Toxoplasma
(protist: apicomplexan)

Overview

Protists are single-celled organisms with membrane-bound nuclei (eukaryotes). One protistan supergroup known as SAR comprises the Stramenopiles (with heterokont flagella), Alveolata (with cortical alveoli) and Rhizaria (with fine pseudopodia). Three major alveolate groups are recognized: ciliates, apicomplexans and dinoflagellates. Apicomplexan cells possess a distinctive apical complex of organelles, comprising a conoid, polar ring, rhoptries, micronemes and subpellicular microtubules, which facilitate entry into host cells as they are obligate intracellular parasites for most of their life-cycles. There are three main apicomplexan groups: gregarines, coccidia and haematozoa. Coccidia form non-motile resistant oocysts that contain infective sporozoites usually confined within secondary spores (sporocysts). Tissue cyst-forming coccidia have heteroxenous (2-host) life-cycles alternating between enteric stages in predators (definitive hosts) and encysted stages in prey (intermediate) hosts. *Toxoplasma gondii* will only form oocysts in cats – merogony (= schizogony), gamogony (male microgametes fertilize female macrogametes) and oocyst formation occur in the intestinal epithelia. Sporogony occurs exogenously and mature oocysts contain 2 sporocysts each with 4 sporozoites (1:2:4 configuration). Thin-walled tissue cysts filled with bradyzoites (= cystozoites) are formed in the striated muscles and neurons of many different vertebrate hosts (mammals and birds) following merogonous division of tachyzoites in macrophages. Infections in cats are asymptomatic while infections in intermediate hosts (including humans) have been associated with mild to severe clinical disease (systemic, neurological or reproductive toxoplasmosis).

Classification:

Domain:	Eukaryota (membrane-bound nucleus)
Supergroup:	SAR (Stramenopiles + Alveolata + Rhizaria)
Group:	Alveolata (with cortical alveoli)
Phylum:	Apicomplexa (with apical complex, all parasitic, sexual development (gamogony))
Class:	Coccidiomorphea [Conoidasida] (with conoid)
Subclass:	Coccidia [Coccidiasina] (small intracellular gamonts)
Order:	Eucoccidiorida (cyclic merogony (schizogony), gamogony, sporogony)
Suborder:	Eimeriorina (no syzygy, many microgametes)
Family:	Sarcocystidae (heteroxenous, oocysts with two sporocysts, tissue cyst formation in intermediate host)
Subfamily:	Toxoplasmatinae (metrocytes not present, thin cyst walls)
Genus:	*Toxoplasma* (tissue cyst-forming coccidian parasite of mammals)
Species:	*T. gondii* (causes toxoplasmosis in humans and animals)

Parasite biodiversity and host range: Protists are unicellular eukaryotes that move using undulipodia (flagella or cilia), pseudopodia (false-feet) or a unique gliding motion. Cells with different modes of locomotion do not form separate monophyletic assemblages as previously thought, but rather are distributed across several disparate supergroups (as evidenced by recent molecular phylogenetic analyses). One protistan supergroup known as SAR comprises the Stramenopiles (with heterokont flagella), Alveolata (with cortical alveoli) and Rhizaria (with fine pseudopodia). Three diverse alveolate groups are recognized: Ciliophora (with cilia), Dinoflagellata (with flagella) and Apicomplexa (with gliding motion, some also with flagellated microgametes). Over 4,000 species of Apicomplexa have been described as obligate parasites from vertebrate and invertebrate hosts. At some stage in their development, these possess unique cytoskeletal and membrane-bound organelles (conoid, rhoptries, micronemes, subpellicular microtubules) forming an apical complex that facilitates host cell invasion. Apicomplexans undergo cyclic development involving up to three different divisional processes: asexual merogony (schizogony) either by fission (splitting of maternal cell) or endogeny (internal formation of daughter cells); gamogony involving formation of gametes (macrogametes = female, microgametes = male) which undergo fertilization to recombine by fusion (syngamy) with or without paired alignment (syzygy); and sporogony (formation of infective sporozoites).

Three main apicomplexan groups are recognized: haematozoa, gregarines, and coccidia. Haematozoa are small blood-borne parasites in vertebrates which complete their development in blood-sucking invertebrate vectors; with pleomorphic haemosporidia being transmitted by insects and pear-shaped piroplasms being transmitted by ticks. Gregarines are lumen-dwelling parasites that form large extracellular (sometimes septate) gamonts with an anterior holdfast organelle (mucron or epimerite) used to attach to the gut or body cavity of invertebrates. Coccidia are tissue-invading parasites that form small intracellular gamonts (lacking a mucron or epimerite) and most species undergo sexual reproduction by anisogamous fusion without syzygy forming non-motile resistant spores (oocysts) containing infective sporozoites usually confined within secondary spores (sporocysts). Three groups of coccidia are recognized: coelotrophiid coccidia in marine annelids; adeleid coccidia in marine and terrestrial animals (including blood parasites paradoxically known as ‘haemogregarines’ in reptiles and amphibians with leech or arthropod vectors); and eimeriid coccidia in vertebrates. Many eimeriid coccidia are monoxenous gut parasites undergoing faecal-oral transmission, but some are heteroxenous alternating between enteric stages in predators and encysted stages in prey (there are also a few enigmatic ‘haemococcidia’ in the blood of reptiles and birds).

Higher taxonomy	Family	Genera	Hosts	Site	Trans-mission*
Class: Gregarinomorphea (gregarines, trophonts with specialized attachment epimerite or mucron, syzygy)					
Subclass: Cryptogregaria (epicellular parasites of vertebrates with feeder organelle but lacking apicoplast)					
	Cryptosporidiidae (naked sporozoites)	*Cryptosporidium*	vertebrates	gut, lungs	direct (f-o)
Class: Coccidiomorphea [Conoidasida] (with conoid)					
Subclass: Coccidia [Coccidiasina] (small intracellular gamonts)					
Order: Eucoccidiorida (cyclic merogony (schizogony), gamogony, sporogony)					
Suborder: Adeleina (syzygy, 1-4 microgametes)	Haemogregarinidae (ookinete, gamonts in blood cells, invertebrate vectors)	*Haemogregarina*	reptiles, amphibia, fish	tissues, blood	indirect (v-b)
		Hepatozoon	mammals, reptiles	tissues, blood	indirect (v-b)
	Klossiellidae (sporocysts)	*Klossiella*	mammals	kidney	direct (f-o)
Suborder: Eimeriorina (no syzygy, >4 microgametes)	Eimeriidae (monoxenous, endogenous merogony and gamogony, exogenous sporogony)	*Caryospora*	birds, reptiles	gut	direct (f-o)
		Cyclospora	mammals, reptiles	gut	direct (f-o)
		Isospora	birds, reptiles	gut	direct (f-o)
		Eimeria	vertebrates	gut, tissues	direct (f-o)
		Epieimeria	fish	gut	direct (f-o)
		Goussia	fish	gut	direct (f-o)
	Sarcocystidae (heteroxenous, 1:2:4 oocyst:sporocyst:sporozoite configuration)				
	subfamily Cystoisosporinae (monozoic cysts)	*Cystoisospora* (no Stieda bodies)	carnivores, omnivores	gut, tissues	direct (f-o), indirect (p-p)
	subfamily: Sarcocystinae (thick-walls, metrocytes)	*Sarcocystis* (*Frenkelia*)	mammals, birds, reptiles	gut, muscles	indirect (p-p)
	subfamily: Toxoplasmatinae (thin-walled cysts without metrocytes)	*Besnoita*	mammals, reptiles	gut, tissues	indirect (p-p)
		Hammondia	mammals	gut, tissues	indirect (p-p)
		Neospora	herbivores, dogs	gut, tissues	indirect (p-p)
		Toxoplasma	vertebrates, cats	gut, tissues	indirect (p-p)
Class: Aconoidasida (asexual stages without conoid)					
Subclass: Haematozoa (clade of vector-borne spore-forming haemo-protozoa)					
Order: Haemosporida (pleomorphic blood stages, insect vectors, motile ookinete)	Plasmodiidae (schizogony in tissues then blood cells, haemozoin pigment)	*Plasmodium*	mammals, birds, reptiles	liver, erythrocytes	indirect (v-b)
	Haemoproteidae (schizogony in tissues, haemozoin pigment)	*Haemoproteus*	birds	endothelia, erythrocytes	indirect (v-b)
	Leucocytozoidae (schizogony in tissues, no haemozoin pigment)	*Leucocytozoon* (*Akiba*)	birds	tissues, leucocytes	indirect (v-b)
Order: Piroplasmorida (pear-shaped blood stages, tick vectors)	Babesiidae (merogony in erythrocytes, trans-stadial + trans-ovarian transmission)	*Babesia*	mammals	erythrocytes	indirect (v-b)
	Theileriidae (merogony in leucocytes, trans-stadial transmission in ticks)	*Theileria*	ruminants	leucocytes, erythrocytes	indirect (v-b)

* f-o = faecal-oral transmission; p-p = predator-prey transmission; v-b = vector-borne transmission.

Numerous species of coccidia have been described from a wide range of vertebrate and invertebrate hosts. Some 50 genera have been classified in 11 families in the suborder Eimeriorina, including nine genera in the family Sarcocystidae. These apicomplexans are often referred to as cyst-forming coccidia, as they undergo gamogony and sporogony producing oocysts (1:2:4 oocyst:sporocyst:sporozoite configuration) in the intestines of carnivorous definitive hosts (DHs) as well as merogony and tissue cyst formation in the tissues of omnivorous or herbivorous intermediate hosts (IHs). They have heteroxenous (two-host) life-cycles with cyclic transmission between predatory animals and their prey. Two main subfamilies are recognized mainly on the basis of differences in cyst development (metrocytes present or absent) and site of oocyst sporulation (endogenous or exogenous). Members of the subfamily Sarcocystinae form cysts with metrocytes within the tissues of their intermediate hosts, and their oocysts sporulate endogenously before being voided from the definitive host. Members of the subfamily Toxoplasmatinae form cysts without metrocytes within the tissues of their intermediate hosts, and their oocysts sporulate exogenously after being voided from the definitive host. A third subfamily has recently been added with the discovery that some *Isospora* spp. in mammals form encysted

monozoic stages (cystozoites) in the tissues of paratenic (transport) hosts (esp. rodents), prompting their classification with the tissue cyst-forming coccidia under the name *Cystoisospora* in the new subfamily Cystoisosporinae.

Parasite genera	No. spp.	Life-cycle	Definitive Hosts (DH) Intermediate Hosts (IH) Paratenic Hosts (PH)	Oocyst configuration*
Family: Sarcocystidae (3 subfamilies)				
Subfamily: Cystoisosporinae (monozoic cysts in PH, sporocysts without Stieda bodies)				
Cystoisospora	50	heteroxenous	vertebrate DH (carnivores, primates), vertebrate PH (mammals, birds)	1:2:4
Subfamily: Sarcocystinae (metrocytes, endogenous sporulation)				
Sarcocystis (incl. *Frenkelia*)	135	heteroxenous	vertebrate DH (predatory mammals, birds, reptiles), vertebrate IH (mammals, birds, reptiles)	1:2:4
Subfamily: Toxoplasmatinae (no metrocytes, exogenous sporulation)				
Toxoplasma	1	heteroxenous	vertebrate DH (felids), vertebrate IH (mammals), invertebrate PH (annelids, insects)	1:2:4
Hammondia	3	heteroxenous	vertebrate DH (canids, felids), vertebrate IH (mammals)	1:2:4
Neospora	2	heteroxenous	vertebrate DH (canids), vertebrate IH (mammals)	1:2:4
Besnoitia	7	heteroxenous	vertebrate DH (felids), vertebrate IH (mammals, reptiles), possibly invertebrate PH (insects)	1:2:4
Hyaloklossia	1	monoxenous	vertebrates (amphibians)	1:2:4
Nephroisospora	1	monoxenous	vertebrates (bats)	1:2:4

*1:2:4 = one oocyst contains 2 sporocysts, each sporocyst contains 4 sporozoites

The genera *Toxoplasma*, *Hammondia*, *Neospora* and *Besnoitia* are obligatory or facultatively heteroxenous with cyclic predator-prey transmission usually between carnivorous definitive hosts (DH) and herbivorous intermediate hosts (IH). Transmission from IH to DH occurs carnivorism (predator consuming cysts in tissues of prey) and transmission from DH to IH occurs via faecal-oral contamination (excretion of oocysts/sporocysts in faeces of predators to contaminate foodstuffs of prey). Several species are also di-heteroxenous (less common term di-homoxenous), meaning that infections can be passed horizontally between intermediate hosts by carnivorism (ingestion of tissue cysts in IH or PH) or vertically from mother to offspring (via transplacental or transmammary infection). These heteroxenous genera within the subfamily Toxoplasmatinae form tissue cysts without metrocytes, the bradyzoites undergo asexual division before gamete formation and the oocysts sporulate exogenously after being voided. More recently, encysted stages of two monoxenous genera (*Hyaloklossia* and *Nephroisospora*) have been found in the tissues of amphibians and bats, prompting their placement in the subfamily Toxoplasmatinae.

Toxoplasma infections have been detected worldwide in a diverse range of warm-blooded vertebrate hosts; mostly mammals (carnivores, omnivores, herbivores, insectivores, rodents, primates including humans) and occasionally birds. Sexual development and oocyst formation only occurs, however, in feline hosts. One species is currently considered valid: *T. gondii* which is facultatively heteroxenous (and diheteroxenous) using a wide range of mammals and birds as intermediate hosts and felids as definitive hosts. *Hammondia hammondi* exhibits many similarities to *T. gondii,* but is obligatorily heteroxenous cycling between some rodents and cats. Other *Toxoplasma* species have been reported but they are considered as *species inquirenda* or *nomen dubium* due to a lack of descriptive or biologic information. Laboratory studies have recognized various strains of *T. gondii* on the basis of their variable infectivity, growth, virulence and gene expression. Recent genetic studies indicate that *T. gondii* propagates primarily by clonal, asexual or uniparental clonal reproduction, and various strains have been allocated to three clonal lineages (Types I, II and III) on the basis of analyses of multiple independent single-copy loci as well as microsatellite markers. Type I strains are most often associated with disease in immunocompetent adults and in congenital infections, type II strains with immunocompromised individuals, and type III strains with patients with ocular toxoplasmosis. The prevalence of infections varies according to host populations and geographic location but seroprevalence estimates range from 5-75% in many countries.

***Toxoplasma* species**	**Intermediate hosts (IH)**	**Definitive hosts (DH)**	**Distribution**
T. gondii (type species)	Warm-blooded vertebrates, including Primates (humans, apes, monkeys, lemurs, lorises, tarsiers), Chiroptera (megabats, microbats), Cetacea (whales, dolphins, porpoises), Carnivora (canids, mephitids, mustelids, procyonids, ursids, pinnipeds, felids, herpestids, hyaenids, viverrids), Artiodactyla (camelids, suids, cetaceans, hippopotamids, tragulids, antilocaprids, giraffids, cervids, bovids), Perissodactyla (equids, rhinocerotids, tapirids), Proboscidea (elephants), Rodentia (mice, rats, squirrels, prairie dogs, chipmunks, porcupines, beavers, guinea pigs, hamsters, gerbils, capybaras), Lagomorpha (rabbits, hares, pikas), Monotremata (echidnas, platypus), Diprotodontia (macropodids, phalangerids, vombatids), Dasyuromorphia (dasyurids, myrmecobiids), Peramelemorphia (bandicoots, bilbies), Didelphimorphia (opossums), Cingulata (dasypodids, chlamyphorids), Pilosa (anteaters, sloths), Scandentia (treeshrews), Soricomorpha (shrews, moles), Afrosoricida (tenrecs, golden moles), Erinaceomorpha (hedgehogs, gymnures); Aves: Anseriformes (ducks), Accipitriformes (hawks), Casuariiformes (cassowaries), Charadriiformes (gulls, terns), Ciconiiformes (egrets), Columbiformes (pigeons, doves), Falconiformes (vultures), Galliformes (chickens, bowerbirds, partridges, pheasant), Gruiformes (coots), Strigiformes (owls), Passeriformes (crows, ravens, bulbuls, canaries, sparrows, finches, shrikes, jays, starlings, thrushes, tits, robins, tanagers, grackles, blackbirds, mynahs), Pelecaniformes (boobies). Psittaciformes (parrots, budgerigars, lories), and Sphenisciformes (penguins). Facultatively heteroxenous (involving diheteroxenous (IH-IH) horizontal transmission (via carnivorism or ingestion of paratenic hosts) and vertical transmission (via transplacental or transmammary infection). Paratenic hosts include Insecta: diptera (filth flies), blattodea (cockroaches) and Annelida: oligochaeta (earthworms).	Carnivora: felid (domestic cat, African wild cat, European wild cat, bobcat, Geoffroy's cat, iriomote cat, leopard cat, Amur leopard cat, Pampas cat, Pallas cat, cheetah, cougar, jaguar, jaguarundi, leopard, lion, ocelot, tiger)	worldwide

Some workers have proposed as many as 6 named *Toxoplasma* species in poikilotherms, but most remain convinced that there is only one species in mammals (*T. gondii*) with a worldwide distribution.

***Toxoplasma* species inquirenda, nomen dubium**	**Intermediate hosts (IH)**	**Distribution**
T. alencari (maybe *Lankesterella*)	pseudocysts in brain of Anura: leptodactylid (butter frog)	South America
T. brumpti	zoites in circulating white blood cells in Sauria: iguanid (common green iguana)	Americas
T. colubri (syn. *T. plimmeri*)	zoites in circulating white blood cells in Serpentes: colubrid (pine snake, green whip snake)	Europe
T. ranae	pseudocysts in tissues of Anura: ranid (northern leopard frog)	North America
T. serpai (maybe *Dactylosoma*)	zoites in blood cells and tissues of Anura: bufonid (cane toad)	Americas
T. wassilewsky (maybe *Eimeria*)	zoites in tissues of Cypriniformes: cyprinid (bream)	Eurasia

Parasite morphology: Four developmental stages are formed; schizonts, tissue cysts, gamonts and oocysts. Schizonts (sometimes called meronts) appear as small basophilic intracellular bodies which divide rapidly to form small collections of merozoites (usually called tachyzoites – 'tachy' meaning 'fast') measuring 4-5 x 1-2 μm. Tissue cysts (measuring 10-100 μm in diameter) are surrounded by a thin primary cyst wall (< 0.5 μm thick) and contain hundreds of basophilic cystozoites (usually called bradyzoites – 'brady' meaning 'slow') measuring 3-4 by 1-2 μm. Gamonts exhibit sexual differentiation, with microgamonts (male) apparent as multinucleate basophilic stages ultimately shedding small biflagellated microgametes; and macrogamonts (female) evident as uninucleate eosinophilic cells with a single ovoid nucleus. Oocysts are small ovoid stages (10-13 x 9-11 μm) and contain two round sporocysts (without Stieda bodies), each sporocyst containing four elongate sporozoites (isosporid-like 1:2:4 configuration).

Site of infection: In cats, parasites undergo asexual and then sexual multiplication in intestinal epithelial cells culminating in the formation of oocysts 3-5 days after infection. The parasite patent period (during which oocysts are shed) lasts several days to weeks and then cats become immune to infection. In all other vertebrate hosts, parasites undergo asexual multiplication in a wide range of extra-intestinal locations (cells of the lymphatic and circulatory systems, nervous tissue, skeletal musculature, etc.). During the acute phase of infection, the parasites divide rapidly forming small groups of 8-32 tachyzoites which lyse the host cells. As infections become chronic, the parasites divide more slowly forming large accumulations of bradyzoites particularly within the brain, heart and skeletal muscle. These tissue cysts are surrounded by a thin cyst wall and they persist for months or even years after infection. Cyst formation (change from tachyzoite to bradyzoite stages) coincides with the development of host protective immunity (not a sterile immunity where the infection is eliminated, but a state of premunition or concomitant immunity where some parasites persist within hosts that are resistant to super-infection). In cats, both the sexual (enteroepithelial) and asexual (extraintestinal) phases of infection may occur simultaneously.

Pathogenesis: Many host species exhibit an age-related resistance to disease therefore most infections in adults and weaned individuals are asymptomatic. In susceptible hosts, symptomatic infections may be acute, subacute or chronic. Acute infections by proliferating tachyzoites cause flu-like symptoms, including lymphadenitis, fever, headache, muscle pain, malaise and anaemia. Symptoms generally subside with the development of immunity, but may sometimes persist producing subacute disease, characterized by extensive lesions in the lung, liver, heart, brain or eyes. Postnatal infections often involve lymphadenitis, myocarditis, central nervous system involvement and retinochoroiditis. Chronic infections by encysted bradyzoites usually cause few clinical signs, although degenerating cysts have been associated with hypersensitive inflammatory reactions, resulting in, for example, encephalitis, myocarditis and/or chorioretinitis. The tissue cysts lay quiescent (dormant) in the tissues for some time, occupying little space and apparently causing few functional deficits, although there is contradictory evidence that infections may be associated with some learning disabilities, slower reflexes and altered behaviour in intermediate hosts (such as increased movement and diminished fear in rodents possibly leading to their enhanced predation by felines). In immunocompetent hosts, concomitant immunity provides protection against clinical toxoplasmosis and appears to be mediated primarily through cellular responses involving both CD4+ and CD8+ T lymphocytes and gamma-interferon. Latent cyst infections may be reactivated in immunocompromised patients (i.e. those undergoing immunosuppressive therapy or with acquired immunodeficiencies) resulting in cell lysis, expanding focal lesions, rapid dissemination, encephalopathy and meningoencephalitis. Infections may also be transmitted transplacentally, but only if the mother/dam contracts infection during pregnancy. In these situations, the invading parasites may cross the placenta and infect the foetus with dire consequences depending on the trimester of pregnancy. Infections in the first trimester may lead to foetal death and spontaneous abortion, infections in the second trimester may also lead to foetal death resulting in stillbirth or foetal retention and mummification, while infections acquired in the third trimester may not kill the developing foetus but the newborn may exhibit profound congenital abnormalities, such as hydrocephalus, brain calcification, chorioretinitis and mental retardation. If the mother/dam is infected prior to pregnancy, her immunity is transferred to her foetus which is consequently protected. Nevertheless, the parasite is considered to be a major abortifacient in domestic livestock, with the exception of cattle (where *Neospora* causes reproductive losses). Infections in cats by enteric sexual developmental stages are generally subclinical, transient and leave the cat with a strong protective immunity against subsequent oocyst production. The duration of protection has not been demonstrated unequivocally, although laboratory studies indicate it may last several years but not be life-long.

Developmental cycle and mode of transmission: Infections are transmitted horizontally between hosts by the ingestion of oocysts excreted by cats, and vertically between mother and offspring by transplacental or even transmammary transmission of proliferative tachyzoites. Infections may also be transferred between intermediate hosts through the food chain via carnivorism (the ingestion of fresh or undercooked meat containing viable cysts). Bradyzoites released during digestive processes are resistant to enzymatic digestion and revert back to tachyzoite stages which infect the host, multiply, spread and lead to new cyst formation. Infections are more prevalent in human populations which have traditional cultural practices involving the consumption of raw or partially cooked meat (e.g. steak tartare, partly cured smallgoods). When intermediate hosts ingest sporulated oocysts, excystation occurs in the small intestines resulting in the release of the infective sporozoites. These stages penetrate the gut wall and may establish infections within a variety of host cells, notably macrophages, where they undergo asexual multiplication via endodyogeny (internal formation of two daughter cells) within parasitophorous vacuoles. Mature schizonts eventually lyse the host cell releasing tachyzoite stages which invade neighbouring cells or disseminate via the circulatory system to infect other organs. After several cycles of tachyzoite proliferation, the host mounts an immune response which suppresses tachyzoite growth. This coincides with their transformation to

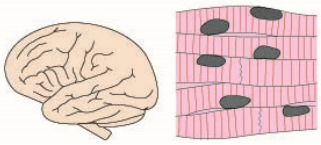
bradyzoite stages which sequester and multiply slowly within host cells to produce tissue cysts, particularly within nervous tissue and striated musculature. In immunocompetent intermediate hosts, these cysts persist as quiescent or dormant stages for years. When felid definitive hosts consume infected flesh, the parasites are released from cysts by enzymatic digestive processes and invade small intestinal cells. Here they undergo asexual multiplication followed by sexual reproduction involving the formation of female (macro-) and male (micro-) gametes which undergo fertilization to produce zygotes (immature oocysts). Oocysts excreted by cats take 1-5 days to sporulate before they become infective and they are resistant to external environmental conditions and may remain viable in contaminated soil and water for some time. They can survive periods of freezing at -20°C and temperatures as high as 50°C, and may even remain viable in seawater for several months. Infective oocysts have also been shown to be transmitted via paratenic (transport) hosts, including insects (filth flies, cockroaches) and oligochaetes (earthworms).

Differential diagnosis: Parasites may be detected in autopsy or biopsy material by histology, immunolabelling, *in vitro* tissue culture (e.g. in HeLa cells) or *in vivo* following inoculation into laboratory rodents. Zoites in smears stain well with Giemsa and other Romanowsky stains while cysts in sections have silver-positive walls and the bradyzoites are strongly PAS (periodic acid-Schiff) positive. Monoclonal and polyclonal antibody labels have also been used to detect parasites in tissue sections, and molecular studies using polymerase chain reaction (PCR) amplification techniques have detected parasite DNA (targeting the B1 repetitive sequence, P30 (SAG1) surface antigen or 18S ribosomal RNA genes). Given the low sensitivity of microscopic techniques, the long duration of culture techniques, the technical difficulty of molecular techniques and the invasive nature of specimen collection, most ante-mortem infections are diagnosed serologically using a range of immunoassays (dye tests; fluorescent-antibody tests; enzyme-linked immunosorbent assays; direct, indirect and modified agglutination tests; and Western immunoblotting techniques). It is important that sequential (longitudinal) samples be examined to establish the time course of infection. Recent/acute infections are indicated by a 4-16 fold increase in specific antibody titre over a two-week period, or by the detection of specific IgM antibody titres.

Treatment and control: Chemotherapy is successful when diaminopyrimidines (pyrimethamine) and sulfonamides (sulfadiazine) are given together as they act synergistically. The toxic side-effects of bone marrow depression can be relieved by the administration of folinic acid. Clindamycin, spiramycin and azithromycin have also been reported to be effective. The risk of transmission can be reduced by maintaining high standards of hygiene (particularly where cats are involved), by thoroughly cooking or deep-freezing meat prior to consumption, treating potable water (filtration and chlorination) and washing foodstuffs potentially contaminated by oocysts (e.g. vegetables from the garden). Many health agencies publish recommended hygiene/safety guidelines for patient groups considered to be most at risk (e.g. pregnant women and HIV-infected individuals). Molecular vaccines are currently being developed for high-risk patient groups, and a live vaccine using a low-virulent non-persistent strain has been marketed to protect sheep against toxoplasmosis.

Toxoplasma

heteroxenous (2-host) cycle
predator-prey transmission
(predator ingests tissue cysts in prey)
(prey ingests sporocysts shed by predator)
plus vertical transmission in prey
(transplacental/transmammary)
plus horizontal transmission between IHs
(via ingestion of bradyzoites in tissue cysts)

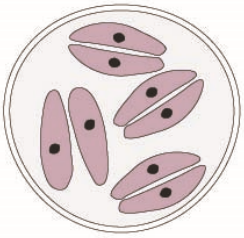


brain, muscles
(lymphadenitis, myocarditis,
chorioretinitis,
encephalopathy,
abortion, neonatal
mortalities)

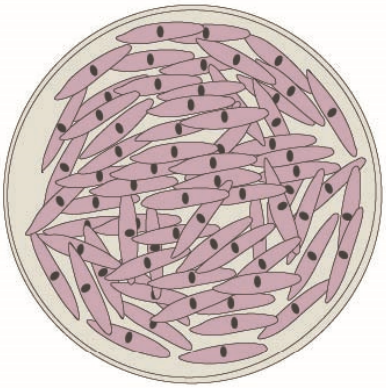
Intermediate Hosts (IH)
(mammals, birds)

disseminated
asexual merogony
(facilitates vertical
transmission)

tissue cyst
formation
in nerve &
muscle cells



meronts (5-20 µm)
filled with merozoites
(called tachyzoites))



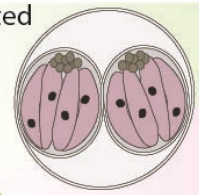
thin
cyst
wall

filled with
bradyzoites
(cystozoites)

tissue cysts
(10-100 µm)

excystation

oocysts
ingested



oocyst
(10-13 µm)

exogenous
sporulation

oocysts
excreted

sporoblast

fertilization

oocyst:sporocyst:sporozoite
configuration = 1:2:4

tissue cysts
ingested

meronts (8-15 µm)

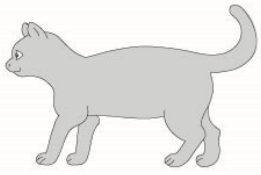
male

female

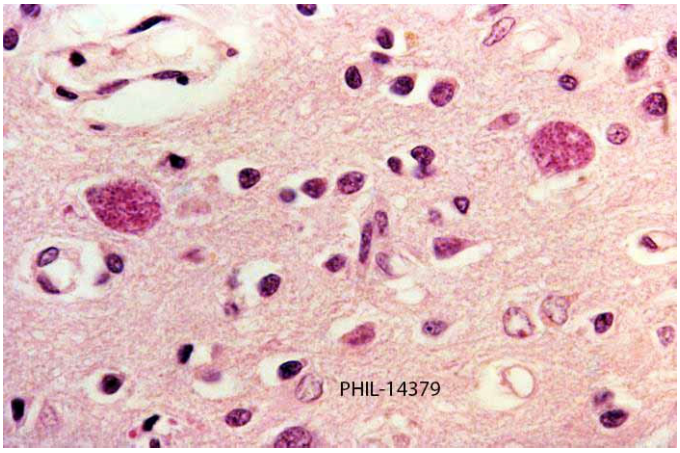
gamonts
(~ 10 µm)

sexual
gamogony

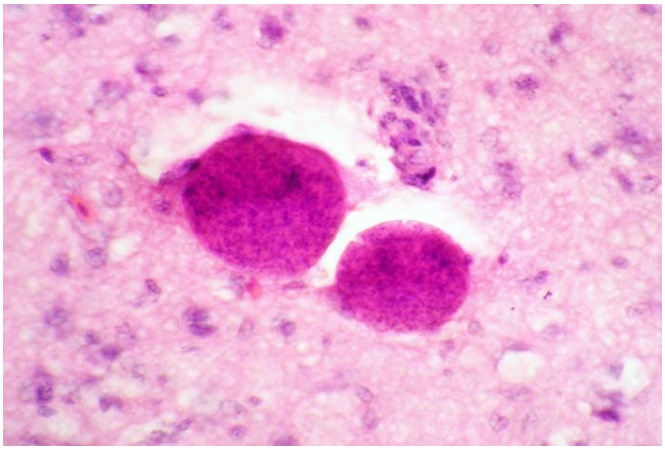
Paratenic Hosts
(flies, cockroaches, earthworms)
(intestines)



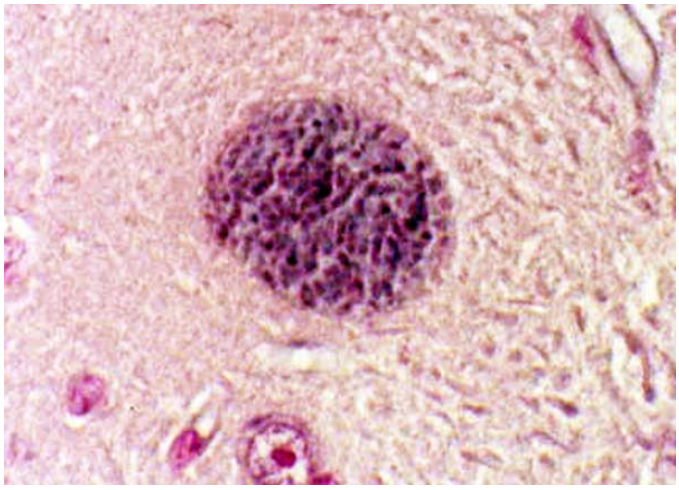
Definitive Hosts
(felids)
(intestines)



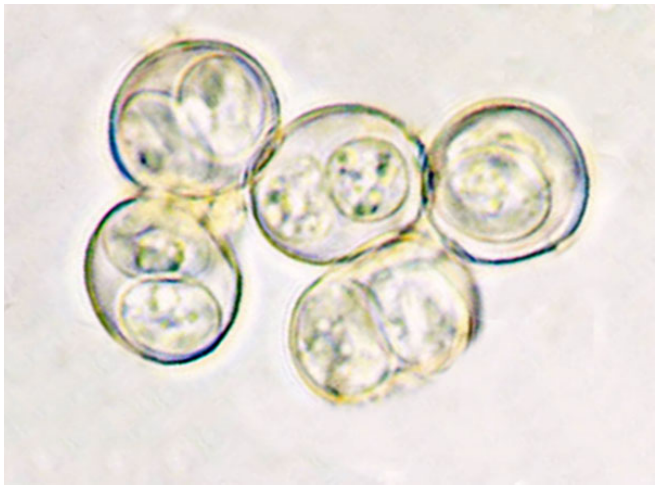
Toxoplasma cysts in brain



Toxoplasma cysts in owl brain



Toxoplasma cyst in mouse brain



Toxoplasma oocysts from cat faeces