Thelazia
(helminth: nematode)

Overview

Nematodes are triploblastic pseudocoelomate unsegmented worms that undergo protostomial embryonic cleavage and grow by cuticular moulting (ecdysis). Two groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Many phasmidian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including tylenchinids, rhabditinids and spirurinids. The latter contains the infraorder Spiruromorpha: an enigmatic clade linked by molecular characters, but all having indirect life-cycles involving one or more intermediate hosts, the first invariably being an arthropod. Most possess two trilobed lips (sometimes greatly reduced), a bipartite oesophagus (anterior muscular, posterior glandular) and non-bursate males with coiled tails and two dissimilar spicules. Several superfamilies are recognised: including both oviparous and viviparous thelazioids (lacking lips). The latter are found around the eyes of mammals and are transmitted by muscid flies feeding on ocular secretions (containing L1 released by female worms). Infections by *Thelazia* spp. have been associated with eye conditions ranging from conjunctivitis to corneal opacities mainly in cattle and horses.

Classification:

Domain:	Eukaryota (membrane-bound nucleus)
Supergroup:	Amorphea (unikonts with single flagellum, or nonflagellated amoebae)
Kingdom:	Metazoa (multicellular eukaryotes, heterotrophs, notably animals)
Group:	Protostomia (triploblastic, spiral cleavage)
Subgroup:	Ecdysozoa (cuticle moulted = ecdysis)
Phylum:	Nematoda (unsegmented, pseudocoelomate roundworms, tubular digestive tract, dioecious)
Class:	Chromadorea (spiral amphids, three oesophageal glands, usually annulated bodies, free-living and parasitic)
Order:	Rhabditida (Secernentea, Phasmidea) (secretors, with phasmids, bipartite oesophagus, single testis)
Suborder:	Spirurina (mostly parasitic in vertebrate hosts)
Infraorder:	Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily:	Thelazioidea (eye-worms of birds and mammals, transmitted by insects)
Family:	Thelaziidae (hexagonal mouth, lacking lips, conspicuous transverse anterior striations, live on surface of eye)
Genus:	*Thelazia* (parasitic in conjunctiva of cattle/horses)
Species:	various species cause eye conditions in cattle/horses

Parasite biodiversity and host range: Most Metazoa are multicellular triploblastic animals with differentiated tissues, many being bilaterally symmetrical with a body cavity. Most invertebrate animals are protostomes as their embryonic development involves spiral determinate cleavage. Those that moult their external cuticles during their life-cycles (process known as ecdysis) are grouped together in the unique clade Ecdysozoa, including the nematodes (roundworms), onychophorans (velvet worms), tardigrades (water bears) and arthropods (myriapods, chelicerates, crustaceans and hexapods, all with jointed limbs). Nematodes (roundworms) are unsegmented tubular worms with a fluid-filled body cavity (pseudocoelom) that acts as a hydrostatic skeleton. They have longitudinal muscles and typically exhibit a sideways thrashing motion. They have well developed digestive tracts with various partitions: the foregut comprising the mouth (often with lips and papillae), buccal capsule (sometimes with ridges, rods, plates, spears, stylets or teeth) and oesophagus (glandular, muscular or both); the midgut (nonmuscular absorptive section); and hindgut (rectum) emptying through a subterminal anus (cloaca in males). Most nematodes are dioecious and form separate sexes. Male worms have a single testis (sometimes 2), an elongate vas deferens often equipped with a seminal vesicle and ejaculatory duct (glandular and/or muscular), 1-2 copulatory spicules (sometimes with an accessory gubernaculum), and bursate species with elaborate posterior claspers. Female worms are usually didelphic (some monodelphic or polydelphic) with 2 ovaries, 2 oviducts usually with spermatheca, 2 uteri opening into a common vagina and a vulva often equipped with a muscular ovejector. Female worms are oviparous or viviparous and produce numerous eggs or larvae, respectively. Larval stages undergo several moults (L1-L4) before maturing into adult worms. Some nematodes have direct life-cycles where eggs or larvae infect definitive hosts (per os or per cutaneous), but many have indirect cycles where larvae first develop in invertebrate intermediate hosts before infecting definitive hosts (by ingestion, injection or deposition). Many nematode species are free-living in terrestrial and aquatic habitats, while some species from diverse groups have become plant or animal parasites. Two nematode groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Most Enoplia are free-living marine organisms but some are found in freshwater, and on land as plant parasites. The Dorylaimia comprise numerous freshwater and terrestrial species, including major groups of plant and animal parasites. The Chromadoria is represented by many marine groups as well as a terrestrial group of plant and animal parasites. The taxonomic ranks of many nematode assemblages vary considerably depending on which classification system has been followed. Molecular phylogenetic studies, however, have supported the separate

classification of most groups, particularly at the level of superfamily. Collectively, species from at least 16 superfamilies are considered to pose serious threats to human and animal health as infectious diseases.

CLASSIFICATION* OF SUPERFAMILIES OF PARASITIC NEMATODES
Class: Enoplea (Aphasmidea, Adenophorea) (gland-bearers, cylindrical oesophagus, no phasmids, setae, two testes)
Subclass: Dorylaimia (five or more oesophageal glands, buccal stylet (odontostyle), free-living or parasitic)[clade I(2)]
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short anterior muscular and long posterior glandular portions)
Class: Chromadorea (spiral amphids, 3 oesophageal glands, usually annulated bodies, free-living and parasitic)
Order: Rhabditida (Secernentea, Phasmidea) (secretors, phasmids present, amphids anterior, bulbous oesophagus)
Suborder: Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)[clade V(9)]
Infraorder: Rhabditomorpha ('rod-shaped' buccal cavity)
Superfamily: Rhabditoidea (open tube stoma, excretory system with lateral canals)
Superfamily: Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Suborder: Spirurina (animal parasites, many use invertebrate intermediate hosts (IH))[clade III(8)]
Incertae sedis Superfamily: Dracunculoidea (elongate parasites of vertebrate tissues, freshwater crustacean IH)
Infraorder: Ascaridomorpha (large roundworms, three large lips, numerous caudal papillae)
Superfamily: Ascaridoidea (ascarids, eggs thick-shelled, larvae may undertake hepato-pulmonary migration)
Superfamily: Heterakoidea (preanal sucker anterior to cloaca in males, direct cycle, infection by egg ingestion)
Infraorder: Gnathostomatomorpha ('jaw-mouthed' due to unique bulbous armed heads)
Superfamily: Gnathostomatoidea (first IH copepod, often use paratenic hosts)
Infraorder: Oxyuridomorpha (pinworms, pointed tails, oesophagus with terminal bulb, males with single spicule)
Superfamily: Oxyuroidea (common in mammals, birds, reptiles, amphibians)
Infraorder: Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily: Acuarioidea (small parasites mostly of birds, with cephalic cordons, ptilina or serrated shields)
Superfamily: Camallanoidea (conspicuous phasmids, L1 with dorsal tooth, ovoviviparous, L1-L3 in copepod)
Superfamily: Filarioidea (tissue-dwelling filarial parasites, lack lips, infect tissues/vessels, arthropod IH)
Superfamily: Habronematoidea (unique head structures with small pseudolabia and median lips)
Superfamily: Physalopteroidea (stomach worms in mammals, insect IH)
Superfamily: Spiruroidea (pseudolabia, bipartite oesophagus, infect birds (crop/gizzard), arthropod IHs
Superfamily: Thelazioidea (eye-worms of birds and mammals, transmitted by insects)
Suborder: Tylenchina (fungal, plant and animal parasites)[clade IV(10,11,12)]
Infraorder: Panagrolaimomorpha (free-living or parasitic (insects, reptiles, amphibians, mammals))
Superfamily: Strongyloidoidea (dauer stages, lip region without processes, striated cuticle)

*Contemporary genotypic classification schemes recognize strong monophyletic clades at the level of superfamily and infraorder, while previous phenotypic classification schemes had ranked many as separate orders.

Molecular phylogenetic studies have grouped a variety of superfamilies into the infraorder Spiruromorpha whose members are parasites of vertebrates with indirect life-cycles involving larval development within invertebrate intermediate hosts. Most members were previously classified within the order Spirurida: either within the suborder Camallanina (worms with conspicuous phasmids, uninucleate oesophageal glands, larvae without cephalic hooks, usually with copepodid intermediate hosts); or the suborder Spirurina (worms with inconspicuous phasmids, multinucleate oesophageal glands, larvae with cephalic hooks or spines, usually with non-copepodid intermediate hosts). Ten spirurinid superfamilies are recognised: Gnathostomatoidea and Physalopteroidea (buccal cavity weakly cuticularized, 2 large lateral pseudolabia); Habronematoidea and Acuarioidea (buccal cavity well cuticularized, 2 large lateral pseudolabia); Filarioidea, Rictularioidea, Aproctoidea and Diplotriaenoidea (buccal cavity well cuticularized, without pseudolabia); Thelazioidea (long cylindrical buccal cavity well cuticularized, body without caudal alae); and Spiruroidea (short buccal cavity well cuticularized, body with caudal alae).

The superfamily Thelazioidea comprises medium-sized worms with hexagonal or subspherical mouths without pseudolabia infecting the eyes or lungs of mammals, the eyes of birds or the intestines of fish, and using arthropods as intermediate hosts for larval development. Three families are recognised: Thelaziidae (buccal capsule well-developed, pharynx not elongated, parasites of eyes of birds and mammals); Rhabdochonidae (buccal capsule well-developed, pharynx cylindrical and elongated, parasites of intestines or organs of fish, sometimes other vertebrates); and Pneumospiruridae (buccal capsule small or absent, 6 lips sometimes well-developed or atrophied, cuticle with sheath, gubernaculum often double, parasites of lungs of mammals). The family Thelaziidae (or eyeworms) have hexagonal mouths and conspicuous transverse anterior striations. Two subfamilies are recognised: Oxyspirurinae (inner surface of buccal capsule often armed with teeth, oesophagus divided, vulva near anus, tail pointed in both sexes); and Thelaziinae (inner surface of buccal capsule without teeth, oesophagus not divided, vulva in anterior half of body, tail rounded in both sexes). The subfamily Thelaziinae contains 4 genera: *Ceratospira, Hempelia, Thelazia* and *Thelazo.* The genus *Thelazia* includes 3 subgenera: *T.* (*Thelazia*) (female tail short, gubernaculum absent, eggs thin-shelled, viviparous, parasites of mammals); *T.* (*Thelaziella*) (female tail long, gubernaculum present, eggs thick-shelled, viviparous, parasites of birds); and *T.* (*Annulofilaria*) (male without caudal alae, parasites of birds).

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Eggs/larvae	Transmission
Subfamily: Thelaziinae						
Thelazia (eyeworms)	43	mammals, birds	eyes	14-21 mm long, cuticle with anterior striations, males with coiled tails, 2 dissimilar spicules, ovoviviparous	larvae (L1) 220-280 µm sheathed	indirect (L1 in dipteran IH, esp. muscids)
Subfamily: Oxyspirurinae						
Oxyspirura (eyeworms)	81	birds	eyes	9-20 mm long, smooth cuticle, males with coiled tails, 2 spicules, some with lateral alae, oviparous	eggs 55-60 x 40-45 µm, ellipsoidal, thin-shelled	indirect (L3 in insect IH, esp. cockroaches)

Some 43 *Thelazia* spp. have been described from the eyes of numerous species of mammals and birds around the world. While 4 subgenera have been named, most authors have synonymized them into 2 subgenera: *T.* (*Thelazia*) syn. *T.* (*Pericyema*) (female tail short, male gubernaculum absent, ovoviviparous, thin-shelled eggs *in utero*, parasites of mammals); and *T.* (*Thelaziella*) syn. *T.* (*Isothela*) (female tail long, male gubernaculum present, oviparous, thick-shelled eggs, parasites of birds). Infections are transmitted by muscid flies which feed on ocular secretions ingesting parasite eggs and supporting larval development. Several species cause clinical disease in domestic livestock, mostly ungulates, producing mild to severe conjunctivitis and blepharitis. Zoonotic transmission to humans has also been reported for several species.

***Thelazia* species**	**Definitive hosts**	**Location [Clinical signs]**	**Intermediate hosts**	**Distribution**
T. anadorhynchi	Psittaciformes: psittacid (hyacinth macaw)	eyes		South America
T. annamensis	Galliformes: phasianid (Burmese peacock-pheasant); Passeriformes: muscicapid (hill blue flycatcher)	conjunctiva, orbit, nasal cavity		Asia
T. (*Thelaziella*) *anolabiata* (syn. *T.* (*Isothela*) *lutzi*)	Galliformes: cracid (Belem curassow, bare-faced curassow, Chaco chachalaca, rusty-margined guan); Passeriformes: cotingid (Andean cock-of-the-rock); Piciformes: ramphastid (black-necked aracari); Psittaciformes: psittacid (hyacinth macaw)	eyes		South America
T. anadorhynchi	Psittaciformes: psittacid (hyacinth macaw)			South America
T. (*Thelaziella*) *aquilina*	Accipitriformes: accipitrid (bicoloured hawk, great black hawk); Falconiformes: falconid (yellow-headed caracara, southern crested caracara)			South America
T. balayi	Artiodactyla: bovid (black-fronted duiker)			Africa
T. bubalis	Artiodactyla: bovid (water buffalo)			India
T. buteonis	Galliformes: cracid (blue-throated piping-guan); Accipitriformes: accipitrid (Swainson's hawk)	orbit		Americas
T. californiensis (California eyeworm)	Carnivora: canid (dog, coyote), felid (cat), ursid (American black bear); Artiodactyla: bovid (sheep), cervid (mule deer); Lagomorpha: leporid (European rabbit, jackrabbit); Primates: hominid (human)	eye, conjunctival sac, lachrymal duct [lacrimation, conjunctivitis]	Diptera: fannid (canyon fly, *Fannia benjamini, canicularis*), muscid (face fly, *Musca autumnalis*)	North America
T. (*Thelazia*) *callipaeda* (Oriental eyeworm) (syn. *T.* (*Pericyema*))	Carnivora: canid (dog, raccoon dog, wolf, American red fox), felid (cat, wildcat); Lagomorpha: leporid (European rabbit), Artiodactyla: bovid (sheep), cervid (deer); Primates: hominid (human)	eye, conjunctival sac, lachrymal duct [lacrimation, conjunctivitis]	Diptera: drosophilid (vinegar fly, *Phortica* (= *Amiota*) *variegata*, *okadai*)	Eurasia
T. campanulata	Accipitriformes: accipitrid (roadside hawk, gray-headed kite, Pallas's fish eagle); Tinamiformes: tinamid (Brazilian tinamou)			Asia, Americas

T. cheni (syn. *Annulofilaria*)	Accipitriformes: accipitrid (northern goshawk)			Asia
T. cholodkowskii	Caprimulgiformes: caprimulgid (European nightjar); Strigiformes: strigid (tropical screech-owl)			South America
T. chungkingensis	Galliformes: cracid (Alagoas curassow); Passeriformes: dicrurid (Indian hair-crested drongo)	eyes		South America, Asia
T. cuculina	Cuculiformes: cuculid (large hawk-cuckoo)			Asia
T. dacelonis	Coraciiformes: alcedinid (blue-winged kookaburra); Tinamiformes: tinamid (grey tinamou); Trogoniformes: trogonid (black-tailed trogon)			South America, Australia
T. dentifera	Piciformes: picid (Burmese black-naped green woodpecker)	conjunctiva		Asia
T. depressa	Carnivora: herpestid (mongoose); Accipitriformes: accipitrid (hooded vulture, red-headed vulture)	orbit		Africa, Asia
T. digiticauda	Caraciiformes: alcedinid (ruddy kingfisher)			Asia
T. digitata	Galliformes: cracid (red-throated piping guan); Piciformes: picid (ringed woodpecker, red-stained woodpecker), ramphastid (Toco toucan); Trogoniformes: trogonid (black-tailed trogon)			Holarctic
T. dollfusi	Pelecaniformes: threskiornithid (crested wood ibis)			Africa
T. erschowi	Artiodactyla: suid (pig)			Russia
T. gulosa (syn. *T. alfortensis*) (cattle eyeworm)	Artiodactyla: bovid (cattle, yak, European bison, sheep); Primates: hominid (human)	eye, conjunctival sac, lachrymal duct [lacrimation, conjunctivitis, photophobia]	Diptera: muscid (face fly, *Musca autumnalis, amica, domestica, larvipara, osiris, vitripennis*)	worldwide
T. iheringi	Rodentia: dasyproctid (agouti, Azara's agouti)			South America
T. (*Thelaziella*) *kaimurensis*	Caprimulgiformes: caprimulgid (nightjar)			Americas
T. lacrymalis (equine eyeworm)	Perissodactyla: equid (horse); Artiodactyla: bovid (cattle, yak)	eye, conjunctival sac, lachrymal duct [lacrimation, conjunctivitis, photophobia]	Diptera: muscid (*Musca autumnalis, osiris*)	Eurasia, Americas
T. leesei (eyeworm)	Artiodactyla: camelid (Bactrian camel, dromedary)	conjunctival sac [conjunctivitis]	Diptera: muscid (*Musca lucidulus*)	Africa, Asia, Russia
T. longicauda	Strigiformes: strigid (Asian barred owlet)	conjunctiva		Asia
T. (*Thelaziella*) *lutzi* (syn. *T.* (*Isothela*))	Galliformes: cracid (rusty-margined guan)	eye		South America
T. nyctardeae	Pelecaniformes: ardeid (black-crowned night heron, grey heron)			Eurasia, Africa
T. (*Thelaziella*) *orissae*	Accipitriformes: accipitrid (crested honey buzzard)			Eurasia
T. papillosa	Perissodactyla: equid (horse)			South America
T. philippinensis	Piciformes: picid (woodpecker)			Philippines
T. pittae	Accipitriformes: accipitrid (black-and-white hawk-eagle); Passeriformes: pittid (Papuan pitta)			Central America, Australia
T. platyptera	Accipitriformes: accipitrid (broad-winged hawk)			Eurasia
T. (*Thelazia*) *rhodesii* (cattle eyeworm)	Artiodactyla: bovid (cattle, zebu, European bison, water buffalo, sheep, goat, roan antelope, Kafue lechwe, Cape bushbuck,	eye, conjunctival sac, lachrymal duct [lacrimation,	Diptera: muscid (*Musca autumnalis, convexifrons,*	Eurasia, Africa

	greater kudu), camelid (dromedary, vicuna), cervid (red deer, moose); Perissodactyla: equid (horse)	conjunctivitis, photophobia]	*crassirostris, domestica, herveia, larvipara, sorbens*)	
T. sicki	Strigiformes: strigid (scops owl)			South America, Indo-China
T. skrjabini (cattle eyeworm)	Artiodactyla: bovid (cattle, yak, sheep), cervid (white-tailed deer)	eye, conjunctival sac, lachrymal duct [lacrimation, conjunctivitis, photophobia]	Diptera: muscid (face flies, *Musca amica, autumnalis, corvina, herveia, larvipara, osiris, viscinia, vitripennis*)	Eurasia, North America
T. (*Thelaziella*) *spizaeti*	Accipitriformes: accipitrid (ornate hawk-eagle); Piciformes: ramphistid (black-necked aracari)			South America
T. (*Thelaziella*) *stereura*	Accipitriformes: accipitrid (Pallas's fish eagle)			Asia
T. tonkinensis	Passeriformes: cotingid (Amazonian umbrellabird)			South America
T. travassosfreitasi	Rodentia: dasyproctid (Azara's agouti)			South America
T. ugandensis	Accipitriformes: accipitrid (hooded vulture)			Africa

Parasite morphology: *Thelazia* spp. form 3 different types of morphological stages during their development: eggs (produced *in utero*); larvae (4 consecutive stages encoded L1-L4); and adult worms. Gravid females contain numerous ovoid eggs measuring around 60 x 55 μm which have thin shells (in members of the subgenus *T.* (*Thelazia*)) or thick shells (subgenus *T.* (*Thelaziella*)). The eggs embryonate *in utero* but there is continuing debate about whether the worms are oviparous (releasing eggs) or ovoviviparous (releasing larvae), as no true hatching event seems to occur *in utero* or *ex utero*. The embryonated eggs transform within the uterus becoming coiled first-stage larvae (L1) still encased (encysted or ensheathed) in the shell membrane. When laid, the surrounding membrane becomes loose and often expanded at one end allowing the L1 to move about inside, sometimes even becoming reflexed. L1 are elongate cylindrical stages measuring from 220-280 μm, and the surrounding shell of some species develops conspicuous transverse folds or striations. Early L1 often have enlarged heads, sometimes with a central notch, while later L1 have grown substantially in width becoming stout with a central longitudinal oesophagus and intestines. The surrounding shell (sheath) is usually shed after ingestion of the L1 by dipteran intermediate hosts. L2 are transient developmental stages in the intermediate hosts, while L3 are long-lasting encapsulated stages. Freed L3 are elongate cylindrical stages ranging in length from 2-5 mm and surrounded by tough cuticles with prominent transverse striations. They have a short buccal cavity, a muscular oesophagus and a short bluntly tapered or rounded tail. L4 are transient parasitic stages in final hosts and they have begun to show oral structures similar to adults as well as genital primordia. Adults are small yellow-white worms with thin cylindrical filiform bodies 4-21 mm long and characterised by the possession of numerous prominent transverse striations of the anterior cuticle. They have hexagonal mouths, lacking lips but surrounded by 2 lateral amphids and 4 submedian cephalic papillae. In some species, the anterior edge of the mouth was thickened and recurved, sometimes forming up to 6 festoons. The buccal cavity is thick-walled, deep, cup-shaped and unarmed (lacking teeth). The cylindrical oesophagus appears undivided and the tail is rounded in both sexes. Adult worms are sexually dimorphic, with males being smaller than females (4-12 cf. 8-21 mm). Mature males have recurved coiled tails with variable numbers (5-33 pairs) of precloacal papillae and 2-3 pairs postcloacal papillae and 2 asymmetrical spicules (long slender left spicule, short stout right spicule). Members of the subgenus *T.* (*Thelazia*) lack a gubernaculum (present in the subgenus *T.* (*Thelaziella*)), and some species have small narrow caudal alae. Mature females are didelphic with 2 ovaries and 2 uteri directed posteriorly but connected to a common anterior vulva. Members of the subgenus *T.* (*Thelazia*) have short conical tails (long in the subgenus *T.* (*Thelaziella*)), but neither possessed caudal alae.

Site of infection: Adult eye-worms occur in the orbits of birds and mammals, being found on the cornea, under the eyelids, conjunctiva, nictitating membrane, in the lachrymal glands and ducts, and occasionally in the vitreous cavity of the eyeball itself. Larval stages develop in the haemocoel and internal organs of dipteran intermediate hosts, before migrating to their mouthparts.

Pathogenesis: Many infections remain asymptomatic, even when eye-worms are observed in the eye, but heavy and chronic infections may cause ocular disease. It is thought that active young adult worms are most pathogenic, while older adult worms are better tolerated by hosts (effectively making some of them asymptomatic carriers). Eye-worms are secretophagous consuming ocular/lachrymal secretions and their movement causes local irritation and inflammation, initially stimulating excessive lachrymation followed by catarrhal and/or petechial conjunctivitis, then chronic follicular conjunctivitis, blepharitis, lachrymal duct inflammation with necrotic exudates and obstruction, and keratitis (potentially leading to corneal opacities and ulceration, and occasionally perforation and permanent fibrosis). Clinical signs may develop after a short 3-5 day incubation period with mild to

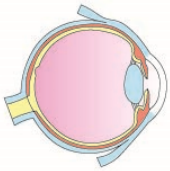
severe conjunctivitis with lymphoid hyperplasia and seromucoid exudates, congestion, localized oedema, epiphora with excessive lachrymation and ocular secretions, photophobia and periorbital pruritus. Clinical signs may progressively worsen over 1-2 weeks resulting in ophthalmia, even panophthalmia, purulent discharges, corneal ulcers and opacities, and sometimes subconjunctival cysts. Infected animals may become listless, distressed, anorexic and lose condition (weight loss, reduced milk production), but many infections resolve spontaneously in about 2 months, although some corneal opacities may remain. Eye-worm infections are also thought to predispose hosts to secondary infections, especially infectious keratoconjunctivitis (pink-eye) caused by *Moraxella* bacteria. Humans may also become infected as aberrant hosts, developing mild to severe symptoms (including lachrymation, epiphora, conjunctivitis, keratitis, and corneal ulcers).

Developmental cycle and mode of transmission: *Thelazia* spp. have indirect heteroxenous life-cycles involving the formation of adult worms in vertebrate definitive hosts (birds and mammals) and the development of larvae in invertebrate intermediate hosts (dipteran insects). Female worms produce thin-shelled eggs which hatch *in utero* discharging sheathed L1 into ocular secretions. The L1 are ingested by various dipteran species (face flies, vinegar flies, canyon flies) which do not bite or suck blood but are secretophagous and cluster around the eye to feed on ocular secretions. Ingested L1 exsheath in the gut and invade the haemocoel and internal organs (fat bodies, testes, ovarian follicles) where they moult twice to form L3 in thin-walled capsules over 15-30 days. Encapsulated L3 may survive over winter in the pupal stages of flies. When adult flies feed on final hosts, infective L3 migrate to the mouthparts and emerge from the labellum to be mechanically deposited in the eye. They develop through 2 moults to form adult worms in ocular tissues (mostly the conjunctival sac) and do not undertake any extra-ocular migration. The prepatent period (time from infection to first release of L1) ranges from 20-25 days in cattle and 21-42 days in horses, and adult worms may live longer than 1 year. The intensity of infection may increase with advancing host age, reaching maximum levels in 2-3 year old animals, due primarily to repeated exposure as the parasites appear to elicit little protective immunity. While infections may be detected throughout the year, clinical disease outbreaks are often seasonal and coincident with warm summers when flies are most abundant and active.

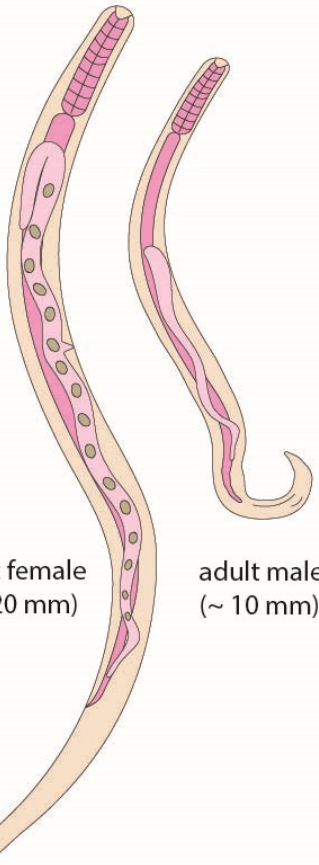
Differential diagnosis: The occurrence of conjunctivitis in livestock coincident with the fly season is generally indicative of infection, but other conditions need to be discounted (especially pink-eye). Physical examination of the eyes (using topical anaesthetics to allow manipulation of the third eyelid) may reveal worms in the conjunctival sac, but some species are more invasive and are less likely to be observed. Worms may even be found incidentally on periorbital skin or hair during surgery or upon necropsy. On occasion, larvae have been detected in lachrymal fluids on microscopic examination, but they need to be differentiated from *Onchocerca* microfilariae and *Draschia* or *Habronema* infective larvae. Molecular biological techniques have been used to examine parasite phylogenetic relationship by polymerase chain reaction (PCR) amplification and sequencing of nuclear (ribosomal RNA) and mitochondrial genes (cytochrome c oxidase subunit I), but they are not used for routine diagnosis.

Treatment and control: The location of the parasites in the superficial structures of the eye (an immunologically privileged location) makes treatment of eye-worms difficult. For many years, treatment was based on mechanical removal of worms under local anaesthesia, often combined with topical applications (eye washes, ointments) of antiseptics, antibiotics, steroidal anti-inflammatories and cicatrizants (healing promoters). Nowadays, modern anthelmintic drugs may be applied topically or systemically to treat infections in livestock and companion animals, including the macrocyclic lactones (ivermectin, doramectin, milbemycin, moxidectin, eprinomectin), imidazothiazoles (levamisole, tetramisole), isoquinolines (praziquantel) and some benzimidazoles (fenbendazole). The regular use of some anthelmintics (especially the macrocyclic lactones) may also help reduce fly populations as drug residues excreted in faeces appear to suppress the development of muscid flies in dung. Clinical infections often occur seasonally during warm months when flies are active, so various preventive strategies may be adopted to interrupt transmission between fly vectors and final hosts, either by reducing fly populations (restricting breeding areas, removing organic waste), protecting animals from face flies (indoor housing, eye shields/covers, chemical repellents/insecticides (impregnated ear-tags, pour-on formulations, spraying holding facilities), or stock/pasture management (animals on dry open pastures have fewer face flies than those on shaded moist pastures).

Thelazia

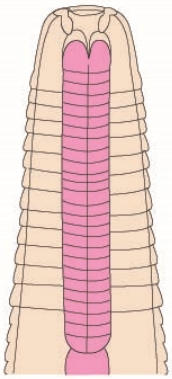


eye
(conjunctivitis,
keratitis,
corneal opacities)

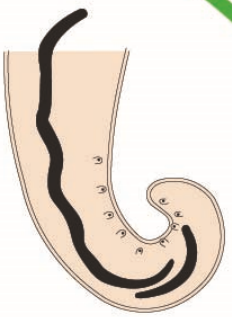


adult female
(~ 20 mm)

adult male
(~ 10 mm)



head



male tail
(lateral)

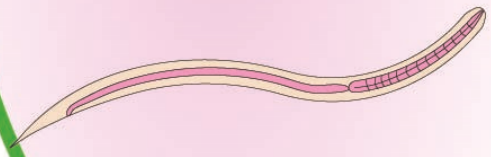
Definitive Hosts
(ungulates, birds)

L1
released

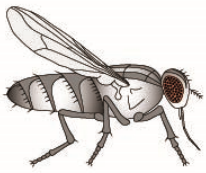
eggs hatch *in utero*
discharging L1 in ocular secretions

first-stage larvae
(L1) (~ 250 µm)
(indistinct sheath)

L3
deposited
in eye



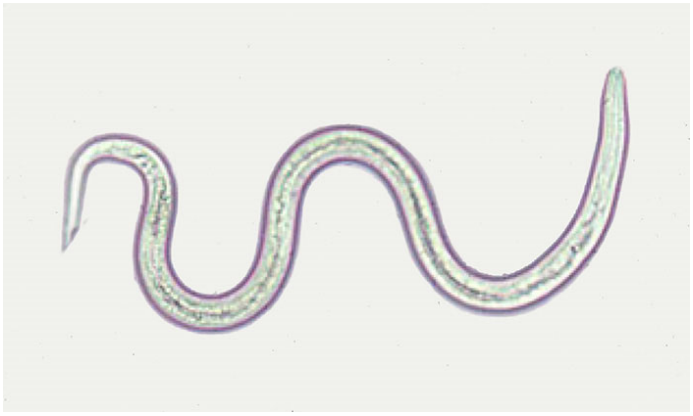
third-stage larvae
(L3) (~ 3 mm)



Intermediate Hosts (IH)
(muscid flies)
(haemocoel, viscera,
then mouthparts)

L1 ingested
by IH

Thelazia larvated egg



Thelazia larva

Thelazia adult worm in eye