasionally, infection can cause acute abdominal pain and intestinal obstruction; rarely cholangitis or cholecystitis may be produced by migrating proglottids. This patient presented with diarrhoea and slight abdominal discomfort. With globalization, more Malaysians are exposed to different cuisines including raw fish. Clinicians should be aware of the likelihood of *D. latum* infection.

Source: Rohela, M., I. Jamaiah, K. W. Chan, and W. S. Yusoff. "Diphyllobothriasis: The first case report from Malaysia." The Southeast Asian Journal of Tropical Medicine and Public Health (2002) Jun; 33(2):229–30.

Case report 2: A 37-year-old Chinese male was seen with a complaint of passing white flat worms in his stool. He had no abdominal symptoms. He was not anaemic. The rest of his physical examination was normal. The specimen received was identified as *Diphyllobothrium latum.* The diagnosis was confirmed after examination of the gravid proglottids which came out in chains and the typical oval operculated eggs that were expelled after rupturing the gravid proglottids. The egg measures 71 μm by 50 μm. The eggs are broadly ovoid, operculated with moderately thick-shelled. The segments or proglottids are greater in breadth than in length. Laboratory investigations showed a haemoglobin level of 13.3 g/dL, an eosinophil of 4%, serum vitamin B_{12} of 217 pmol/L, and serum folate of 21.4 nmol/L. The laboratory results were within normal limits. A single dose of praziquantel 10 mg/kg was given to the patient and discharged. Stool examinations of his family members were negative. The patient revealed that he travelled to Thailand quite often and enjoyed eating raw fish there. In Malaysia, he frequently ate raw fish in Japanese restaurants and had been consuming raw fish for years.

Source: Rohela M, Jamaiah I, Goh KL, Nissapatorn V. A second case of diphyllobothriasis in Malaysia. The Southeast Asian Journal of Tropical Medicine and Public Health (2006) Sep; 37(5): 896–8.

Learning Points

1. Being a connoisseur of raw fish is a well-known risk factor for this parasitic infection.
2. A patient with diphyllobothriasis often remains asymptomatic for a long time.
3. It is necessary to check vitamin B_{12} level of infected patients as infection with this parasite can cause vitamin B_{12} deficiency.

Case 18: Liver Cirrhosis and Splenomegaly Associated with Schistosomiasis mansoni

Case report: A 52-year-old Sudanese woman was admitted with a complaint of left hypochondrium pain a day prior to admission. She denied fever, jaundice, vomiting, bleeding tendency, diarrhoea and dysuria. Systemic review was unremarkable. Her vital signs were normal. There were no stigmata of chronic liver disease and infective endocarditis. She was anicteric. She had no evidence of skin itching, fever or

bloody stool. On abdominal examination, there was massive splenomegaly without signs of decompensated liver disease and portal hypertension and she was not in hepatic encephalopathy state. Her admission blood test showed pancytopenia. Abdominal ultrasound scan demonstrated appearances of liver cirrhosis with splenomegaly, gastric and splenic varices.

On further questioning the patient said that she lives in Rabak region, Sudan, where her daily routine are cow rearing and farming. Her sources of drinking water are from canals and wells, where both are infested with snails. Sanitation is poor and canals are used as toilets. She said she had been exposed to the snail infested water for many years. While in Sudan, the patient had a history of contracting malaria and was treated with intravenous artesunate. Viral screening for hepatitis B and C was negative. Thick and thin blood films for malaria were negative. Blood was sent to a diagnostic laboratory for serological tests to rule out leishmaniasis and schistosomiasis. Leishmaniasis was negative. However, the serological test by ELISA for schistosomiasis was positive. *Schistosoma mansoni* eggs were detected in the stool by Kato-Katz thick smear stool examination confirming the diagnosis of schistosomiasis. The egg of *S. mansoni* has a characteristic lateral spine. Following the diagnosis, the patient was treated with praziquantel 40 mg/kg of body weight in a single dose and the patient progressed well. Stool examination after anthelminthic treatment was negative for *S. mansoni* eggs.

Source: Rajoo, Yamuna, Rohela Mahmud, Ng Rong Xiang, Sharifah FS Omar, G. Kumar, Yvonne AL Lim, Arine Fadzlun Ahmad, Amirah Amir, Zurainee Mohamed Nor, and Romano Ngui. "Liver cirrhosis and splenomegaly associated with *Schistosoma mansoni* in a Sudanese woman in Malaysia: A case report." Asian Pacific Journal of Tropical Medicine 8, no. 4 (2015): 334–6.

Learning Points

1. There are various causes of portal hypertension and one must consider the aetiology of schistosomiasis when seeing patients from endemic areas. While schistosomiasis is rare in Malaysia, it is one of the commonest causes of portal hypertension in endemic areas.
2. Other parasitic infections causing splenomegaly include visceral leishmaniasis and tropical splenomegaly syndrome (TSS), which is caused by malaria.
3. Schistosomiasis remains a significant public health concern in endemic areas.

Case 19: Acute Cholecystitis Caused by *Clonorchis sinensis*

Case report: A 43-year-old Chinese man from Hong Kong, presented with an acute onset of severe upper abdominal pain. On admission, an ultrasound scan showed nodular lesions in the gallbladder and an enlarged dilated gallbladder which was consistent with acute cholecystitis. His liver function test was normal and he had no clinical jaundice. On the second day, he developed jaundice and the pain became much worse. The patient underwent emergency cholecystectomy the same night, and the liver was noted to be congested and friable, with features of fatty liver. The gallbladder was tense, dilated, and edematous. On exploration of the common bile

duct, lancet-shaped worms were seen emerging from it, some of them were noted to be swimming in the washing solution. No stones were found. Lancet-shaped adult worms were also found in parts of the gallbladder. Forty-five adult worms were sent to the diagnostic laboratory. The worms were identified as *Clonorchis sinensis*, measuring an average of 18 mm long by 4 mm wide and appeared flat, transparent, attenuated anteriorly, and rounded posteriorly. Branched testes was seen in the posterior part of the body. The eggs retrieved from the ruptured uterus measured an average of 28 μm long by 14.5 μm wide and were operculated. The histopathology report showed no evidence of malignancy and histopathological findings of the gallbladder was consistent with acute-on-chronic cholecystitis and cholesterosis. On further questioning, the patient gave a history of travelling to China and Hong Kong 1 month before admission and had consumed raw fish while visiting these places. After the operation, the patient was treated with praziquantel 25 mg/kg t.i.d. for 2 consecutive days. He had an uneventful recovery.

Source: Rohela, M., J. Surin, I. Jamaiah, I. Init, and S. H. Lee. "Acute cholecystitis caused by *Clonorchis sinensis*." Southeast Asian Journal of Tropical Medicine and Public Health 37, no. 4 (2006): 648–51.

Learning Points

1. Clonorchiasis is commonly reported in the Far East and is acquired by ingestion of raw/undercooked freshwater fish.
2. Clonorchiasis is known to be associated with cholangiocarcinoma.

Acknowledgement

We are grateful to Dr. Benedict Sim Lim Heng, Consultant Infectious Diseases Physician, Hospital Sungai Buloh, Selangor, Malaysia for providing the learning points.

Case 20: Visceral Leishmaniasis

Case report: A previously healthy 40-year-old gentleman was referred to the hospital with 1-month history of fever with chills and rigors, significant weight loss and non-productive cough. He received multiple courses of antibiotic (ampicillin/sulbactum, ceftriazone, piperacilin/tazobactam) but to no avail. On examination, he was febrile (38.5 °C), blood pressure 110/70 mmHg, oxygen saturation of 99%. He was pale but not jaundiced. There was non-tender hepatomegaly measuring 3 finger breadth. The Traube's space was dull. Auscultation of the lungs revealed bibasal crepitations. Otherwise, jugular venous pressure was not raised and there was no pitting ankle oedema. Blood investigations demonstrated pancytopenia (white blood cells $3.2 \times 10^3/\mu L$, haemoglobin 9.5 g/dL, platelets $39 \times 10^3/\mu L$) and alkaline phosphatase 110 IU/L. Total bilirubin, alanine transaminase, and renal profile were normal. Blood cultures and blood film for malaria were repeatedly negative. HIV serology was negative. A CT scan of chest and abdomen demonstrated hepatomegaly with multiple calcifications in the spleen, pericardial effusion, and consolidations in bilateral lung bases with minimal pleural effusion. Echocardiography

confirmed the presence of pericardial effusion. On further questioning, he said that he had worked in Rio De Janeiro, Brazil for 5 months and since his return, he had been working in Singapore. The new information has led us to investigate for leishmaniasis. Intravenous deoxycholate amphotericin B (1 mg/kg/day) was initiated empirically. Fever subsided at the third dose of therapy. Amastigotes were not noted in full blood picture, bone marrow aspirates and trephine biopsy. However, PCR for *Leishmania* on peripheral blood was positive. This confirmed our diagnosis of visceral leishmaniasis. At this point, serial echocardiography showed worsening of pericardial effusion. Drainage was performed after consultation with a cardiologist. Interestingly, very scanty acid fast bacilli was noted from one of the many sputum specimens. There were conflicting opinions about commencement of anti-tuberculous treatment at this point as bronchoscopic examination was unremarkable. Bronchio-alveolar lavage, pericardial fluid, peripheral blood, and bone marrow aspirates for acid fast bacilli, mycobacterium culture, and PCR were all negative. He was discharged after receiving a total of 18 doses of amphotericin B. On discharge, his white blood cells was $3.61 \times 10^3/\mu L$, haemoglobin was 9.4 g/dL, and platelets was $97 \times 10^3/\mu L$.

Two months later, he was readmitted for fever, chills and rigors with worsening pancytopenia (white blood cells $2.26 \times 10^3/\mu L$, haemoglobin 8.6 g/dL, platelets $90 \times 10^3/\mu L$). Echocardiography showed reaccumulation of pericardial effusion but was not causing cardiac tamponade. Intravenous amphotericin B was re-initiated. However, he did not demonstrate response to amphotericin this time. A repeated leishmania PCR on blood was negative, indicating the possibility of co-infection. Anti-tuberculosis treatment was initiated. He improved dramatically with this therapy. At 56th dose of intensive anti-tuberculosis therapy, he remained asymptomatic. Echocardiography showed complete resolution of pericardial effusion. A clinic review 2 years later showed his blood counts were within normal range (white blood counts $13.2 \times 10^3/\mu L$, haemoglobin 13.2 g/dL, platelets $229 \times 10^3/\mu L$).

Learning Points

1. Clinicians should maintain a high index of suspicion for visceral leishmaniasis in a patient who has returned from an endemic country and presents with fever, hepatosplenomegaly, and pancytopenia.
2. PCR-based assays can be performed on peripheral blood and bone marrow aspirates to detect leishmania DNA.
3. Visceral leishmaniasis may trigger an overt T-cell response, exhausting the body immune system. This immunosuppressive stage may render patient more susceptible to other infections, e.g., Tuberculosis.

Acknowledgement

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Question Bank

1. This protozoa causes dysentery:

A.	*Giardia lamblia*	F
B.	*Cystoisospora belli*	F
C.	*Entamoeba histolytica*	T
D.	*Blastocystis hominis*	F
E.	*Balantidium coli*	T

2. *Plasmodium falciparum*

A.	causes enlargement of the infected red blood cells	F
B.	causes cerebral malaria	T
C.	has a hypnozoite stage in the liver	F
D.	has crescent-shaped gametocytes	T
E.	can cause recrudescence in human	T

3. Regarding Chagas' disease:

A.	It is caused by *Trypanosoma brucei* complex	F
B.	Human acquires the disease via the bites of infected sandflies	F
C.	It causes megasyndrome in patients with prolonged illness	T
D.	The most common clinical manifestation is Winterbottom's sign	F
E.	It can be diagnosed by detecting the promastigote in the spleen	F

4. Regarding intestinal nematodes of man:

A.	*Enterobius vermicularis* is not a soil-transmitted helminth	T
B.	*Strongyloides stercoralis* is the smallest intestinal nematode	T
C.	*Capillaria philippinensis* lives in the lumen of the small intestine	F
D.	*Trichinella spiralis* is oviparous	F
E.	*Trichuris trichiura* has a similar mode of transmission as *Ascaris lumbricoides*	T

5. Regarding *Brugia malayi*:

A.	It causes lymphatic filariasis	T
B.	Its infection is transmitted by the black flies	F
C.	Its microfilaria has two terminal nuclei	T
D.	Its microfilaria shows periodicity phenomenon	T
E.	Microfilaria is the infective stage to human	F

6. Regarding human blood fluke:

A.	It is the only fluke in which the sexes are separated	T
B.	It requires a second intermediate host to complete its life cycle	F
C.	The infective stage to human is metacercaria	F
D.	Its egg is operculated	F
E.	Its adult lives in venous blood vessels of human	T

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7. Regarding *Taenia solium:*

A.	Cow is its intermediate host	F
B.	Human is its definitive host	T
C.	Its infection can cause vitamin B_{12} deficiency	F
D.	Its larval stage is not found in human	F
E.	Its egg cannot be differentiated from that of *Taenia saginata*	T

8. Regarding parasitic infections in the respiratory system:

A.	Tropical pulmonary eosinophilia is caused by strongyloidiasis	F
B.	Ascariasis causes Loeffler's syndrome	T
C.	Pulmonary oedema is a complication of falciparum malaria	T
D.	Paragonimiasis causes haemoptysis	T
E.	Pulmonary amoebiasis is an extension of amoebic liver abscess	T

9. Regarding the life cycle of malaria parasite:

A.	*Aedes* mosquito is the vector	F
B.	Human is the intermediate host	T
C.	The complete life cycle requires two hosts	T
D.	Trophozoite is the natural infective stage to human	F
E.	Gametocyte is the infective stage to the vector mosquito	T

10. This parasite undergoes lung migration phase in its life cycle:

A.	*Ascaris lumbricoides*	T
B.	Hookworm	T
C.	*Trichuris trichiura*	F
D.	*Enterobius vermicularis*	F
E.	*Strongyloides stercoralis*	T

11. Regarding *Wuchereria bancrofti:*

A.	It causes river blindness	F
B.	It is transmitted to human via mosquito	T
C.	Its clinical manifestations are caused by microfilaria	F
D.	The adult stage is found in the lymph nodes	T
E.	Its infection can be diagnosed via blood examination	T

12. This is a clinical feature of African trypanosomiasis:

A.	Winterbottom's sign	T
B.	Chagoma	F
C.	Chancre	T
D.	Onchocercoma	F
E.	Romana's sign	F

13. *Mansonia* mosquito is the vector for

A.	Dengue haemorrhagic fever	F
B.	Dengue fever	F
C.	Malaria	F
D.	Lymphatic filariasis	T
E.	Onchocerciasis	F

14. Human is a definitive host for this tapeworm:

A.	*Taenia solium*	T
B.	*Spirometra* spp.	F
C.	*Hymenolepis nana*	T
D.	*Diphyllobothrium latum*	T
E.	*Echinococcus granulosus*	F

15. Regarding *Entamoeba histolytica*:

A.	Its trophozoites are seen in loose stools	T
B.	Its natural infective stage is the trophozoite	F
C.	Red blood cells are found in the trophozoites	T
D.	Its trophozoites can invade the mucosa of the large intestine of human	T
E.	Its cysts are easily distinguishable by the presence of more than 4 nuclei	F

16. *Plasmodium falciparum*

A.	causes relapse after a primary infection	F
B.	causes malignant tertian malaria	T
C.	has a band-shaped trophozoite	F
D.	causes knobs to be formed on the infected red blood cells	T
E.	has crescent-shaped schizonts	F

17. *Ascaris lumbricoides*

A.	is found in the lumen of the small intestine	T
B.	lays infective eggs which are passed out in the stool	F
C.	is transmitted via faecal oral route	T
D.	adults can cause ectopic migration	T
E.	sucks human blood	F

18. Regarding *Taenia saginata*:

A.	Pigs are its intermediate host	F
B.	Humans are its definitive host	T
C.	Its infection can cause vitamin B_{12} deficiency	F
D.	Its larval stage is cysticercus cellulosae	F
E.	Its adult stage lives in the ileum of humans	T

19. This parasite causes lymphatic filariasis:

A.	*Loa loa*	F
B.	*Brugia timori*	T
C.	*Onchocerca volvulus*	F
D.	*Brugia malayi*	T
E.	*Wuchereria bancrofti*	T

20. Regarding *Schistosoma* spp.:

A.	The diagnostic stage is the egg	T
B.	The infective stage to human is miracidium	F
C.	Albendazole is the drug of choice for the treatment of its infection	F
D.	Its infection can be prevented by eating cooked meat	F
E.	The intermediate host is snail	T

21. The larva of this worm can cause cutaneous larva migrans:

A.	*Ancylostoma caninum*	T
B.	*Ancylostoma duodenale*	F
C.	*Ancylostoma braziliense*	T
D.	*Strongyloides stercoralis*	F
E.	*Necator americanus*	F

22. In intestinal amoebiasis, there is

A.	invasion of the mucosa by the trophozoite	T
B.	blunting and shortening of villi	F
C.	formation of flask-shaped ulcers	T
D.	mechanical blockage affecting the absorption of fats	F
E.	inflammation which leads to toxic megacolon	T

23. This parasite causes malabsorption syndrome:

A.	*Giardia lamblia*	T
B.	*Cryptosporidium parvum*	T
C.	*Strongyloides stercoralis*	T
D.	*Balantidium coli*	F
E.	*Trichuris trichiura*	F

24. Regarding malaria parasite:

A.	Asexual cycle occurs in human	T
B.	Hypnozoite is found in *Plasmodium vivax* infection	T
C.	The natural infective stage to human is the merozoite	F
D.	*Plasmodium malariae* infection commonly causes the highest parasitaemia	F
E.	Schizonts of *Plasmodium falciparum* are frequently found in the peripheral blood	F

25. Infection with this parasite can cause extensive damage to human urogenital structures:

A.	*Schistosoma haematobium*	T
B.	*Wuchereria bancrofti*	T
C.	*Ascaris lumbricoides*	F
D.	*Toxoplasma gondii*	F
E.	*Naegleria fowleri*	F

26. Regarding cerebral malaria:

A.	It is a complication of *Plasmodium vivax* infection	F
B.	It is fatal if not treated	T
C.	All stages of the infected red blood cells develop knobs on their surface	F
D.	Intravenous artesunate is given for its treatment	T
E.	Cerebrospinal fluid findings are abnormal in most cases of cerebral malaria	F

27. This helminth inhabits the bile duct of humans:

A.	*Fasciola hepatica*	T
B.	*Clonorchis sinensis*	T
C.	*Opisthorchis viverrini*	T
D.	*Fasciolopsis buski*	F
E.	*Ascaris lumbricoides*	F

28. This parasite causes cutaneous lesions:

A.	*Loa loa*	T
B.	*Leishmania tropica*	T
C.	*Trichuris trichiura*	F
D.	*Ancylostoma braziliense*	T
E.	*Onchocerca volvulus*	T

29. Amoebic keratitis

A.	has been associated with the use of contact lens	T
B.	can spread and cause amoebic encephalitis	F
C.	is caused by *Acanthamoeba* spp.	T
D.	is diagnosed by detection of the amoebic cyst in corneal scrapings	T
E.	is frequently reported in AIDS patients	F

30. This parasitic infection causes high eosinophilia:

A.	Toxocariasis	T
B.	Trichinosis	T
C.	Malaria	F
D.	Giardiasis	F
E.	Trichomoniasis	F

31. This parasitic disease causes intracerebral lesions in AIDS patients:

A.	Amoebiasis	F
B.	Cystoisosporiasis	F
C.	Toxoplasmosis	T
D.	Malaria	F
E.	Cryptosporidiosis	F

32. This parasite can cause ocular lesion:

A.	*Naegleria fowleri*	F
B.	*Toxocara canis*	T
C.	*Toxoplasma gondii*	T
D.	*Onchocerca volvulus*	T
E.	*Wuchereria bancrofti*	F

33. This parasite can cause abscess formation in the liver:

A.	*Giardia lamblia*	F
B.	*Cystoisospora belli*	F
C.	*Entamoeba histolytica*	T
D.	*Hymenolepis nana*	F
E.	*Ascaris lumbricoides*	T

34. Infection with this parasite causes splenomegaly:

A.	*Plasmodium vivax*	T
B.	*Trichuris trichiura*	F
C.	*Fasciolopsis buski*	F
D.	*Leishmania donovani*	T
E.	*Trypanosoma cruzi*	T

35. This parasite lives in the biliary tract of human:

A.	*Ascaris lumbricoides*	F
B.	*Heterophyes heterophyes*	F
C.	*Clonorchis sinensis*	T
D.	*Fasciola hepatica*	T
E.	*Paragonimus westermani*	F

36. This is the effect on the renal system in urinary schistosomiasis:

A.	Hydrocele	F
B.	Chyluria	F
C.	Bladder calculi	T
D.	Haematuria	T
E.	Bladder cancer	T

37. Blackwater fever

A.	occurs in patients infected with *Plasmodium falciparum*	T
B.	is caused by prolonged and inadequate quinine treatment	T
C.	can cause acute renal failure	T
D.	occurs in patients infected with quartan malaria	F
E.	is a serious syndrome in patients with G6PD deficiency	T

38. This parasite can infect human muscle:

A.	*Toxoplasma gondii*	T
B.	*Wuchereria bancrofti*	F
C.	*Sarcocystis*	T
D.	*Trichinella spiralis*	T
E.	*Taenia saginata*	F

39. The classic triad of congenital toxoplasmosis include:

A.	Retinochoroiditis	T
B.	Endocarditis	F
C.	Hydrocephalus	T
D.	Gastroenteritis	F
E.	Myositis	F

40. Cerebral malaria

A.	shows sign of neck stiffness	F
B.	is treated with chloroquine	F
C.	is a complication of *Plasmodium falciparum* infection	T
D.	is diagnosed by blood culture	F
E.	causes abnormal changes in the cerebrospinal fluid	F

41. Iron deficiency anaemia

A.	is the result of hypersplenism	F
B.	causes a high serum ferritin level	F
C.	can occur in chronic hookworm infection	T
D.	is normally associated with chronic blood loss	T
E.	is associated with *Diphyllobothrium latum* infection	F

42. Regarding *Giardia lamblia:*

A.	Trophozoites are seen in loose stools	T
B.	Cyst is the infective stage	T
C.	Red blood cells are found in the trophozoites	F
D.	Its trophozoites can invade the mucosa of the large intestine of human	F
E.	In severe infection, it can cause dysentery	F

43. Amoebic liver abscess

A.	can be diagnosed by serological test	T
B.	has cyst stage in the pus	F
C.	causes pain in the right hypochondrium	T
D.	is treated with metronidazole	T
E.	is usually located in the left lobe of the liver	F

44. This is the clinical feature of late lymphatic filariasis:

A.	Haemoptysis	F
B.	Haematemesis	F
C.	Hydrocele	T
D.	Haematuria	F
E.	Chyluria	T

45. Regarding *Giardia lamblia*:

A.	Its infection causes blunting and shortening of villi	T
B.	It is an intracellular parasite	F
C.	Its infection causes malabsorption of fats	T
D.	Trophozoite is commonly found at the rectosigmoid region	F
E.	Its infection is routinely diagnosed using serological test	F

46. Congenitally acquired parasites include:

A.	*Toxoplasma gondii*	T
B.	*Toxocara canis*	F
C.	*Cryptosporidium parvum*	F
D.	*Plasmodium falciparum*	T
E.	*Taenia solium*	F

47. This parasite causes space-occupying lesions in the liver:

A.	*Entamoeba histolytica*	T
B.	*Toxoplasma gondii*	F
C.	*Plasmodium falciparum*	F
D.	*Echinococcus granulosus*	T
E.	*Leishmania major*	F

48. Enlarged lymph nodes are found in the following parasitic diseases:

A.	Toxoplasmosis	T
B.	Ascariasis	F
C.	Kala azar	T
D.	Giardiasis	F
E.	Filariasis	T

49. This parasite causes ocular infection:

A.	*Onchocerca volvulus*	T
B.	*Toxoplasma gondii*	T
C.	*Naegleria fowleri*	F
D.	*Toxocara canis*	T
E.	*Cysticercus cellulosae*	T

50. Iron deficiency anaemia can be caused by

A.	*Ancylostoma duodenale*	T
B.	*Necator americanus*	T
C.	*Plasmodium falciparum*	F
D.	*Diphyllobothrium latum*	F
E.	*Trichuris trichiura*	T

51. *Cryptosporidium*

A.	is transmitted via water	T
B.	is an intracellular parasite	T
C.	can cause chronic diarrhoea	T
D.	is only found in humans	F
E.	can be killed by boiling the water	T

52. A 24-year-old woman at 32 weeks gestation was confirmed through ultrasound that her foetus had hydrocephaly. This clinical manifestation is thought to be due to an infection acquired during her current pregnancy.

The organism which causes this congenital anomaly is

A.	*Trypanosoma cruzi*	F
B.	*Plasmodium vivax*	F
C.	*Toxoplasma gondii*	T
D.	*Trypanosoma brucei*	F
E.	*Leishmania donovani*	F

53. This parasite is acquired by humans via ingestion of infected fish:

A.	*Clonorchis sinensis*	T
B.	*Taenia saginata*	F
C.	*Diphyllobothrium latum*	T
D.	*Paragonimus westermani*	F
E.	*Schistosoma japonicum*	F

54. Regarding hookworm anaemia:

A.	The condition is due to vitamin B_{12} deficiency	F
B.	It is seen in chronic hookworm infection	T
C.	Infected patient may present with pallor and tiredness	T
D.	Red blood cells are microcytic and hypochromic	T
E.	It is caused by *Necator americanus*	T

55. Microfilariae of this filarial worm show nocturnal periodicity:

A.	*Loa loa*	F
B.	*Brugia timori*	T
C.	*Onchocerca volvulus*	F
D.	*Brugia malayi*	T
E.	*Wuchereria bancrofti*	T

56. Six months after a 2-week vacation in the countryside in central India, a 22-year-old female patient developed irregular fever with chills and rigors, abdominal discomfort with hepatosplenomegaly. These clinical manifestations are thought to be due to an infection acquired via insect bite.

The likely organism to cause these clinical manifestations is

A.	*Trypanosoma cruzi*	F
B.	*Loa loa*	F
C.	*Leishmania donovani*	T
D.	*Toxoplasma gondii*	F
E.	*Trypanosoma brucei*	F

57. The diagnosis of this parasite involves the use of cellophane tape to recover the eggs in the perianal region:

A.	*Ascaris lumbricoides*	F
B.	Hookworm	F
C.	*Trichuris trichiura*	F
D.	*Enterobius vermicularis*	T
E.	*Strongyloides stercoralis*	F

58. Mosquito is the definitive host of this parasite:

A.	*Plasmodium vivax*	T
B.	*Plasmodium falciparum*	T
C.	*Plasmodium ovale*	T
D.	*Brugia malayi*	F
E.	*Wuchereria bancrofti*	F

59. *Plasmodium malariae* causes

A.	quartan malaria	T
B.	zoonotic malaria	F
C.	cerebral malaria	F
D.	recrudescence after primary attack	T
E.	infected red blood cells to be enlarged	F

60. Tropical pulmonary eosinophilia (TPE) is caused by

A.	*Strongyloides stercoralis*	F
B.	*Brugia malayi*	T
C.	*Wuchereria bancrofti*	T
D.	*Loa loa*	F
E.	*Toxocara canis*	F

61. A 28-year-old-woman at 20 weeks gestation returned from Ethiopia and presented with a history of fever, soft-tissue swelling of the forehead with severe regional lymphadenopathy. Blood smear shows *Trypanosoma brucei*.

The treatment of choice is

A.	albendazole	F
B.	ivermectin	F
C.	suramin	T
D.	mebendazole	F
E.	praziquantel	F

62. This is a specific characteristic for human trematodes:

A.	*Schistosoma japonicum* has ova with a lateral spine	F
B.	Miracidium is an infective stage to human	F
C.	All trematode eggs are operculated	F
D.	All trematodes are hermaphrodites	F
E.	Snail is the first intermediate host	T

63. The control measures for the following parasites include periodical deworming, health education and improved sanitation to reduce soil contamination with infective eggs:

A.	*Ascaris lumbricoides*	T
B.	*Enterobius vermicularis*	F
C.	*Capillaria philippinensis*	F
D.	*Trichinella spiralis*	F
E.	*Trichuris trichiura*	T

64. Regarding *Plasmodium knowlesi*:

A.	It has a 48-h asexual life cycle	F
B.	It causes enlargement of the infected red blood cells	F
C.	It is a zoonosis	T
D.	It has a band-shaped trophozoite	T
E.	Its gametocyte stage is not found in the peripheral blood	F

65. *Toxoplasma gondii*

A.	is an intracellular parasite	T
B.	is transmitted via cat bite	F
C.	infection is routinely diagnosed by serological test	T
D.	infection in humans can be prevented with vaccination	F
E.	infection can be treated with a combination of pyrimethamine and sulfadiazine	T

66. Scabies

A.	is caused by *Sarcoptes scabiei*	T
B.	is transmitted to human by close contact with an infected person	T
C.	presents with pruritus of the lesions on the body	T
D.	is diagnosed by serological test	F
E.	causes high eosinophilia	F

Note: We acknowledge the contributions of the past and present academic staff at the Department of Parasitology, Faculty of Medicine, University of Malaya. These questions have been modified from the archived questions bank of previous curriculum.

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