Atlas of Medical Helminthology and Protozoology
Fourth Edition

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Medical Helminthology and Protozoology

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Illustrated by Robert Britton
Preface

Since this atlas was first published, major advances in immunology and molecular biology have transformed our understanding of the parasitic diseases which affect humans. The programme to eradicate Guinea worm is well advanced and real progress is being made towards a malaria vaccine. However, none of the parasites described in the first edition have yet been consigned to history. Indeed, *Cyclospora* and the microsporidia are newly recognised as important human pathogens even since the third edition, and in some geographical areas the malaria situation is worse, with the spread of multi-drug resistant *Plasmodium falciparum* malaria. There is a great deal left to be done.

Effective action against parasitic disease requires a team approach, including epidemiologists, biologists, diagnostic laboratory workers and clinicians. Common to all these disciplines is a need to understand the life cycles and morphology of the organisms they confront. It is hoped that this edition of the atlas will provide an appropriate introduction. The strong emphasis on diagnosis has been retained and since diagnostic parasitology still relies heavily on morphology, we have strengthened this area with the introduction of colour illustrations and photomicrographs.

We hope this book will help to kindle enthusiasm for the effort to control these parasites and the diseases they cause.

London
2001

P. L. C.
A. H. M.
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Acknowledgement

This atlas first originated from the Royal Army Medical College, London. The late Major-General HC Jeffrey and the late RM Leach wrote the first two editions. Colonel, later Major-General, GO Cowan undertook revision for the third edition and an abridged version of his introduction is included in this latest edition.
Introduction

The protozoan and the helminth, as regards tropical pathology, are in the ascendand.

Sir Patrick Manson (1899)

Parasites to the Ancient Greeks were those who sat at another’s table and paid for their meal with flattery. In biology, a parasite is an animal or plant living in or on another (the host) and drawing nourishment from it. This definition could include viruses, bacteria and fungi as well as protozoa and helminths, but historically the first group has been studied in microbiology, the second in parasitology. In tropical diseases, Manson’s dictum remains valid today.

Protozoa are small, unicellular organisms, which contain a nucleus and functional organelles. They reproduce quickly and asexually in the host, but may have a sexual phase of their life cycle in another host or vector.

Helminths (worms), which are metazoa, are larger, multicellular organisms, normally visible to the naked eye in their adult form. They reproduce sexually, usually within the host, and have pre-adult stages (ova, larvae) which live externally or in other hosts.

Transmission of parasites requires:
- a source or reservoir which may be human or animal
- a route of infection, e.g. ingestion, penetration or an insect vector.

The definitive host is that in which sexual reproduction occurs (e.g. mosquitoes for malaria) or in which the mature form of the parasite occurs (e.g. humans for African trypanosomiasis). An intermediate host is another animal essential to the completion of the life cycle (e.g. snails for schistosomiasis).

Parasites cause disease in humans by:
- mechanical effects, e.g. hydatid cyst
- invasion and destruction of host cells, as in malaria
- allergic or inflammatory immune reaction by the host to the parasite, e.g. toxocariasis and trypanosomiasis
- competition for specific nutrients, e.g. *Diphyllobothrium latum* for vitamin B₁₂
- or there may be no obvious disease, as in *Taenia saginata* in humans.

Diagnosis in parasitic diseases depends on:
- a history of exposure and the clinical pattern of illness in the patient
- identification of the parasite itself in excreta (stool, urine), blood, or specific tissues
- indirect evidence of the parasite by testing the patient’s blood for antibodies
- detection of parasite antigens in clinical specimens
- detection of parasite DNA or RNA in clinical specimens.
Helminthology
Worms of medical importance

Nematodes (round worms)
- Unsegmented
- Possess mouth, oesophagus and anus
  - Important in further diagnosis
- In general, sexes separate
- Reproduction
  - Oviparous
  - Larviparous
- Infection by
  - Ingestion of eggs, or
  - Penetration of larvae through surfaces, or
  - Arthropod vector, or
  - Ingestion of encysted larvae

Cestodes (tape worms)
- Segmented
- Possess scolex, neck and proglottids
- Hermaphroditic
- Reproduction
  - Oviparous
  - Sometimes multiplication within larval forms
- Infection generally by encysted larvae

Trematodes (flukes)
- Unsegmented
- Leaf-like or cylindrical
- Generally hermaphroditic
- Reproduction (digeneric)
  - Oviparous
  - Multiplication within larval forms
- Infection mainly by larval stages entering intestinal tract, sometimes through skin
Nematode (round) worms

*Enterobius vermicularis* (thread or pin worm)

**Life cycle**

1. **Maturation in humans** 15–26 days
2. **Caecum and lower ileum**
3. **Gravid female crawls through anus to oviposit on perianal skin**
4. **Mature in hours (viable for months)**

**Distribution**

350 million infected worldwide, often group or institutional infection.

**Pathology and Clinical features**

Most infections are asymptomatic. Perianal itching may be troublesome. In females, migrating worms may cause pruritis vulvae or vaginitis. Rarely, urinary tract infection or appendicitis can occur. Migration into the peritoneal cavity has been recorded.

**Laboratory diagnosis**

Mild eosinophilia.

Ova can be recovered from the perianal area using clear adhesive tape or a cotton swab moistened with saline. Early morning collection before washing gives best recovery. In females, ova may occasionally be recovered from urine.
Pathology and Clinical features

Light infections may be asymptomatic. Heavy infections can result in the trichuris dysentery syndrome, rectal prolapse, rectal bleeding, anaemia, growth stunting and growth retardation in children.

Laboratory diagnosis

Eosinophilia may occur. Ova may be recovered in faeces by concentration methods.

Distribution

1.3 billion infected worldwide.
**Pathology and Clinical features**

Larvae can cause pneumonitis with eosinophilia. Adult worms can cause obstruction of the small intestine, bile ducts and trachea; also appendicitis, pancreatitis and peritonitis. Children may vomit up a bolus of adult worms, or cough up immature worms.

**Laboratory diagnosis**

Ova may be recovered from faeces by concentration methods. Rarely larvae can be found in sputum, and must be distinguished from those of *Strongyloides*. Eosinophilia is present in the larval invasion stage.

No specific serology is currently available.

**Distribution**

1.47 billion infected worldwide.
**Pathology and Clinical features**

Ground itch may follow skin penetration by filariform larvae. Pneumonitis can result from larval migration through the lungs. Adult worms in the jejunum ingest blood. Occult gastrointestinal bleeding occurs. Iron deficiency anaemia and its sequelae in heavy infections.

**Distribution**

900 million infected worldwide.

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**Laboratory diagnosis**

Eosinophilia.

Ova may be recovered from faeces by concentration methods. Rhabditiform larvae may be seen in old faecal specimens and must be distinguished from *Strongyloides* by the appearance of the buccal cavity.
**Strongyloides stercoralis**

**Life cycle**

- **Larvae mature in duodenum (or bronchus)**
- **Eosinophilia**
- **Larvae enter circulation and via heart, lungs, respiratory tree and oesophagus reach intestine. Maturation in humans 17 days**
- **Rhabditiform larvae passed in faeces**
- **Rhabditiform larvae metamorphose in bowel to filariform larvae**
- **Passed in faeces**
  - **New host**
  - **Same host skin**
  - **Same host bowel wall**
- **Direct cycle**
  - **Autoinfection**
- **Indirect cycle**
  - **Free living**

**Pathology and Clinical features**

Skin penetration by larvae may cause local irritation. Migrating larvae can cause pneumonitis, and ectopic larvae can sometimes be found in the brain and other viscera. A characteristic serpiginous urticarial rash (larva currens) is seen on the trunk and buttocks.

Established infection may have no signs or symptoms, or present with larva currens alone. Diarrhoea, abdominal pain, bloating and sometimes malabsorption can be found. The *Strongyloides* hyperinfection syndrome results from massive autoinfection with filariform larvae in the presence of severe immunosuppression or cachexia. Risk factors include steroid and/or cytotoxic therapy, HTLV1 infections, HIV infections, malignancy, severe malnutrition and other severe systemic disorders. Clinical features include diarrhoea, gastrointestinal haemorrhage or perforation, pneumonitis, Gram-negative bacterial meningitis or septicaemia with high mortality.

**Distribution**

70 million infected worldwide.

**Laboratory diagnosis**

Eosinophilia may be present, but its absence does not exclude diagnosis. It is essential to examine fresh specimens. Rhabditiform larvae can be seen in faeces by direct microscopy or by concentration methods. Filariform larvae may also be seen in faeces, sputum and other body fluids, particularly in immunocompromised hosts. Faecal culture using charcoal is an important diagnostic method. Duodenal aspiration and the 'string test' are also recommended isolation methods. Serology by ELISA is useful in chronic infection.
Trichinella spiralis

Life cycle

A given host can be definitive or intermediate, but two hosts, both carnivores, are required to complete the cycle.

- horses
- dogs
- foxes
- cats
- wild pigs
- bears
- badgers
- seals

Swill, calf, etc.

Domestic pig

Rat

Humans are infected by eating raw or undercooked infected pork, pork products or horsemeat.

Infected flesh is digested by gastric juices; the larvae are set free and develop into adults in duodenum. The gravid female burrows into mucosa and releases larvae which enter circulation and are disseminated throughout the body.

Laboratory diagnosis

Eosinophilia and high serum CPK in the acute phase. At the encystment stage, use muscle biopsy, muscle crush preparation and serology (IFAT or ELISA).

Distribution

50 million infected worldwide.
Pathology and Clinical features

Invasion

Intestinal inflammation leading to diarrhoea. Inflammatory response leading to periorbital oedema, haemorrhages under nails, muscle pains and myocarditis.

Dissemination

Migration may occur through any tissue but larval encystment is only in striated muscle. A granulomatous response develops elsewhere.

Localization

Especially muscles of respiration and tongue. Long term: eventual fibrosis and degeneration, resulting in calcification.

Organization

Laboratory diagnosis

At the diarrhoeal stage, adults and larvae may be found occasionally in faeces. Eosinophilia is high. At the encystment stage, use muscle biopsy, muscle crush preparation and serology (IFAT or ELISA).
**Pathology and Clinical features**

Adult worms in the lymphatic channels cause proliferation of the lining of the endothelium. Surrounding infiltration of eosinophils, macrophages, lymphocytes and giant cells causes filarial granulation tissue leading to obstruction, secondary infection, fibrosis and calcification. The results of this are acute lymphangitis, filarial abscess, lymphadenopathy, elephantiasis, hydrocele and chyluria. Tropical pulmonary eosinophilia (TPE) occurs in individuals who are hyper-responsive to filarial antigens, giving rise to nocturnal cough, wheeze and low-grade fever.

**Development in mosquito**

- Maturation time: 2–3 weeks
- May survive several months

*Development in mosquito*:
- The larvae penetrate stomach, migrate to thoracic muscles, develop, then migrate to head, mature and become infective.

*Adults*:
- Nocturnal periodicity
- Head bluntly rounded
- Head: 85–100 x 0.25 mm
- Tail: 40 x 0.1 mm

**Localization**

- Microfilariae appear in the blood 1 year after infection

**Microfilariae**

230–320 μm x 10 μm

- Tail pointed, free from nuclei
- Sheathed

**Distribution**

90 million infected worldwide.

**Laboratory diagnosis**

Eosinophilia.

Microfilariae are found in peripheral blood collected between 10pm and 2am, or at midday for *W. bancrofti var.pacific*. Thick blood films are examined stained or unstained, concentration by Knott's method will increase sensitivity. Filtration of citrated blood through a 5 micron pore size polycarbonate membrane is the method of choice.

Microfilariae can also be found in chylous exudate, chylous urine and in hydrocoele fluid.

**Serology.** ELISA is of use. Patients with TPE have high filarial antibody levels. A specific *W. bancrofti antigen immuno* chromatographic test is now commercially available.
**Brugia malayi**

**Life cycle**

- Nocturnal periodicity
- Life cycle as for *W. bancrofti* (p. 12)

**Laboratory diagnosis**

As for *Wuchereria bancrofti* except for the specific antigen test.

**Distribution**

**Pathology and Clinical features**

These are similar to those of *Wuchereria*, but *Brugia* more commonly affects the upper limbs. Hydrocoele, other genital lesions and chyluria are rare.
**Pathology and Clinical features**

Transient subcutaneous (Calabar) swellings due to hypersensitivity to adult excretory products.

The adult worm may appear under the conjunctiva and can be removed surgically. Symptoms include fatigue, chronic pruritus, rarely encephalopathy or nephropathy.

**Laboratory diagnosis**

Eosinophilia.

Microfilariae are found in blood by day (between noon and 14:00 hours). Nucleopore membrane filtration or centrifugation after lysis of the blood (Knott's method) can be used.

**Seroology.** ELISA detects antibodies to filarial antigens but is non-specific.

**Distribution**

33 million infected, mostly in the great river basins of Africa, e.g. Congo, Niger.
Pathology and Clinical features

Fibrous nodules develop round the adult worms, especially over the iliac crests. There may be some lymphatic obstruction; elephantiasis has been noted in Africa. The microfilariae cause itching, excoriation, urticaria, depigmentation, lichenification, ‘sowda’ and lymphadenopathy. When invading the eye, they can cause inflammatory lesions in any part of the eye such as sclerosing keratitis, choroidoretinitis and optic atrophy. Blindness may ensue.

Where microfilariae cannot be demonstrated, a Mazzotti test (DEC provocation test) can be useful.

Laboratory diagnosis

Eosinophilia.

Adult worms can be detected in excised nodules, microfilariae in the anterior chamber of the eye (slit lamp), skin snips and rarely in blood and urine.

Specific serodiagnosis by ELISA and PCR for parasite DNA on skin samples is in use.

Distribution

17 million infected worldwide.
Other filarial worms

These worms are much less pathogenic. Microfilariae of other species are unsheathed, may be found in the blood and tissues and differentiation from Wuchereria and Brugia is necessary. Filtration requires 3 micron pore size membrane, because of the smaller size of these microfilariae. No periodicity.

**Mansonella perstans**

Found in Tropical Africa and the coasts of Central and South America. The vector is the midge *Culicoides*. Microfilariae can be found in the blood.

**Mansonella streptocerca**

Found in Africa. The vector is the midge *Culicoides*. Microfilariae can be found in the skin.

**Mansonella ozzardi**

Found in South America and the Caribbean. The vector is the midge *Culicoides*. Microfilariae can be found in the blood and skin.
Pathology and Clinical features

The gravid female causes itching, urticaria and a burning sensation. A blister appears which bursts to become an ulcer (usually leg) with discharge of embryos and some fibrosis. The adult female may be seen protruding from the ulcer. There is often secondary bacterial infection, and sometimes arthritis of the knee and ankle. Worms may fail to emerge, die and calcify.

Laboratory diagnosis

Eosinophilia.
Larvae may be found in fluid from the ulcer.

Distribution

70,000 infected worldwide.

Areas where dracunculiasis is endemic (based on reported cases in 1997). (Map reprinted from Weekly Epidemiological Record 1997; 72(6):33-35; prepared by WHO/UNICEF HealthMap Programme & CTD/DRA, Geneva: WHO.)
**Phasmid Nematodes**

*Toxocara canis* (dog round worm)

**Morphology**

*Toxocara*: body is bent ventrally. *Toxascaris*: body is bent dorsally.

**Life cycle and occurrence**

Ocular larva migrans (OLM) and visceral larva migrans (VLM) usually occur as distinct entities without overlap. VLM occurs in younger children and gives rise to fever, pneumonitis and hepatomegaly. Myocarditis, convulsions, psychiatric changes or encephalopathy may occur. OLM presents as unilateral visual loss, often with squint. Retinal detachment, endophtalmitis or papillitis may occur.

**Laboratory diagnosis**

Eosinophilia.

**Serology.** Antibody detection by ELISA on serum. A vitreous sample may be required in OLM. Examination of environmental soil samples for ova by concentration techniques may be an aid to control.

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**Toxocara cati** (cat round worm)

**Life cycle**

In an incompatible host, the larvae hatch in intestine, gain circulation and are carried to viscera where they cause granulomata.
**Gnathostoma spinigerum**

### Morphology
Stout, reddish-coloured worms

- **♂** 11–25 mm
  - Cesophagus
  - Salivary gland
  - Cervical constriction

- **♀** 25–54 mm

### Life cycle and occurrence

- **Cats and dogs** Adults live in tumours in stomach wall
- **Ova in faeces** Hatches to larvae armed with spines
- **Ingested by cyclops** Stage larvae

Occasionally humans are infected by 3rd stage larvae but they cannot reach maturity. The larvae migrate to skin, subcutaneous tissue, muscle and brain.

- **Cutaneous larva migrans**
- **Visceral larva migrans** (or gnathostomiasis)

#### Laboratory diagnosis
ELISA for antibody detection. Histology or morphology of worm if excised.

#### Distribution
South East Asia, mainly Thailand.

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**Cutaneous Larva Migrans (creeping eruption)**
Caused by non-human hookworm larvae.

- **Ancylostoma braziliense**
- **Ancylostoma caninum**
- **Uncinaria stenocephala**

If they successfully invade humans, the intensely itchy infection lasts for months.
Cestode (tape) worms

*Taenia solium* (pork tape worm)

**Life cycle**

- **Usual** Intermediate host: liberated embryo, via bloodstream to tissue, especially muscle.
- **Measly pork**
- **Definitive host** (and reservoir)

**Ovum**

31-43 µm

Cysticercus is liberated, scolex evaginates, attaches itself to mucosa of small intestine. Develops to adult. Maturation time 3 months. Life span up to 25 years.

**Human cysticercosis**

Development of cysticercus

*Cysticercus cellulosae*—5 x 8–10 mm

**Section of human brain showing viable larva of T. solium**

**Infection with adult**

**Pathology and Clinical features**

**Infection by larvae (cysticercosis).** Cysticerci, generally multiple, may occur in any site but are more frequent in the brain and muscle. They excite reaction in the area, especially when they die, which manifests as inflammation, fibrosis and later some calcification. This leads to focal CNS syndromes, especially epilepsy.

**Infection with adults.** Often there can be no pathology, but there might be mild irritation of intestinal mucosa.

**Laboratory diagnosis**

Eosinophilia.

Larval infections. There are several methods, including histological examination of biopsy material, serology (IFAT, ELISA, EITB) and radiology (CT or MRI scan of the brain, X-ray of the thigh muscles).

Pure infection with the adult. Gravid segments, ova and scolex can be found in faeces. The uterine branches of the mature segments can be demonstrated by injection of Indian ink through the uterine pore.

**Distribution**

5 million people infected worldwide. *Taenia solium* is endemic in pig-rearing areas of the world where hygiene and animal husbandry are poor.
**Taenia saginata** (beef tape worm)

**Life cycle**

1. **Intermediate host, liberated embryo**
2. **Humans infected by eating undercooked beef**
3. **Definitive host and reservoir**
4. **Muscle segments rupture and release eggs**
5. **Scolex evaginates in small intestine and attaches itself to mucosa of jejunum**

**Pathology and Clinical features**

Usually there is no pathology as *Cysticercus bovis* is unknown in humans. Occasionally there is vague alimentary upset.

**Laboratory diagnosis**

Gravid segments, ova and scolex can be found in faeces. Uterine branches of the mature segments may be seen in a crush preparation between two glass slides, or by Indian ink preparation, as in *T. solium*. Ova are also found on the perianal skin (on clear adhesive tape slides).

**Distribution**

*Taenia saginata* is found in beef-eating areas, especially in the tropics.
**Dwarf tape worms**

**Hymenolepis nana**

**Life cycle**

- Ova ingested in contaminated food via hands etc.
- Ova passed in faeces 30 days after infection
- Liberated embryo penetrates villus and becomes cysticercoid in 4 days. Cysticercoid re-enters lumen, attaches itself to mucosa and develops into adult worm in 10–12 days.

**Pathology and Clinical features**

Often there are none, but with heavy infection there may be abdominal pain and diarrhoea. Anaemia and nervous symptoms, including dizziness and irritability, can occur in children.

**Laboratory diagnosis**

Eosinophilia may be present. Ova found in faeces.

**Distribution**

36 million people are infected worldwide.

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**Hymenolepis diminuta (rat tape worm)**

**Life cycle**

- Accidental ingestion by human of infected insect
- Cysticercoid liberated, attaches itself to mucosa and develops to adult worm
- Embryo hatched in gut, penetrates intestinal wall, develops into cysticercoid in body cavity

**Pathology and Clinical features**

Generally there is no effect on the host.

**Laboratory diagnosis**

Ova in faeces.

**Distribution**

Worldwide, but rare in humans.
**Pathology and Clinical features**

Generally there is none, but occasionally there can be megaloblastic anaemia (through absorption of vitamin B₁₂ by the worm).

**Laboratory diagnosis**

Eggs and gravid segments can appear in faeces. Megaloblastic anaemia (low serum B₁₂).

**Distribution**

16 million infected worldwide in eastern seaboard of Canada and America, Brazil, Baltic States, parts of West Africa, North Siberia and South East Asia.
Larval forms of cestode infection in humans

Sparganosis

Life cycle of such tapeworms

Sparganosis is caused by the extra-intestinal presence in the human body of larvae of non-human tapeworms of the genus *Spirometra.*

By ingestion

2nd intermediate hosts:
- Plerocercoid (sparganum) in frogs, reptiles (snakes), mammals

1st intermediate host:
- Procercoid in cyclops

By ingestion

Humans becoming infected with plerocercoid larvae by a route other than the intestine
- e.g. infected frog flesh applied to wound

Procercoid liberated in intestine penetrates intestinal wall

Develops into plerocercoid in subcutaneous tissue, muscle, fascia, etc.

Morphology of spargana
- 1–3 x 0.2–0.7 cm
- White, ribbon-like, motile structures

Pathology and Clinical features

Infestation with living larvae causes a painful oedematous reaction. Dead larvae cause intense local inflammatory reactions. There are numerous eosinophils and there can be abscess formation. There can be ocular sparganosis in the soft tissues near the eye, resulting in severe damage. Invasion of the CNS may occur.

Types of spargana

Most Spargana do not proliferate in human tissues. *Sparganum proliferum* is a very rare parasite in which sparganum proliferates by lateral budding.

Laboratory diagnosis

Diagnosis of the disease is by examination of biopsy material or excised larvae.

Distribution

The Far East mainly but occasionally elsewhere.
**Echinococcus granulosus (dog tape worm)**

**Life cycle**

_Echinococcus granulosus_ causes hydatid disease.

- **Ovum**: 30–37 μm
- **Definitive host**: Dog and other canines
- **Intermediate host**: Sheep, cattle etc. and other herbivores

**Adult**
- 30–36 hooks in two rows
- 4 suckers
- Immature
- Mature
- Proglottids
- Length 3–8 mm

**Hydatid cyst**
- Surrounding host tissue reaction forming false capsule
- Laminated membrane
- Germinal membrane
- Brood capsule
- Scolices

**Hydatid sand**
- Remains of germinal epithelium
- Brood capsules
- Protoscolices

- Invaginated in cyst
- Evaginated on entry into host

**Brood capsules of Echinococcus granulosus**

**Cestode (tape) worms** 25
Echinococcus multilocularis

Pathology and Clinical features of hydatid disease

Echinococcus granulosus

Unilocular cysts. There is usually surrounding inflammatory reaction and fibrosis. After years, the cyst may die, shrink and calcify. There is general allergic reaction with eosinophilia, bronchospasm, etc. Pressure effects can cause local tissue damage and obstruction of natural channels. Rupture or leakage of the cyst can accentuate the allergic reaction. There can be anaphylactic shock and sometimes secondary implantation, for example in the peritoneal region. There can also be secondary infection with formation of abscess.

Osseus cysts. Usually there is no fibrosis although there is some cellular infiltration. Destruction of the bone can sometimes lead to spontaneous fracture.

Echinococcus multilocularis

Alveolar cysts. There are local pressure effects and allergy. Germinal epithelium can act like a neoplasm with local infiltration or distant metastases.

Laboratory diagnosis of hydatid disease

Use serological tests on serum (e.g. ELISA, complement fixation, counter current immunoelectrophoresis for Arc 5 or immunoblot). Microscopy of cyst fluid from operative specimens can be used to assess viability of protoscolices. Histological examination of a removed specimen is another possibility.

Distribution

1 million infected worldwide. E. multilocularis is rare in humans, but occurs in Northern Europe, Asia, North America and Arctic regions. E. granulosus is widespread in sheep-rearing areas of the world. Eradication is well advanced in Australia and New Zealand.
Trematode (flat) worms

Schistosoma species (blood flukes)

Life cycle for all species

Vary in size according to species and sex
Range 6.4–20 x 0.25–1 mm

Ovum
Few minutes
Miracidium
16 hours

Development within snail host
4–8 weeks
Primary sporocysts 1
Secondary sporocysts 2
Developing cercariae 3

Cercaria
1–3 days
375–500 x 36–100 μm

Life cycle in humans

Immature schistosomes
Carried in circulation throughout body, generally only survive and mature in portal veins

Mature adults
Migrate to pelvic or mesenteric venous plexuses, ♂ lays eggs in small venules

Ova
1. Pass through tissue to lumen of viscera and are voided
2. Some gain general circulation and may land up anywhere

Cercariae
Lose tails, penetrate skin of host in 3–5 minutes and enter circulation via lymphatics
Schistosoma species (blood flukes) (Continued)

**Morphology**

*S. haematobium*

- **Female**:
  - Ovary posterior half

- **Male**:
  - 4–5 testes
  - Tegument slightly tuberculated
  - Terminal spine 112–170 x 40–70 μm

- **Ovum**:
  - 20–30 ova in uterus

*Host: Bulinus*

*S. mansoni*

- **Female**:
  - Ovary anterior half

- **Male**:
  - 8–9 testes
  - Tegument coarsely tuberculated

- **Ovum**:
  - 1–4 ova in uterus
  - Lateral spine 140–180 x 45–70 μm

*Host: Biomphalaria*

*S. japonicum*

- **Female**:
  - Ovary central

- **Male**:
  - 6–8 testes
  - Tegument smooth

- **Ovum**:
  - 50–100 ova in uterus
  - Lateral knob 70–105 x 50–80 μm

*Host: Oncomelania*

**Distribution**

*S. haematobium*: 78 million

*S. mansoni*: 57 million

*S. japonicum*: 69 million
Schistosomiasis

Pathology

Penetration of the skin by cercariae (1)
Skin penetration may not be apparent. Human and some non-human Schistosoma species cause cercarial dermatitis (swimmer’s itch). This manifests with papules, macules, vesicles and intense itching.

Migration and maturation of immature worms (2)
There are general toxic and allergic symptoms including urticaria with eosinophilia, fever, abdominal pain and tender hepatosplenomegaly. This is known as Katayama or snail fever.

Damage by eggs in tissue (3)
Resulting damage depends on the severity of the parasite load. An inflammatory granuloma forms with epithelial, giant, plasma and eosinophil cells and fibroblasts (Hoepppli reaction). There is subsequent fibrosis and calcification. Such damage may be local and/or ectopic.

Urinary schistosomiasis (4)
Caused by S. haematobium. Initial toxic and allergic symptoms are not marked, but the bladder and ureter are typically involved with hyperaemia, terminal haematuria, dysuria and frequency of micturition, papules, papillomata and ulceration. Hypertrophy of the bladder can lead to later contraction. There may be cystitis and calulus formation, with calcification and squamous cell carcinoma. Fistulae may develop. There can also be hydronephrosis and hydronephrosis. Ectopic lesions are less severe than in other species. Genital schistosomiasis may lead to lumpy semen, haematosperma or wart-like lesions on the vulva.

Intestinal schistosomiasis (5)
Caused by S. mansoni. There are marked initial toxic and allergic symptoms. The large intestine and rectum are typically involved with polyps, papules, abscesses, ulcers, papillomata, fistulae and ova in faeces. The bladder is sometimes involved, with pathology as for urinary schistosomiasis as above. There can be ectopic lesions; the liver is frequently involved (receiving eggs via the portal vein with inflammatory reaction and fibrosis leading to periportal ‘pipe-stem’ fibrosis with portal hypertension, oesophageal varices, splenomegaly and ascites; there can also be lesions in the brain, spinal cord and lungs.

Oriental schistosomiasis (6)
Caused by S. japonicum. Initial toxic and allergic symptoms are marked and can lead to myocarditis and death. Intestinal lesions are similar to those with S. mansoni infection, and the small intestine is often involved. The liver is infected as in S. mansoni. Hepatic involvement occurs as for S. mansoni. The brain may also become involved.

Laboratory diagnosis

Eosinophilia may be present.

Ova found in terminal urine by Nuclepore filtration or after centrifugation. Ova may also be found in semen. Ova may also be found in faeces directly or using formalin-ether concentration, rectal scrapings or biopsies.

Serology. ELISA tests (using soluble egg antigen) are useful 6–12 weeks post-exposure. In many chronic cases, the diagnosis will be made by serology alone.
**Pathology and Clinical features**

Adult flukes inhabit the distal bile ducts with epithelial proliferation, surrounding inflammatory reaction and ascending cholangitis. Sometimes there is secondary bacterial infection with jaundice and septicaemia. There can also be eosinophilia. All this can lead to thick, dilated fibrous ducts with adenomata of epithelium, bile duct stenosis and cholangiocarcinoma. Many cases are asymptomatic. Acute infection may lead to tender hepatomegaly. Chronic infection can result in anorexia, low-grade fever, epigastric pain and tender hepatomegaly.

**Laboratory diagnosis**

Ova are found in faeces and in bile (via duodenal aspiration or 'string test').

**Distribution**

28 million infected worldwide.
Clonorchis sinensis (continued)

**Morphology**
- Adult
- Ovary lobed
- Testes branched
- 10–20 x 3–4 mm
- Oral sucker
- Ceca
- Ventral sucker
- Uterus coiled
- Vitellarium in middle third

**Opisthorchis felineus, Opisthorchis viverrini (cat liver fluke)**

**Morphology**
- Adult
- Ovary lobed
- Testes lobed obliquely placed
- Lance-shaped
- 7–12 x 2–3 mm
- Oral sucker
- Ventral sucker
- Uterus coiled
- Vitellarium transverse in middle third
- Excretory bladder, long and sac-like

**Life cycle**
- Definitive host: Cat, Dog, Seal
- Direct into Bulinus 1st intermediate host
- Cercaria released after 2–3 months
- Humans often infected by eating raw fish
- Metacercariae excyst in duodenum
- Migrate through common bile duct to the smaller intrahepatic ducts
- Mature in 3–4 weeks

**Pathology and Clinical features**
There are proliferative changes in the bile ducts. If the infection is massive or repeated then there may be chronic cholangitis. Clinical features are similar to those of clonorchiasis.

**Laboratory diagnosis**
Ova can be found in faeces.

**Distribution**
- *O. felineus* is found mainly in Eastern Europe and Russia.
- *O. viverrini* occurs in Thailand.
Pathology and Clinical features

Transit of immature worms through the liver can cause mechanical and toxic irritation with toxaemia, necrosis and secondary fibrosis. Development in the bile ducts causes cystic enlargement, endothelial hyperplasia and adenomata, and secondary inflammatory infiltration causing fibrosis and cholangitis. There can be secondary bacterial infection causing abscesses. Eosinophilia is marked. Worms can appear ectopically in lungs, brain, eyes, etc. with similar reactions. If raw sheep or goat’s liver, infected by the adult fluke, is eaten there can be local irritation and pharyngeal infection (Halzoun).

Acute infection may present with fever, tender hepatomegaly, epigastric pain, anorexia and vomiting. Jaundice may occur. In chronic infection, there may be no symptoms or epigastric/right upper quadrant pain, hepatomegaly and vomiting.

Laboratory diagnosis

Ova are found in faeces. Serology (IFAT) is available.

Distribution

The fluke is found in all sheep-rearing countries. About 1 million people are infected worldwide.
**Pathology and Clinical features**

There is localized inflammation at the site of attachment with haemorrhages and occasional abscesses. There is also eosinophilia. Lightly infected individuals may be asymptomatic. Diarrhoea, abdominal pain, anorexia, nausea and vomiting may occur.

**Laboratory diagnosis**

Ova, and sometimes adults, are found in faeces.

**Distribution**

15 million infected worldwide.
**Heterophyes heterophyes**

**Morphology**

- **Adult**
  - Oral sucker
  - Scales, especially anterior
  - Caecum
  - Ventral sucker
  - Genital sucker armed with spines
  - Uterus, coiled
  - Vitellaria in posterior third

- **Ovary round**
  - O

- **Testes round**
  - **TT**

- **Ovum**
  - 28–30 x 15–17 μm
  - Operculate Embryonated

- **Cercaria**
  - Tail keeled
  - Armed with spines
  - Pigmented eyespots

- **Pathology and Clinical features**
  - There is a mild inflammatory reaction. Infected individuals may be asymptomatic or have abdominal pain, diarrhoea, anorexia and nausea. Ectopic ova have been found in the heart and brain.

**Life cycle**

Definitive hosts: Uncooked fish

**Distribution and laboratory diagnosis**


---

**Metagonimus yokogawai**

**Morphology**

- **Adult**
  - Oral sucker
  - Pharynx
  - Caecum
  - Ventral sucker
  - Uterus coiled
  - Conspicuous seminal receptacle

- **Ovary round**
  - O

- **Testes round**
  - **TT**

- **Ovum**
  - 27 x 16 μm
  - (like Heterophyes)
  - Operculate Embryonated

- **Cercaria**
  - (like Heterophyes)
  - Tail keeled
  - Spines
  - Eyespots

- **Pathology and Clinical features**
  - Causes mild inflammatory reaction in the intestine.
  - Occasionally ectopic ova can cause granulomata in other organs of the body, especially the liver and brain.

**Life cycle**

Definitive hosts: Uncooked fish

**Distribution**

- Prevalent in the Far East.
**Paragonimus westermani** (lung fluke)

### Life cycle

1. **Also other mammals, e.g. civet cat**
2. **Exocyst in small intestine, pass through intestinal wall, penetrate diaphragm and pleural cavity, come to rest in lung**
3. **Ova voided in sputum or swallowed and voided in faeces**
4. **Main snail hosts:** *Melania* (Semisulcospira) spp.
5. **Cercaria**
6. **1st intermediate host:** Snail
7. **2nd intermediate host:** Crustacean, e.g. crabs
8. **Ovum matures in water and hatches in 20 days to:**
   - **Sporocyst** → **Radula** → **Cercariae**
   - **Metacercaria 250-500 µm**
   - **Miracidium which is ingested by:**
   - **Adult**
   - **Ovum 80-120 x 50-60 µm**

### Pathology and Clinical features

The initial invasion has little pathological effect on the host. On localization in the lungs, there is tissue reaction leading to formation of a fibrous tissue capsule (of a slate blue colour) containing worms (generally in pairs), ova and inflammatory infiltrate. The capsule is connected with the respiratory passages. Secondary complications of these lung cysts include bronchiectasis, abscess formation and haemoptysis. Localization in other sites can cause cysts in any part of the body (for example the brain, causing epilepsy). Eosinophilia is a general manifestation. Chronic infection may be asymptomatic. Cough, brown gelatinous sputum, chest discomfort, shortness of breath and pleuritic chest pain may occur.

### Laboratory diagnosis

Ova are found in sputum after KOH digestion or faeces after formalin-ether concentration. Serological tests, when available, are CF or ELISA (using extract of adult flukes as antigen) or gel diffusion. Chest X-ray or CT can also be used.

### Distribution

5 million infected worldwide.
(a) *Ascaris* ovum

(b) *Trichuris* ovum

(c) *Hymenolepis nana* ovum

(d) *Schistosoma mansoni* ovum

(e) *Toxocara canis* ova

(f) Hookworm (*Ancylostoma*) ovum

(g) *Schistosoma haematobium* ovum

(h) *Fasciola hepatica* ovum
Protozoology
An outline classification of the parasitic protozoa of humans

<table>
<thead>
<tr>
<th>Empire</th>
<th>Kingdom</th>
<th>Phylum</th>
<th>Class</th>
<th>Order</th>
<th>Genus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eukaryota</td>
<td>Archezoa Haackei 1894</td>
<td>Metamonada</td>
<td>Trepomonadaea</td>
<td>Diplomonadida</td>
<td>Giardia</td>
</tr>
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<td></td>
<td>Enteromonas</td>
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<td></td>
<td>Chilomastix</td>
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<td></td>
<td></td>
<td>Retortamonas</td>
</tr>
<tr>
<td>Microspora</td>
<td>Microsporea</td>
<td>Microsporide</td>
<td>Microsporida</td>
<td>Enteroctozoona</td>
<td>Encephalitozoon</td>
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<td></td>
<td>Nosema</td>
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<td></td>
<td>Septata</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trichileptophora</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Parabasala</td>
<td>Trichomonadae</td>
<td>Trichomonadida</td>
<td>Leishmania</td>
<td>Naegleria</td>
</tr>
<tr>
<td>Goldfuss 1818</td>
<td>Heterolobosea</td>
<td>Schizopyridia</td>
<td>Serpentinea</td>
<td>Dientamoeba</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trichomonas</td>
</tr>
<tr>
<td></td>
<td>Euglenozoa</td>
<td>Kinetoplastida</td>
<td>Trypanosomatida</td>
<td>Leishmania</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciliophora</td>
<td>Litolomatea</td>
<td>Vestibuliformia</td>
<td>Trypanosoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Apicomplexa (Sporozoa)</td>
<td>Coccidea</td>
<td>Elmerida</td>
<td>Balantidium</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Haematozoea</td>
<td>Haemosporida</td>
<td>Plasmodium Babesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lobosea</td>
<td>Acanthopodida</td>
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<tr>
<td></td>
<td>Entamoebida</td>
<td>Euamoebida</td>
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<td></td>
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<tr>
<td>Rhizopoda</td>
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</tr>
</tbody>
</table>
Intestinal protozoa

Coccidia

Classification

Phylum

Apicomplexa

Class

Coccidea
- Sexual-asexual cycle in same host
- Parasitize intestinal epithelium

Order

Eimerida
- Growth period in host cell

Genus

Isospora Sarcocystis Toxoplasma Cryptosporidium Cyclospora

Isospora belli (causing coccidiosis in humans)

Life cycle

Pathology and Clinical features

Small bowel mucosal atrophy. Watery diarrhoea or steatorrhoea, weight loss and sometimes cholecystitis occur in AIDS.

Laboratory diagnosis

Oocysts are seen in formalin–ether concentration of faeces or modified Ziehl-Neelsen or auramine-stained faecal smears. Intraepithelial parasites may be seen in small bowel biopsies.
Cryptosporidium parvum

Pathology and Clinical features
In the immunocompetent, there is short-term enteropathy with self-limiting diarrhoea. In the immunocompromised, for example a patient with AIDS or a child with severe combined immunodeficiency, there is chronic diarrhoea with malabsorption and weight loss. Extraintestinal infection of the respiratory tract, biliary tract and pancreas may occur.

Laboratory diagnosis
Oocysts (4–5 μm in diameter) are found in faeces, using modified Ziehl-Neelsen stain, auramine or specific FITC labelled monoclonal antibody staining. They can also be found in faecal concentrates, duodenal aspirates and duodenal biopsies. The oocysts are very small (5 μm in diameter) and round. Parasites may also be seen in small bowel biopsies. Sucrose flotation is an alternative to formalin–ether concentration.

Distribution
Cryptosporidia have a cosmopolitan distribution. Human and farm animal strains exist; both can cause human disease. Human infection is usually waterborne.
Cyclospora cayetanensis

Life cycle

Cyclospora

Oocysts are 8–10 μm in diameter with a central morula of refractile spheres when unsporulated. These mature into a final division of 2 sporocysts.

Pathology and Clinical features

Acute onset of diarrhoea, followed by steatorrhoea. Colicky abdominal pain and malaise. Partial villous atrophy may be seen.

Laboratory diagnosis

Oocysts are seen in faeces unsporulated when first passed. Diagnosis is either by formalin–ether concentration, modified Ziehl-Neelsen stain or by autofluorescence.

Distribution

Widespread, probably worldwide.
Coccidia (continued)

Sarcocystis hominis

Probable life cycle

Occasionally humans can act as intermediate hosts for Sarcocystis of other animals.

Morphology

Pathology and Clinical features

The intestinal stages produce diarrhoea and abdominal pain. The clinical significance of muscle cysts is unknown.

Laboratory diagnosis

Oocysts or free sporocysts are found in faeces. Histological examination of biopsy specimens may show the sexual stages in the intestinal epithelium. Histology is the only way to diagnose the presence of sarcocysts, although these are almost invariably incidental findings.
Microsporidia—general characteristics

All are obligate intracellular parasites. The vast majority of species are in invertebrates, especially insects, lower vertebrates and fish. Only a few have been reported from warm-blooded vertebrates.

They are considered to be primitive organisms. Their evolutionary history has been predicted from their prokaryote-like ribosomal characteristics—the absence of a separate 5.8S rRNA and the nucleotide sequence of the small subunit (16S) rRNA. They have no mitochondria. The infective stages are highly-resistant spores. These are very uniform in size for a given species.

When spores are ingested by a new host, the cells are penetrated by means of an apparatus known as the polar tube. When this is fully extended, the sporoplasm passes through the tube, to be inoculated into the cytoplasm of the host cell.

Following infection, there follows a phase of multiplication by binary or multiple fission (merogony). The transition to the spore-producing stage (sporogony) is heralded by the secretion of an electron dense surface coat—this will form the future exospore layer of the spore wall. The primary sporogonic cells are sporonts, which divide into sporoblasts, which mature into spores, which are released when the host cell ruptures.

Common species of microsporidia reported from humans. Most are AIDS associated.

<table>
<thead>
<tr>
<th>Species</th>
<th>Localization</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalitozoon cuniculi</td>
<td>Generalized, brain</td>
<td>Convulsions, etc.</td>
</tr>
<tr>
<td>Encephalitozoon hellem</td>
<td>Corneal epithelia</td>
<td>Keratopathy</td>
</tr>
<tr>
<td>Enterocytozoon bieneusi</td>
<td>Enterocytes—gut</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Encephalitozoon (Septata) intestinalis</td>
<td>Enterocytes—gut</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Nosema cononi</td>
<td>Generalized</td>
<td>Multi-organ</td>
</tr>
<tr>
<td>Nosema corneum</td>
<td>Corneal stroma</td>
<td>Keratitis</td>
</tr>
<tr>
<td>Microsporidum africanum</td>
<td>Corneal stroma</td>
<td>Keratitis</td>
</tr>
<tr>
<td>Pleistophora sp.</td>
<td>Muscle fibres</td>
<td>Myositis</td>
</tr>
</tbody>
</table>

Infections of the gastrointestinal tract and urinary system can be detected by the presence of spores in faeces or urine. Spores from these sites can be visualized by staining them with the modified trichrome stain.

The spores of microsporidia are very small—1 x 0.5 μm (See below)
**Life cycle**

- **Infective stage**
  - Enterocyte
  - Spore
  - Polar filament
  - Sporoplasm injected into host cell

- **Merogony**
  - Production of sporoblasts

- **Sporogony**
  - Production of spores

- Infective spores released into the gut lumen

**Laboratory diagnosis**

Alternative staining methods for microsporidial spores in stool samples are modified trichrome stain and uvitex 2B or calcofluor fluorescence.
Entamoeba
- Generally one nucleus in trophozoite
- Small karyosome at or near centre
- Nuclear membrane lined with chromatin granules
- Forms cysts

Endolimax
- Generally one nucleus in trophozoite
- Large irregular karyosome attached to nuclear membrane
- No peripheral chromatin
- Forms cysts

Iodamoeba
- Generally one nucleus in trophozoite
- Large karyosome surrounded by achromatic granules
- No peripheral chromatin
- Forms cysts

Dientamoeba
- Minute
- Generally binucleate
- Central particulate karyosome
- No peripheral chromatin
- No cystic stage

Species
- Entamoeba histolytica/dispar
- Entamoeba coli
- Entamoeba hartmanni
- Entamoeba polecki

Intestinal protozoa 47
Entamoeba histolytica (causing amoebiasis)

**Life cycle**

- **Extraintestinal lesions**
- **Cysts from the environment**

**Invasion of large intestine**
- **Discharge in necrotic debris**
- **Ulceration, occasionally amoebomas formation**

**Excystation in small intestine**
- **Metacyst liberated from cyst wall**
  - Cytoplasm divides forming metacytic trophozoites

**Encystation when dehydrated in bowel lumen**
- **Discharges undigested food**
- **Passed in diarrhoea**
- **Passed in semi-formed stool**
  - **Precyst Condenses to spherical mass**
  - **Cyst Secretes tough cyst wall**
  - **Food inclusions glycogen - chromatidial bars**
  - **Two consecutive mitoses - produce 4 nuclei**
  - **Glycogen and chromatidial bars - less conspicuous - may disappear**
  - **Passed in semi-formed or formed stool**

**To the environment in faeces**

**Important note**
*E. dispar has a similar life cycle but is regarded as non-invasive and not responsible for clinical disease*

**Outside the host**
- **Trophozoite**
  - **Die rapidly**
  - **Not infective by natural route**

- **Precyst**
  - **Not infective**

- **Cyst**
  - **Resistant**
  - **Infective**

**Cysts in the environment**
- **Via**
  - **Polluted water**
  - **Infected food handlers**
  - **Flies contaminating food**
  - **Night soil cultivation**
  - **Direct contact**

**Patient or carrier**

**New host**

**Viability**
- **Moist, cool conditions up to 12 days**
- **In water 9-30 days**

48 Protozoology
**Morphology**

**General—nomenclature**

- **Trophozoite (Vegetative)**
  - Pseudopodia
  - Endoplasm with inclusions
  - Ectoplasm
  - Cytoplasm
  - Nucleus
  - Membrane
  - Chromatin lining membrane
  - Fibril network
  - Karyosome

- **Precyst or unripe cyst**
  - Glycogen mass
  - Cyst wall
  - Nuclei
  - Chromidial bodies and bars

- **Ripe cyst**

**Important note**

*E. dispar* is morphologically identical to *E. histolytica* but the trophozoites are not haematophagous.

---

**Particular—Includes differentiation from Entamoeba coli, an intestinal commensal.**

**Unstained preparations**

<table>
<thead>
<tr>
<th><em>E. histolytica</em></th>
<th><em>Trophozoite</em></th>
<th><em>E. coli</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular</td>
<td>Cytoplasm</td>
<td>Conspicuously granular</td>
</tr>
<tr>
<td>Clear finger-like</td>
<td>Pseudopodia</td>
<td>Blunt</td>
</tr>
<tr>
<td><strong>Active</strong></td>
<td>Movement</td>
<td><strong>Sluggish</strong></td>
</tr>
<tr>
<td>Purposeful</td>
<td>Nucleus</td>
<td>Not purposeful</td>
</tr>
<tr>
<td>Generally invisible</td>
<td>Inclusions</td>
<td>Ring refractile granules with eccentric karyosome</td>
</tr>
<tr>
<td><strong>Red blood cells (RBCs)</strong></td>
<td></td>
<td>Vacuoles, crystals, vegetable cells, bacteria, no RBCs</td>
</tr>
</tbody>
</table>

15–60 μm

<table>
<thead>
<tr>
<th><em>Precyst and unripe cyst</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular</td>
</tr>
<tr>
<td>May be refractile ring</td>
</tr>
<tr>
<td>Rod-like refractile chromidial bars</td>
</tr>
<tr>
<td>Glycogen masses</td>
</tr>
<tr>
<td>Cytoplasm</td>
</tr>
<tr>
<td>Nucleus</td>
</tr>
<tr>
<td>Inclusions</td>
</tr>
</tbody>
</table>

Granular
Visible as refractile ring
May be slender refractile chromidial bars
Glycogen masses

<table>
<thead>
<tr>
<th><em>Ripe cyst</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Round</td>
</tr>
<tr>
<td>Refractile</td>
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<tr>
<td>1–4 refractile nuclei with central karyosome</td>
</tr>
<tr>
<td>Refractile chromidial bars often present</td>
</tr>
<tr>
<td>Shape</td>
</tr>
<tr>
<td>Wall</td>
</tr>
<tr>
<td>Nuclei</td>
</tr>
<tr>
<td>Inclusions</td>
</tr>
</tbody>
</table>

Round
Conspicuous refractile double outline
1–8 refractile nuclei with eccentric karyosomes
Only rudimentary slender chromidial bars

10–33 μm

**Intestinal protozoa 49**
Invasion of the large intestine

**Site of entry**
Initially minute then irregular ulcer shape, typically flask-like edges overhanging floor; necrotic-laden tissue; amoebae invading around discharge; necrotic debris, mucus and amoebae

**Invasion elsewhere in large bowel**

**The primary ulcer**
- Invasion of mucosa via crypts
- Repair may:
  - overtake necrosis with healing
  - keep pace with necrosis causing persistent superficial lesions

**Flask-shaped**
Lag behind — extension

**Extension in mucosa**
Muscularis mucosae relatively resistant
Accumulation of amoebae superficial to it
Lateral extension of lytic necrosis

**Formation of sinuses**
Abscesses may coalesce under intact mucosa
Later mucosa may slough with widespread ulceration

**Deep extension**
Muscularis mucosae eventually pierced (directly or via vessels)
Deep necrosis of sub-mucosa, even muscle and sub-serosa

Complications and sequelae

**Perforation**
Haemorrhage (rare)

**Secondary infection**

**Amoeboma (rare)**
(Clinically simulates neoplasm)
- intussusception
- obstruction

**Invasion of blood vessels**
Direct extension outside bowel

**Peritonitis**
Haemorrhage

**Surrounding inflammatory reaction and fibroblastic proliferation**
A mass under oedematous mucosa with
- internal abscesses of necrotic tissue and amoebae
- surrounding granulomatous tissue zone with eosinophils, lymphocytes and fibroblasts
- outer firm nodular fibrous tissue

Extraintestinal lesions—page 52
Entamoeba histolytica (causing amoebiasis) (continued)

Extraintestinal lesions in amoebiasis

Haematogenous spread

Further haematogenous spread

Further haematogenous spread

Invasion of large intestine

Secondary invasion, especially in liver

Formation of abscesses

Direct extension

Cutaneous amoebiasis

- Spreading ulcer
- Irregular margins
- Necrotic floor
- Amoebae laterally

Fibrin thrombus containing amoebae trapped in small vessels
- Amoebae digest pathways into tissue
- Multiple small foci of necrosis
- Essentially no surrounding reaction

Almost normal tissue invaded by amoebae
- Later some (slight) polymorph infiltration
- Red brown fluid
- Cellular debris with stromal trabeculae
- Usually bacterially sterile

Zone of stroma of organ

Direct extension

Haematogenous spread

Lung

Brain

Ectopic sites

Skin of abdominal wall after rupture or surgery

Peritoneal cavity and other abdominal organs

Perianal skin, balanitis, vulvitis

May rupture into bronchus (anchovy sauce sputum)

Pleuro-pulmonary abscess

Pericardium (Cardiac tamponade)

Sub-diaphragmatic abscess

Progression to abscess(es)

Secondary to
- Concomitant with
- Independent of

Liver involvement
Laboratory diagnosis

Diagnosis depends primarily on demonstration of haematophagous trophozoites of *E. histolytica* in stool samples, aspirates from intestinal and other organs, biopsy material (pinch biopsy at proctoscopy or sigmoidoscopy and surgical biopsy from elsewhere) and in mucus from rectal ulcers. ELISAs are available for the detection of *Entamoeba* antigen and specific *E. histolytica* lectin antigen in faecal samples. Serology is the method of choice for diagnosis of amoebic liver disease.

<table>
<thead>
<tr>
<th>Faecal appearances in amoebic dysentery</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naked eye</td>
<td></td>
</tr>
<tr>
<td>Faecal matter</td>
<td>Always present</td>
</tr>
<tr>
<td>Mucus</td>
<td>Not tenacious</td>
</tr>
<tr>
<td></td>
<td>Not abundant</td>
</tr>
<tr>
<td>Microscopic</td>
<td></td>
</tr>
<tr>
<td>1. Bacteria</td>
<td>Numerous</td>
</tr>
<tr>
<td>2. Pus cells</td>
<td>Scanty, well preserved</td>
</tr>
<tr>
<td>3. Red blood cells</td>
<td>Often in roeules</td>
</tr>
<tr>
<td>4. Large macrophages</td>
<td>Not a feature</td>
</tr>
<tr>
<td>5. Charcot-Leyden crystals</td>
<td>May be present but are non-specific</td>
</tr>
<tr>
<td>6. Haematophagous trophozoites of <em>E. histolytica</em></td>
<td>Present</td>
</tr>
<tr>
<td>Culture</td>
<td></td>
</tr>
<tr>
<td>Usually limited to reference or research laboratories; lectin ELISA is used for specific identification of <em>E. histolytica</em> from cyst or trophozoite. Enzyme electrophoresis from cultured trophozoite is an alternative.</td>
<td></td>
</tr>
</tbody>
</table>

Haematophagous amoebic trophozoites.

Notes

Vegetative *E. histolytica* when seen is actively motile and moves purposefully. There are finger-like, clear pseudopodia and ingested red cells. No nucleus can be seen. Precysts or cysts found in semi-formed or solid stool have typical nuclear characteristics (1–4 nuclei) and glycogen and chromidial bars can be demonstrated.

Diagnostic tests

Polymorph leucocytosis. Examination of stool samples may show cysts and trophozoites of *E. histolytica*. Serological tests (IFAT, ELISA, cellulose acetate precipitin, latex agglutination) but serology is positive in no more than 75% of cases of amoebic colitis. Examine aspirated material for *E. histolytica*. Histology of rectal and colon biopsy material.
**Other intestinal amoebae**

### Life cycle

- **Cysts** (vegetative forms of *D. fragilis*) from environment.
- Multiplication of vegetative forms in large intestine.
- **Exocystation** in small intestine.
- **Encystation** (except in *D. fragilis*) if dehydrated.
- Cysts (vegetative forms of *D. fragilis*) to environment in formed stools. Vegetative forms found in diarrhoea.

### Morphology

#### Unstained

<table>
<thead>
<tr>
<th>Vegetative forms (trophozoites)</th>
<th>Entamoeba coli</th>
<th>Endolimax nana</th>
<th>Iodamoeba butschlii</th>
<th>Dientamoeba fragilis</th>
<th>Entamoeba histolytica</th>
<th>Entamoeba dispar</th>
<th>Entamoeba hartmanni</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>15–50 µm</td>
<td>8–10 µm</td>
<td>8–20 µm</td>
<td>5–12 µm</td>
<td>15–60 µm</td>
<td>15–60 µm</td>
<td>15–60 µm</td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td>Sluggish</td>
<td>Sluggish</td>
<td>Fairly active</td>
<td>Very active</td>
<td>Very active</td>
<td>Active</td>
<td>Active</td>
</tr>
<tr>
<td><strong>Ectoplasm</strong></td>
<td>Little</td>
<td>Little</td>
<td>Little</td>
<td>Abundant</td>
<td>Abundant</td>
<td>Abundant</td>
<td>Abundant</td>
</tr>
<tr>
<td><strong>Pseudopodia</strong></td>
<td>Blunt, mainly granular</td>
<td>Blunt, mainly granular</td>
<td>Blunt, clear</td>
<td>Leaf-like, clear</td>
<td>Finger-like, clear</td>
<td>Finger-like, clear</td>
<td>Finger-like, clear</td>
</tr>
<tr>
<td><strong>Endoplasm</strong></td>
<td>All have granular cytoplasm with food particles, bacteria, crystals, vegetable cells, often in vacuoles. No ingested RBCs</td>
<td></td>
<td></td>
<td></td>
<td>Ingested RBCs</td>
<td>No ingested RBCs</td>
<td>No ingested RBCs</td>
</tr>
<tr>
<td><strong>Nucleus</strong></td>
<td>Ring of refractive dots</td>
<td>Generally invisible</td>
<td>Generally invisible</td>
<td>Two, collection of dots</td>
<td>Generally invisible</td>
<td>Generally invisible</td>
<td>Generally invisible</td>
</tr>
<tr>
<td><strong>Precyst</strong> (round up, discharge food particles, bacteria, etc.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Glycogen</strong></td>
<td>Often prominent vacuole</td>
<td>Rare</td>
<td>Conspicuous</td>
<td>None</td>
<td>Diffuse, soon disappears</td>
<td>Diffuse, soon disappears</td>
<td>Diffuse, soon disappears</td>
</tr>
<tr>
<td><strong>Chromidal bars</strong></td>
<td>Rarely seen</td>
<td>Rare</td>
<td>None</td>
<td>None</td>
<td>Large refractive bars</td>
<td>Large refractive bars</td>
<td>Large refractive bars</td>
</tr>
</tbody>
</table>

#### Cysts

| **Size**                       | 10–33 µm       | 5–14 µm       | 5–18 µm       | None          | 10–20 µm       | 10–20 µm       | 8–10 µm       |
| **Shape**                      | Spherical or oval | Oval | Irregular     | None          | Spherical     | Spherical     | Spherical     |
| **Wall**                       | Thick          | Thin          | Thin          | None          | Thin          | Thin          | Thin          |
| **Glycogen**                   | Diffuse central | None          | Well-defined vacuoles | None | Sometimes persists | Sometimes persists | Sometimes persists |
| **Chromidal bars**             | Not usual | None | None | None | Sometimes present | Sometimes present | Sometimes present |
| **Nuclei numbers**             | 1–8            | 4 (at one end) | 1 only        | None          | 1–4           | 1–4           | 1–4           |

54 Protozoology
<table>
<thead>
<tr>
<th>Stained</th>
<th>Entamoeba coli</th>
<th>Endolimax nana</th>
<th>Iodamoeba bütschlii</th>
<th>Dientamoeba fragilis</th>
<th>Entamoeba histolytica</th>
<th>Entamoeba dispar</th>
<th>Entamoeba hartmanni</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cytoplasm inclusions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stain black except glycogen as clear area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With haematoxylin, stains bluish-grey</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nuclear characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thick</td>
<td>Thin</td>
<td>Thick</td>
<td>Very delicate</td>
<td>Delicate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coarse</td>
<td>None</td>
<td>Sometimes granular</td>
<td>None</td>
<td>Fine granules</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large lateral</td>
<td></td>
<td>Central granules</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large irregular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chromatin on membrane</td>
<td>Coarse, generally eccentric</td>
<td>None</td>
<td>Sometimes granular</td>
<td>None</td>
<td>Fine granules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karyosome</td>
<td>Large lateral</td>
<td></td>
<td>Central granules</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Small central</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibril network</td>
<td>May be chromatin particles</td>
<td>No chromatin</td>
<td>No chromatin</td>
<td>Delicate fibrils</td>
<td>Not often seen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathogenicity</td>
<td>Harmless commensal</td>
<td>Harmless commensal</td>
<td>Harmless commensal</td>
<td>Disputed</td>
<td>invasive</td>
<td>Harmless commensal</td>
<td>Non-invasive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Images:**
- Entamoeba coli cysts
- Iodamoeba bütschlii cysts
- Entamoeba histolytical/dispar cysts
Intestinal flagellates

**Diagnosis**

Trophozoites or cysts are found in stool samples or duodenal aspirates. Duodenal string test and stool antigen detection ELISA are also possible for the detection of *Giardia*.

**Distribution**

These protozoa have a worldwide distribution.

---

**Giardia intestinalis (G. lamblia)**

**Life cycle**

- **Cysts from environment**
  - Excreted in stool
- **Excretion**
  - Reingestion of cysts
- **Life cycle**
  - Cysts develop into trophozoites in the small intestine
  - Trophozoites divide by binary fission
  - Trophozoites are motile and can cause diarrhea
  - Cysts are environmentally resistant

**Pathogenicity**

- Common inhabitant of upper part of small intestine
- Enteropathy, diarrhoea, steatorrhoea

---

**Chilomastix mesnili**

**Life cycle**

- **Trophozoite**
  - 6 flagellae
  - 3 free anteriorly
  - 1 in mouth
  - 2 surrounding mouth
- **Cyst**
  - 7–10 μm
  - Thick, unstained cell wall
  - Cystosome and remains of locomotor apparatus

**Pathogenicity**

Commensal—apparently harmless
Trichomonas species

*T. hominis*
This is illustrated above. The trophozoite inhabits the small and large intestine. There is no proof as yet that it has any pathogenicity.

*T. vaginalis*
Morphologically this is the same as *T. hominis* (above) but there is no free posterior flagellum beyond the undulating membrane. There is a marked parabasal body. It inhabits the urethra in the male and the vagina in the female, and is a cause of urethritis and vaginitis.

Demonstration of *T. vaginalis* is made by direct microscopy or after staining with acridine orange fluorescence stain. Cultures can be made using Feinberg-Whittington or Diamond's medium.
Intestinal ciliates

Balantidium coli

Found in South and Central America, parts of Asia and some Pacific islands.

In its vegetative state, recognizable by the oval shape, coarse cilia, contractile vacuoles and the horseshoe- or kidney-shaped macronucleus. Reproduction is by binary fission.

Life cycle

Pathology and Clinical features

Problems occur in the ileum, colon and rectum but there is no extraintestinal spread. The parasite is a cause of dysentery, although the ulcers are wider mouthed than those of amoebic dysentery. Secondary infection is frequent. The main complication is perforation.

Laboratory diagnosis

Trophozoites are found in diarrhoea and, in a fresh specimen, can be seen in active rotational movement. Cysts are found in semi-formed and formed stools.
Tissue protozoa

Toxoplasma gondii

Toxoplasma has a very wide mammalian host range.

**Morphology**

**Tachyzoites**
- Pointed end
- Red nucleus-ovoid, crescentic, or pyriform-nearer one end
- Blue cytoplasm
- Parasitophorous vacuole as a small red dot
- 4–6 x 2–3 µm

**Habitat**
- Tachyzoites: single (free or intracellular) or in masses (pseudocysts)
- Bradyzoites (similar to tachyzoites but less active metabolically) in tissue cysts

**Life cycle**

- Cysts ingested by cat
- Cat is definitive host:
  - Unsporulated oocysts passed in faeces
- Ingested cysts in infective meat (raw or undercooked)
- Tachyzoites transmitted through placenta
- Contaminated food and water
- Infected fetus
- Intermediate hosts
- Oocysts in feed, water, or soil ingested by intermediate host
- Sporulated oocysts
**Laboratory diagnosis**

Diagnosis is usually made serologically by demonstration of specific antibodies. Methods include Latex agglutination, ELISA and ISACA. The ‘gold standard’ for *Toxoplasma* serological diagnosis is the Sabin-Feldman dye test.

Lymph node biopsy should not be required to diagnose *Toxoplasma* but if performed because another diagnosis was suspected, the findings are as stated above.

*Toxoplasma tachyzoites*  
*Toxoplasma pseudocyst (brain)*
### Malaria parasites

#### Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Haematozoa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order</td>
<td>Haemosporida</td>
</tr>
<tr>
<td></td>
<td>- Sexual and asexual generations in different hosts</td>
</tr>
<tr>
<td></td>
<td>- Parasitic in fixed tissue cells and RBCs of vertebrate host</td>
</tr>
<tr>
<td>Family</td>
<td>Plasmodiidae</td>
</tr>
<tr>
<td></td>
<td>- Include human malaria parasites</td>
</tr>
<tr>
<td></td>
<td>- Produce pigment in asexual cycle in RBCs of vertebrates</td>
</tr>
<tr>
<td></td>
<td>- Produce gametocytes in RBCs of vertebrates</td>
</tr>
<tr>
<td></td>
<td>- Sporogony (sexual cycle) in invertebrates</td>
</tr>
<tr>
<td>Genus</td>
<td>Plasmodium</td>
</tr>
<tr>
<td></td>
<td>- Schizogony (asexual cycle) in:</td>
</tr>
<tr>
<td></td>
<td>- RBCs</td>
</tr>
<tr>
<td></td>
<td>- other tissue cells of vertebrate host</td>
</tr>
<tr>
<td></td>
<td>- Pigment derived from haemoglobin of infected RBC</td>
</tr>
<tr>
<td></td>
<td>- Gametocytes develop in some RBCs. These undergo sporogony (sexual cycle) in female anopheline mosquitoes</td>
</tr>
<tr>
<td></td>
<td>- Sporozoites produced in mosquito, infective to vertebrate host</td>
</tr>
<tr>
<td></td>
<td>- All malaria parasites included in this genus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class</th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Causes benign tertian malaria</td>
<td>Causes quartan malaria</td>
<td>Causes malignant tertian malaria</td>
<td>Causes ovale malaria</td>
</tr>
</tbody>
</table>

Malaria parasites 61
Morphology  
Stained by Leishman or Giemsa  

Schizogony (asexual cycle)  

Pre-erythrocytic cycle in liver cells  

Sporozoite → Mature → Ruptured → Releases → Merozoites  
- Schizonts in liver cells  
- No pigment at this stage  

Erythrocytic stage in RBCs  

The parasite  
- Cytoplasm blue  
- Chromatin red  
- Pigment (from haemoglobin) varies in colour and time of appearance  

General features  
- Pink spots in cytoplasm unoccupied by parasite  
- Schüffner's or James' dots  
- Maurer's clefts  
- Brick-red clefts in cytoplasm  

RBC characteristics  

<table>
<thead>
<tr>
<th>RBC characteristics</th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Larger than mature RBC</td>
<td>Smaller, older RBC</td>
<td>Mature RBC</td>
<td>Larger than mature RBC</td>
</tr>
<tr>
<td>Colour</td>
<td>Pale</td>
<td>Normal</td>
<td>Normal</td>
<td>Pale</td>
</tr>
<tr>
<td>Shape</td>
<td>Round</td>
<td>Round</td>
<td>Round, may be crenated</td>
<td>Oval, may be tinfoilated</td>
</tr>
<tr>
<td>Cytoplasmic inclusions</td>
<td>Schüffner's dots present</td>
<td>None</td>
<td>Maurer's clefts may be present in late trophozoites</td>
<td>James' dots conspicuous</td>
</tr>
</tbody>
</table>
Morphology (continued)

Stages in thin films

Ring forms (early trophozoites)

<table>
<thead>
<tr>
<th></th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>1/3 RBC</td>
<td>Up to 1/3 RBC</td>
<td>1/3 RBC</td>
<td>1/3 RBC</td>
</tr>
<tr>
<td>Shape</td>
<td>Delicate ring</td>
<td>Compact ring</td>
<td>Very delicate ring</td>
<td>Dense ring</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Fine dot</td>
<td>One mass often inside ring</td>
<td>Fine dots Frequently two</td>
<td>Dense, well-defined mass</td>
</tr>
<tr>
<td>Accolé forms*</td>
<td>Sometimes</td>
<td>None</td>
<td>Frequent</td>
<td>None</td>
</tr>
<tr>
<td>Pigment</td>
<td>None at this stage</td>
<td>May be present</td>
<td>None at this stage</td>
<td>None at this stage</td>
</tr>
<tr>
<td>Multiple parasitized cells</td>
<td>Sometimes</td>
<td>Rare</td>
<td>Frequently with high parasitaemia</td>
<td>Rare</td>
</tr>
</tbody>
</table>

* Forms situated on margin of RBC

Developing trophozoites

<table>
<thead>
<tr>
<th></th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Large</td>
<td>Small, but appears large relative to size of RBC</td>
<td>Small</td>
<td>Small</td>
</tr>
<tr>
<td>Shape</td>
<td>Very irregular, amoeboid</td>
<td>Compact, often band forms</td>
<td>Compact, with cytoplasmic vacuolation</td>
<td>Compact</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Dots or threads</td>
<td>Prominent, often as a band</td>
<td>Dots or threads</td>
<td>Large irregular clumps</td>
</tr>
<tr>
<td>Pigment</td>
<td>- texture Fine</td>
<td>Coarse</td>
<td>Coarse</td>
<td>Coarse</td>
</tr>
<tr>
<td></td>
<td>- colour Yellow brown</td>
<td>Dark brown</td>
<td>Black</td>
<td>Dark yellow brown</td>
</tr>
<tr>
<td></td>
<td>- quantity Medium</td>
<td>Abundant</td>
<td>Medium</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>- distribution Scattered fine particles</td>
<td>Scattered clumps and rods</td>
<td>Aggregated in one or two clumps</td>
<td>Scattered coarse particles</td>
</tr>
</tbody>
</table>
### Immature schizonts

<table>
<thead>
<tr>
<th></th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Almost fills RBC</td>
<td>Almost fills RBC</td>
<td>Almost fills RBC</td>
<td>Almost fills RBC</td>
</tr>
<tr>
<td>Shape</td>
<td>Somewhat amoeboid</td>
<td>Compact</td>
<td>Compact</td>
<td>Compact</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Numerous irregular masses</td>
<td>Few irregular masses</td>
<td>Irregular masses</td>
<td>Few irregular masses</td>
</tr>
<tr>
<td>Pigment</td>
<td>Scattered</td>
<td>Scattered</td>
<td>Single clump</td>
<td>Scattered</td>
</tr>
</tbody>
</table>

(rarely seen in peripheral blood)

### Mature schizonts

<table>
<thead>
<tr>
<th></th>
<th>P. vivax</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Fills RBC</td>
<td>Nearly fills RBC</td>
<td>Nearly fills RBC</td>
<td>Fills 3/4 RBC</td>
</tr>
<tr>
<td>Shape</td>
<td>Segmented</td>
<td>Segmented daisy head</td>
<td>Segmented</td>
<td>Segmented</td>
</tr>
<tr>
<td>Merozoites</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— range</td>
<td>14–24</td>
<td>6–12</td>
<td>8–32</td>
<td>6–12</td>
</tr>
<tr>
<td>— mean</td>
<td>16</td>
<td>8</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>— size</td>
<td>Medium</td>
<td>Large</td>
<td>Small</td>
<td>Large</td>
</tr>
<tr>
<td>Pigment</td>
<td>Aggregated in centre (yellow brown)</td>
<td>Aggregated in centre (dark brown)</td>
<td>Aggregated in centre (black)</td>
<td>Aggregated in centre (dark yellow brown)</td>
</tr>
</tbody>
</table>

(rarely seen in peripheral blood)
### Morphology (continued)

**Stages in thin films (continued)**

**Microgametocytes (male)**

<table>
<thead>
<tr>
<th>Trait</th>
<th>P. vivax</th>
<th>P. malarias</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of appearance</td>
<td>3–5 days</td>
<td>7–14 days</td>
<td>7–12 days</td>
<td>12–14 days</td>
</tr>
<tr>
<td>Number in bloodstream</td>
<td>Many</td>
<td>Scanty</td>
<td>Many</td>
<td>Scanty</td>
</tr>
<tr>
<td>Size</td>
<td>3/4 fills RBC</td>
<td>1/2 to 2/3 fills RBC</td>
<td>Larger than RBC</td>
<td>1/2 to 2/3 fills RBC</td>
</tr>
<tr>
<td>Shape</td>
<td>Round or oval compact</td>
<td>Round compact</td>
<td>Kidney-shaped Bluntly round ends</td>
<td>Round compact</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Pale blue</td>
<td>Pale blue</td>
<td>Reddish blue</td>
<td>Pale blue</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Single chromatin mass</td>
<td>As for P. vivax</td>
<td>Fine granules scattered throughout</td>
<td>As for P. vivax</td>
</tr>
<tr>
<td>Pigment</td>
<td>Abundant brown granules throughout</td>
<td>As for P. vivax</td>
<td>Dark granules throughout</td>
<td>As for P. vivax</td>
</tr>
</tbody>
</table>

**Macrogametocytes (female)**

<table>
<thead>
<tr>
<th>Trait</th>
<th>P. vivax</th>
<th>P. malarias</th>
<th>P. falciparum</th>
<th>P. ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of appearance</td>
<td>3–5 days</td>
<td>7–14 days</td>
<td>7–12 days</td>
<td>12–14 days</td>
</tr>
<tr>
<td>Number in bloodstream</td>
<td>Many</td>
<td>Scanty</td>
<td>Many</td>
<td>Scanty</td>
</tr>
<tr>
<td>Size</td>
<td>3/4 fills RBC</td>
<td>1/2 to 2/3 fills RBC</td>
<td>Larger than RBC</td>
<td>1/2 to 2/3 fills RBC</td>
</tr>
<tr>
<td>Shape</td>
<td>Round or oval compact</td>
<td>Round compact</td>
<td>Crescentic-sharply rounded or pointed ends</td>
<td>Round compact</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Dark blue</td>
<td>Dark blue</td>
<td>Dark blue</td>
<td>Dark blue</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Compact peripheral mass</td>
<td>As for P. vivax</td>
<td>Compact masses near centre</td>
<td>As for P. vivax</td>
</tr>
<tr>
<td>Pigment</td>
<td>Small masses round periphery</td>
<td>As for P. vivax</td>
<td>Black, rod-like granules round nucleus</td>
<td>As for P. vivax</td>
</tr>
</tbody>
</table>
Morphology in stained thick films

Note that the parasites are not flattened in the film and so appear smaller than in thin film. The red cells are haemolyzed in processing so there is no guide to the size, shape or colour of the RBCs. Schüffner's dots are indefinite and there are no Maurer's clefts.

**P. vivax**

1. Ring forms, small fine rings often broken
2. Trophozoites, markedly irregular cytoplasm
3. Schizonts, many (average 16) small merozoites
4. Gametocytes, compact parasites with features of $\delta$ and $\varphi$ as described
5. White blood cell

**P. malariae and P. ovale**

Almost identical but James' dots may be visible in the latter

1. Ring forms, compact rings
2. Trophozoites, solid regular cytoplasm
3. Schizonts, few (average 8) large merozoites
4. Gametocytes, very difficult to distinguish from *P. vivax*
5. White blood cell

**P. falciparum**

1. Ring forms, very small, fine rings usually unbroken trophozoites (with vacuolated cytoplasm) and schizonts are rarely seen in peripheral blood
2. Gametocytes, characteristic crescentic $\delta$ and $\varphi$ forms
3. White blood cell
Pathology and Clinical features

*Plasmodium vivax*, *P. ovale*, *P. malariae* and uncomplicated *P. falciparum* malaria have similar features with fever, rigors, headache, muscle aches, malaise and anorexia. Anaemia may develop and the liver and spleen may become enlarged. Because the clinical appearances are non-specific, malaria may be misdiagnosed, e.g. as a viral infection, with severe consequences.

*Plasmodium falciparum* infection can readily progress to severe malaria, the clinical criteria of which have been defined by a World Health Organisation working group. One or more of the following features in the presence of asexual parasitaemia indicate severe falciparum malaria: cerebral malaria • severe anaemia • renal failure • pulmonary oedema or adult respiratory distress syndrome • hypoglycaemia • circulatory collapse or shock • spontaneous bleeding from the gums, nose, gastrointestinal tract and/or laboratory evidence of disseminated intravascular coagulation • repeated generalised convulsions (more than two in 24 hours despite cooling) • acidemia (arterial pH < 7.25) or acidosi (plasma bicarbonate < 15 mmol/L) • macroscopic haemoglobinuria.

Other features of severe falciparum malaria include impaired consciousness less severe than coma, prostration, hyperparasitaemia, jaundice and hyperpyrexia.

![Diagram of the pathology of malaria](image)

Sequence of events leading to cerebral malaria

![Diagram of the role of TNF](image)

Role of TNF

Laboratory diagnosis

Malaria parasites in thin blood film. Stained by Leishman or Giemsa at pH 7.2

P. vivax

P. malariae

P. falciparum

Rarely seen in peripheral blood

P. ovale

It is also possible to use thick blood films stained by Field or Giemsa. Bone marrow films may also be examined. Serology (IFAT or ELISA) is not appropriate for the detection of acute malaria but is deployed as a retrospective test for epidemiological use to establish the cause of nephrotic syndrome or hyperreactive malarial splenomegaly (HMS).

Antigen Detection

P. falciparum expresses a specific antigen HRP2 on the surface of the parasitized RBC. This can be detected by using immunochromatographic antigen capture techniques (AMRAD ICT, Becton Dickinson ParaSight F). Parasite lactate dehydrogenase (pLDH) is biochemically and antigenically distinct from human LDH and is produced by all Plasmodium species. Gold-labelled monoclonal and polyclonal antibodies can be used in an immunochromatographic technique to detect pLDH in whole blood (OptiMAL, Flow Inc., Portland OR).
Body-fluid and tissue flagellates

Classification

Phylum: Euglenozoa
Class: Kinetoplastida

Trypanosomatidæ
Single flagellum

Live in bloodstream and tissues
Vector (blood-sucking invertebrates) required

Morphological stages of the Trypanosomatidae affecting humans

Leishmania spp.

Leishmania amastigotes

Amastigote (L-D body) → Intracellular in macrophages in humans

Promastigote → In midgut, then proboscis of sandfly (transfer stage to human, also in culture)

Trypanosoma spp.

Trypanosoma brucei rhodesiense
Trypanosoma brucei gambiense

Epimastigote → In salivary glands and proboscis of tsetse fly (transfer stage to human)

Trypomastigote → In bloodstream, lymph nodes and later CNS of humans

Trypanosoma cruzi

Amastigote → Intracellular in macrophages and tissue cells of humans

Trypomastigote → In midgut, then faeces of bug (transfer stage to humans)
In blood and tissue spaces of humans
Leishmaniasis

<table>
<thead>
<tr>
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</tr>
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<tr>
<td></td>
<td>L. infantum</td>
</tr>
<tr>
<td></td>
<td>L. donovani</td>
</tr>
<tr>
<td></td>
<td>L. chagasi</td>
</tr>
<tr>
<td></td>
<td>L. tropica</td>
</tr>
<tr>
<td></td>
<td>L. major</td>
</tr>
<tr>
<td></td>
<td>L. infantum</td>
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<tr>
<td></td>
<td>L. braziliensis complex</td>
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<td></td>
<td>L. amazonensis</td>
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<tr>
<td></td>
<td>L. mexicana</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Disease</th>
<th>Visceral (Kala Azar)</th>
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<tbody>
<tr>
<td></td>
<td>Cutaneous</td>
</tr>
<tr>
<td></td>
<td>Muco-cutaneous (Espundia)</td>
</tr>
</tbody>
</table>

Distribution

Life cycle and morphology of Leishmania (similar in all three species)

Promastigote form in insect (and culture)

14–20 μm

Nucleus
Axoneme
Kinetoplast

Amastigote in macrophages of humans

3–4 x 2 μm
Vacuole
Remains of axoneme
Nucleus
Kinetoplast (DNA)

Life cycle in insect

Species of sandflies
- Phlebotomus (Old World)
- Lutzomyia (New World)

Blockage of proboscis by promastigotes

Forward migration to pharynx

Change into promastigote

Life cycle in humans and reservoir animals

Blocked sandfly attempts to obtain blood meal Injects promastigotes

Ingested by macrophages Metamorphose into amastigotes

Reproduction by binary fission

Rupture of parasitized cell

Infection of further cells

Core of parasitized cells formed

Lodge in RE cells of various organs
Released into bloodstream in systemic forms
Remains localized to skin in cutaneous forms
Localized to skin, plus metastases to mucosae in mucocutaneous forms

To insect

In blood

In tissue juices

Body-fluid and tissue flagellates 71
Visceral leishmaniasis (kala azar)

**Distribution**

- Parasitized macrophages and endothelial cells
- Splenomegaly, pain from perisplenitis
- Spleen appears congested, dark red, soft and friable. Markedly enlarged
- The capsule is thickened and, later, infarcts and fibrosis occur

**Clinico-pathological correlation**

- Liver
  - Hepatomegaly
  - Liver appears enlarged, fatty congested and later may become cirrhotic
  - Parasitized proliferated Kupffer cells with atrophy of the liver cells and later fibrosis

- Lymph nodes
  - Lymphadenopathy
  - Reactive hyperplasia with parasitized macrophages

**Mechanism of pathology**

- **Offence**
  - Skin and nasal mucosa involvement can occur (especially in Sudan) leading to ulceration

- **Parasitization and breakdown of RE cells. Release of parasites and debris with further parasitization**

- **Secondary effects**
  - Displacement, degeneration of parenchymal tissue
  - Toxaemia, cachexia fever, weight loss, weakness
  - Pallor, cardiac dilatation, tachycardia, low blood pressure, haemorrhagic murrmurs, ankle oedema
  - Replacement of bone marrow
  - Anemia, leucopenia, thrombocytopenia
  - Degenerative myocarditis
  - Stomatitis, cancrum oris, cough, diarrhoea
  - Purpura, epistaxis, melena
  - Pigmentation: darkening of skin at forehead, temples, mouth (Kala azar means 'black fever')

- **Defence**
  - Multiplication and mobilization of RE cells with stimulation of immune response. Enlargement of liver, spleen and lymph nodes

- Later inconstant fibrosis-cemrosis-haemorrhage. Jaundice, ascites, rashes

- Localization in the skin after treatment: Migration of parasites to skin post-kala azar dermal leishmaniasis (PKDL)

Both offensive and defensive processes give rise to increased serum globulin and reversal of a/g ratio.
Visceral leishmaniasis (kala azar)

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Clinico-pathological correlation

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- Splenomegaly, pain from perisplenitis
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Localization in the skin after treatment
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Pigmentation: darkening of skin at forehead, temples, mouth (Kala azar means "black fever")

Both offensive and defensive processes give rise to increased serum globulin and reversal of α/γ ratio.
Cutaneous leishmaniasis

Caused by Leishmania tropica, L. major, L. aethiopica, L. infantum, L. braziliensis complex

Mucocutaneous leishmaniasis (espundia)

Caused by some infections with L. braziliensis (Central and South America), L. aethiopica (Ethiopia), L. mexicana

Diagnosis of Leishmaniasis

Visceral
Amastigotes can be demonstrated by staining bone marrow, lymph node fluid, nasal scrapings (in the Sudan), liver biopsy or splenic aspiration specimens (although this can be a dangerous procedure). Rarely, amastigotes can be demonstrated in buffy coat preparations from peripheral blood.

Cutaneous and mucocutaneous
Demonstration of the parasite is possible in stained films from slit-skin smears taken from the indurated edge of an ulcer, biopsy of the margin of the ulcer and from mucosal scrapings in mucocutaneous type.

Culture (NNN or a liquid medium such as Schneider's Drosophila medium or 199 medium with added fetal calf serum) is used for all types of material for diagnosis. Animal inoculation is rarely used now.

Polymerase chain reaction (PCR) can be used to diagnose and type the species of Leishmania present in biopsy or culture material.

Specific serological tests are IFAT, ELISA, direct agglutination test (DAT), or latex agglutination for IgG antibodies. An immunochromatographic test for rK39 antibody detection is also available.
Trypanosomiasis

African type: sleeping sickness

Caused by either *Trypanosoma gambiense* (chronic sleeping sickness, found in West Africa, the Congo, Zaire) or by *T. rhodesiense* (acute sleeping sickness, found in Zimbabwe, Tanzania, Zambia, Angola). Both have similar life cycle and morphology.

![Life cycle in insect](image)

- Trypanosomes in blood ingested by tsetse fly
- Total developmental cycle in fly 20 days
  - Reproduction by binary fission
  - Migrate forward
  - Enter salivary glands via ducts
  - Metamorphose to epimastigotes and multiply
  - Re-metamorphose to slender metacyclic trypanosomites

![Life cycle in humans](image)

- Reproduction by binary fission as trypanosomites
- Primary stage
  - Metacyclic trypanosomes injected by tsetse fly
    - Multiply at site of injection
  - Secondary stage
    - Invade bloodstream and tissue spaces of various organs particularly lymph nodes initially
  - But do not enter actual cells
  - Third stage
    - Then CNS
### Pathogenesis and pathology

**Primary stage**
- Multiplication at site of injection
- Surrounding inflammatory reaction

**Secondary stage**
- Parasitaemia and toxemiasa
- Invasion of tissue spaces (not cells) of various organs
- Predominantly CNS
- Lymph nodes
- Damage to endothelial cells of blood vessels, surrounding (perivascular) granulomatus reactions and haemorrhages

**Third stage**
- Toxic degeneration and pressure atrophy of tissue cells

---

**Chronic sleeping sickness**  
(Due to *T. gambiense*)

<table>
<thead>
<tr>
<th>Clinico-pathological correlation</th>
<th>Primary stage</th>
<th>Secondary stage—predominantly blood and lymph node involvement</th>
<th>Third stage—CNS involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firm, tender, painful red nodule 1–3 weeks</td>
<td>Trypanosomal chancre</td>
<td>Trypanosomal chancre</td>
<td>Fever</td>
</tr>
<tr>
<td>Fever</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>General toxic symptoms</td>
<td>Backache</td>
<td>Headache</td>
<td>Tachycardia</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td></td>
<td>Irregular skin rashes (circinate)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Transient oedema face</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>Typically post-cervical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Later anaemia monocytosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slight enlargement liver, spleen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Congested, slightly enlarged</td>
<td>Toxic depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toxic depression</td>
<td>Bone marrow</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slightly enlarged</td>
<td>Toxic depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bone marrow</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Acute sleeping sickness**  
(Due to *T. rhodesiense*)

**Note on epidemiology**
- Vectors of *T. gambiense* are riverine species, hence disease often epidemic:
  - *G. palpalis*
  - *G. tachinoides*

- Vectors of *T. rhodesiense* are game-attacking species, hence disease more often sporadic:
  - *G. morsitans*
  - *G. pallidipes*
  - *G. swynnertoni*
South American type: Chagas’ disease

Caused by Trypanosoma cruzi. The parasite is harboured in humans, domestic animals such as cats and dogs, and some wild animals, notably armadillos and opossums.

**Morphology**

Axoneme
Small parabasal body
Large blepharoplast
Trypomastigotes in blood of humans and gut of insect
Resemble African trypanosomes except:
- characteristic C or S shape
- conspicuous kinetoplast
- long and short forms may occur

Amastigotes in cells of humans
Indistinguishable (except for site) from Leishman–Donovan bodies of leishmaniasis

Promastigotes in gut of insect and transitional stage in humans

**Life cycle in insect**

Triatoma spp: the cone bug

Trypomastigotes in blood ingested by bug
Metamorphosis to and multiplication as epimastigotes
Re-metamorphosis to small metacyclic trypomastigotes

8–10 days
Posterior station development
These infective forms passed in faeces

**Life cycle in humans**

Metacyclic trypanosomes in bug faeces deposited on skin
Rubbed into bite puncture, abrasion or conjunctiva
Enter histiocytes locally metamorphose to amastigotes and multiply by binary fission

Carried to regional lymph nodes

Some amastigotes metamorphose to trypomastigotes and invade blood and lymph

Enter cells of many organs, metamorphose to amastigotes and multiply

Parasitized cells rupture

Do not divide in blood
Pathogenesis and pathology

Local invasion of histiocytes
Inflammatory reaction
Fibrosis: lymph blockage
Oedema

Chagoma

Regional lymphangitis and lymphadenitis

Systemic manifestations

Invasion of local lymph nodes
Reticuloendothelial hyperplasia with parasitization

Invasion of blood and lymph vessels by trypansosomal forms

No multiplication in bloodstream

Dissemination to practically any tissue of body

Parasitization of reticuloendothelial and parenchymatous cells by amastigote forms which multiply and destroy cells

Recurring re-invasion of the blood by trypansosomal forms and further dissemination

Acute symptoms
- Fever
- Swelling of eyelids (Romana's sign)

Micro
Similar in all lesions
Amastigote forms in tissue cells e.g.
Pseudocyst
RE cells
CNS
Myocardial fibres
Thyroid
Little surrounding tissue reaction

Acute form (often in children)
- Blood and reticuloendothelial cells predominantly involved
- Fever
- Oedema
- Lymphadenopathy
- Enlargement of liver and spleen
- Sometimes encephalitis

Death or

Chronic form
- General toxic symptoms and focal signs depending on localization
- Predominantly cardiac and CNS manifestations
- May be asymptomatic

Fundamental pathogenesis
Invasion and destruction of tissue cells by multiplying amastigote forms with functional disability

- Myocarditis
- Tachycardia
- Heart block
- Emboli
- Aneurysms

- Generalized lymphadenopathy

- Encephalitis
- General or focal CNS signs and symptoms

- Splenomegaly

- Hepatomegaly

- Toxic depression of bone marrow
- Anaemia

- Destruction of intestinal nerve plexus
- Megesosonephagus
- Megaloclon

Body-fluid and tissue flagellates
Laboratory diagnosis of trypanosomiasis

**African type (sleeping sickness)**

Demonstration of the parasite.
Microscopy of thin and thick blood films anduffy coat preparations.
Trypanosomes can also be seen in smears from bone marrow and centrifuged cerebrospinal fluid (CSF). Culture is possible but difficult.
Microscopic detection of trypanosomes in peripheral blood may be improved by the use of a mini-anion-exchange column or by the use of the QBC11® (Becton Dickinson) to concentrate the parasite.
The CSF might show increased protein and lymphocytes.

**South American type (Chagas' disease)**

Demonstration of the parasite.
Stained smears of peripheral blood show trypanosomal forms in C or S shape. Stained films of lymph node fluid show amastigotes. It is possible to show trypomastigotes by animal inoculation from blood and by culture from lymph node fluid.
Histological methods from biopsy or post-mortem material. It is also possible to demonstrate the parasite through xenodiagnosis: clean bred triatomid bugs fed on the patient's blood develop trypanosomes in the gut.
Serology (e.g. by ELISA or IFAT) is the method of choice for the detection of chronic T. cruzi infection.
Laboratory diagnosis of trypanosomiasis

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Recapitulation

Luminal intestinal protozoa

Refer to text for the following additional stained appearances:
- trichrome stain for coccidia and microsporidia spp.
- modified Ziehl-Neelsen for Cyclospora, Isospora and Cryptosporidium spp.
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Atlas of Medical Helminthology and Protozoology

In this fourth edition provides a unique diagnostic reference source for the microbiologist, tropical disease physician and medical scientist. The entire contents has been revised and re-structured and illustrated with new full colour diagrams and photomicrographs. For each organism there is a schematic life cycle, range map, morphological drawing and microscopic appearance. No diagnostic laboratory should be without this valuable resource.
### Entamoeba histolytica (causing amoebiasis) (continued)

#### Morphology (continued)

<table>
<thead>
<tr>
<th>E. histolytica</th>
<th>Iodine preparations</th>
<th>E. coli</th>
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<tbody>
<tr>
<td><strong>Precyst</strong></td>
<td>Brown, diffuse</td>
<td>Brown, compact</td>
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<tr>
<td></td>
<td>Finely granular yellow green</td>
<td>Conspicuous granularity</td>
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<tr>
<td></td>
<td>Yellow ring with central yellow dot (karyosome)</td>
<td>Nuclear membrane with eccentric karyosome easily recognised</td>
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<tr>
<td><strong>Stained by iron haematoxylin</strong></td>
<td></td>
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<tr>
<td><strong>Trophozoite</strong></td>
<td></td>
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<tr>
<td>Puprilsish brown</td>
<td>Cytoplasm</td>
<td>Greyish blue</td>
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<tr>
<td>Fairly granular</td>
<td>Inclusions</td>
<td>Coarsely granular</td>
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<tr>
<td>RBC black</td>
<td>Nucleus; Membrane</td>
<td>Vacuoles black, as are bacteria etc.</td>
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<tr>
<td>Lined with minute black granules</td>
<td></td>
<td>Thick with plaques of black chromatin</td>
</tr>
<tr>
<td>Small black central dot</td>
<td>Karyosome</td>
<td>Eccentric black dot or plaque</td>
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<tr>
<td>Trace only seen</td>
<td>Fibril network</td>
<td>More conspicuous; may have chromatin plaques</td>
</tr>
<tr>
<td><strong>Precyst</strong></td>
<td>Round</td>
<td>Round</td>
</tr>
<tr>
<td>As trophozoite</td>
<td>Cytoplasm; Nucleus</td>
<td>As trophozoite</td>
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<tr>
<td>Black chromidial bodies or bars</td>
<td>Inclusions</td>
<td>May have slender black chromidial bars</td>
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<td>Glycogen (dissolved) replaced by vacuoles</td>
<td></td>
<td>Glycogen (dissolved) replaced by vacuoles</td>
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<td><strong>Cyst</strong></td>
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<td>Greyish-blue, granular</td>
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<td>Inclusions</td>
<td>As precyst, less conspicuous or absent</td>
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<td>Wall</td>
<td>Unstained, hyaline</td>
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<td>As trophozoite 1–4</td>
<td>Nuclei</td>
<td>As trophozoite 1–8</td>
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