Toxascaris
(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 Ascaridomorpha which includes ascaridoid nematodes (roundworms) characterised by their large size, three prominent anterior lips and the absence of a bursa. They occur in the small intestines of many animals (including humans) and most have simple direct life-cycles involving faecal-oral transmission. Female worms produce numerous eggs which are excreted with host faeces and undergo embryonation to contain infective larvae. When ingested, larvae hatch from the eggs and develop into adult worms in the gut. The larvae of ascaridoid species undergo hepato-pulmonary migration before forming adults, whereas those of heterakoid species do not. Two major ascaridoid families are recognised: ascarids in terrestrial mammals; and anisakids in marine mammals. Infections by *Toxascaris* spp. are unusual in that larvae may be taken up by paratenic (transport) hosts (usually rodents), and they do not undergo hepato-pulmonary migration in the definitive host. Infections in cats and dogs cause unthriftiness, and occasionally diarrhoea.

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:	Ascaridomorpha (large roundworms, mouth surrounded by three large lips, numerous caudal papillae)
Superfamily:	Ascaridoidea (ascarids, eggs thick-shelled, direct cycle but larvae undertake hepato-pulmonary migration)
Family:	Ascarididae (large pale roundworms, in terrestrial mammals)
Genus:	*Toxascaris* (parasitic in small intestines of dogs/foxes/cats)
Species:	*T. leonina* (causes illthrift in carnivores)

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.

The infraorder Ascaridomorpha is characterised by large roundworms with poorly developed buccal cavity with 3 large lips sometimes separated by interlabia, an undivided oesophagus, numerous caudal papillae, nonbursate males often with pre-anal suckers, and females with complex ovejectors. Five superfamilies (conventionally assigned to the order Ascaridida) are recognised as parasites in vertebrates: Ascaridoidea (cylindrical oesophagus often terminated by swelling without bulb, coelomyarian, eggs thick-shelled); Heterakoidea (oesophagus cylindrical or with claviform corpus, short isthmus and valved bulb, coelomyarian, pre-anal sucker, eggs thick-shelled); Seuratoidea (lips absent, oesophagus short, platymyarian, eggs with delicate shells or hatch *in utero*); Cosmocercoidea (oesophagus with cylindrical corpus, elongate isthmus and valved bulb, platymyarian, eggs with delicate shells or hatch *in utero*); and Subuluroidea (well-developed buccal capsule without lips, coelomyarian, pre-anal sucker, eggs thick-shelled). Adult worms of the superfamily Ascaridoidea inhabit the gastrointestinal tract of vertebrate hosts and generally consume food ingested by the host. They may have simple monoxenous life cycles involving faecal-oral transmission, or more complicated heteroxenous life-cycles involving larval development in vertebrate intermediate hosts and sometimes larval transport in invertebrate paratenic hosts. Female worms produce unembryonated eggs which are passed in host faeces into the external environment where they embryonate to first-stage larvae (L1) which grow and moult to infective L2 or L3. Aquatic species produce thin-shelled eggs which hatch in water releasing sheathed L2 that are taken up by suitable hosts, while terrestrial species produce thick-shelled eggs which hatch releasing L3 when ingested by suitable hosts. Ascaridoid larval stages then undertake unique journeys: most involving pulmonary or somatic migration in their definitive hosts before maturing in the gut, sometimes including vertical transmission (transplacental and/or transmammary); many migrating into the tissues of intermediate hosts, sometimes involving larval migrans or encapsulation in 'unsuitable' hosts; and a few undergoing precocious development in invertebrate hosts.

Five ascaridoid families are recognised: Ascarididae (lips often with toothed ridge, oesophagus with or without ventriculus, parasites of mammals, birds, reptiles, amphibians, fishes); Anisakidae (lips with tongue-like prolongations with cuticular thickenings, oesophagus with ventriculus with suture-like depressions, parasites of mammals, birds, reptiles and fishes); Crossophoridae (lips semicircular with toothed combs, fimbriated collar, long oesophagus without ventriculus, parasites of hyracoids); Heterocheilidae (lips with tongue-like prolongations with cuticular thickenings, cylindrical oesophagus without ventriculus, parasites of sirenians); and Acanthocheilidae (lips small with teeth or toothed ridges, oesophagus with ventriculus, parasites of elasmobranchs). The family Ascarididae contains 4 subfamilies: Ascaridinae (oesophagus simple, gubernaculum absent, lips hexagonal with anterior region offset from posterior, parasites of terrestrial mammals); Toxocarinae (oesophagus with globular ventriculus without appendices, gubernaculum absent, parasites of terrestrial or marine mammals or birds); Angusticaecinae (oesophagus simple, gubernaculum absent, lips quadrangular and not divided into anterior and posterior regions, parasites of reptiles and amphibians); and Multicaecinae (oesophagus with globular ventriculus usually with appendices, gubernaculum present, parasites of crocodilians or rarely fish). Ascaridid genera of medical and veterinary significance are compared in the following table.

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Eggs	Transmission
Ascaridinae						
Toxascaris	2	carnivores	small intestines	2-15 cm long, 3 lips, long thin cervical alae, oesophageal ventriculus absent, males lack terminal digitiform appendage, larvae do not undergo hepato-pulmonary migration	70-85 x 60-75 µm, ovoid, thick-shelled	faecal-oral (sometimes ingestion of infected PH)
Ascaris (roundworm)	2 (+ 150 *nomen dubium*)	primates, suids	small intestines	15-50 cm long, 3 small lips, striated cuticle, males with curved tail, simple spicules, females opisthodelphic, larvae undergo hepato-pulmonary migration	50-87 x 35-60 µm, ovoid, thick-shelled	faecal-oral
Parascaris	3	equids	small intestines	10-50 cm long, 3 large lips each with transverse groove, cuticle striated, males abursate, simple spicules, larvae undergo hepato-pulmonary migration	90-120 µm, spherical, thick-shelled	faecal-oral
Toxocarinae						
Toxocara	26	carnivores, ruminants, rodents	small intestines	3-30 cm long, 3 lips, long thin cervical alae, oesophageal ventriculus present, males with terminal digitiform appendage, larvae undergo somatic migration, hypobiosis	64-91 µm, spherical, thick-shelled	faecal-oral, ingestion of PH, transplacental, transmammary

The subfamily Ascaridinae contains 5 genera of large roundworms with well-defined lips and a simple oesophagus (ventriculus absent): namely, *Ascaris* (syn. *Fusaria*, *Lombricoides*, *Stomachida*), *Baylisascaris, Lagochilascaris*, *Parascaris* and *Toxascaris.* The genus *Toxascaris* contain the arrow-headed ascaridoids (cervical alae present) which form smooth-shelled eggs. The lips of adult worms are not deeply indented anteriorly, interlabia and lateral flanges are absent, and the cuticle has funnel-shaped bars reaching the surface in the alae region. Transmission cycles are usually direct (ingestion of eggs containing infective L2) but may sometimes be indirect (ingestion of encapsulated larvae in tissues of small paratenic hosts). The genus *Toxascaris* may be monotypic with a single species *T. leonina* being found as a relatively common cosmopolitan parasite in domestic and wild carnivores, notably felids and less frequently canids. Several species described in ursid and procyonid carnivores have recently been transferred to the genus *Baylisascaris* and the sole report of a species in a bird remains doubtful.

***Toxascaris* species**	**Definitive hosts**	**Location [Clinical signs]**	**Paratenic hosts**	**Distribution**
T. centropusi	Cuculiformes: cuculid (greater coucal)	intestines		India
T. leonina (syn. *T. limbata, marginata, Ascaris anterospiralis, canis, cati, crenata, microptera, teres*)	Carnivora: felid (cat, wild cat, rusty spotted cat, Pallas's cat, Kaffir cat, African wild cat, fishing cat, bobcat, Eurasian lynx, Canada lynx, Iberian lynx, cougar, leopard cat, leopard, snow leopard, clouded leopard, ocelot, serval, jaguar, puma, South American tiger cat, Brazilian chati, Bengal tiger, Siberian tiger, lion, Asiatic lion, cheetah), canid (dog, dingo, Cape hunting dog, wolf, Arctic wolf, coyote, golden jackal, culpeo, raccoon dog, red fox, American red fox, Iberian fox, grey fox, corsac fox, Indian fox, Arctic fox), ursid (American black bear), mephitid (Molina's hog-nosed skunk), viverrid (common genet), mustelid (wolverine); Primates: hominid (human)	small intestines [illthrift]	Rodentia: murid (mouse, rat), cricetid (Siberian brown lemming, tundra vole); Lagomorpha: leporid (rabbit); Diptera: muscid (house fly *Musca domestica*)	worldwide
T. melursus (now *Baylisascaris*)	Carnivora: ursid (sloth bear)			India
T. procyonis (now *Baylisascaris*)	Carnivora: procyonid (raccoon)			North America
T. transfuga (syn. *T. ailuri*, *multipapillata*, *selenarctis*) (now *Baylisascaris*)	Carnivora: ursid (American black bear, brown bear), ailurid (red panda)			North America, Eurasia

Parasite morphology: *Toxascaris* spp. form several different developmental stages: eggs which produce larvae that moult from first-stage (L1) to fourth-stage (L4) before developing into adult worms. Freshly laid eggs are subspherical measuring 70-85 x 60-75 µm, clear and translucent or pale brown in colour, surrounded by a smooth thick shell (rough in *Toxocara*), and are unembryonated containing a central morula. Embryonated eggs contain a coiled L1 which measured from 190-230 µm in length when dissected from eggs and had small cuticular projections around the mouth, lateral alae, and a tapering tail with a small terminal knob. L2 also develop within the egg and upon hatching they ranged in length from 200-600 µm, had rounded heads with conspicuous triangular structures around the mouth (modified lips), a tapering tail with a small terminal knob, and were ensheathed (retained L1 cuticle as protective covering). L3 measured 420-650 µm long and had small lips, a cuticular flange, and a knobbed tail, while L4 ranged in length from 560-1,420 µm and had mouths with distinct lips and sharp dorsally curved tails. Adults are large tan-pink cylindrical worms measuring from 2-15 cm long and they have 2 prominent cervical alae (making them members of the 'arrow-headed' ascaridoids). The alae are lanceolate in shape being long and narrow (those of *Toxocara* are often broader) and the surrounding cuticle has small annulations and funnel-shaped bars reaching to the surface. The worms have 3 lips surrounding the mouth, each with anterior denticulate margins but lacking interlabia and lateral flanges, an inconspicuous buccal capsule, a tubular oesophagus without a posterior bulb (present in *Toxocara*), and short tapering tails. Adult worms are sexually dimorphic, with female worms being larger than males (20-150 x 2 mm cf. 20-70 x 2 mm). Mature females are didelphic with 2 ovaries and uteri lying posteriorly behind the common vulva located in the anterior third of the body. Mature males have simple conical tails without terminal appendages (present in *Toxocara*) and they have 2 subequal curved wingless spicules measuring 0.7-1.5 mm in length.

Site of infection: Adult worms infect the small intestines of their carnivorous hosts, residing within the lumen. Earlier larval stages do not undertake somatic or hepato-pulmonary migration through host tissues, but may undergo a brief histotrophic phase of development in the intestinal wall (sometimes termed local migration). Infective larvae have been detected encysted within the muscles of small vertebrate prey animals which may act as paratenic hosts (carrying L2) or as intermediate hosts (in which L2 develop to L3).

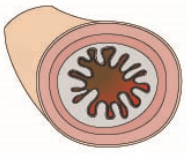
Pathogenesis: Most infections in cats and dogs remain asymptomatic even when moderate numbers of worms may be present. Developing larvae remain within the vicinity of the small intestines (no somatic or hepatic-pulmonary migration) and parasites do not feed on host tissues but absorb nutrients from the lumen. Nonetheless, heavy infections may cause local inflammation interfering with digestive processes with mucoid enteritis, malnutrition, mild diarrhoea, distended abdomens (pot-bellied appearance), dull coat, anorexia, malaise and unthriftiness. Large tangles of worms may sometimes cause intestinal obstruction leading to intussusception and even death. Aberrant migration of worms into the stomach may also cause irritation of the mucosa and vomiting. The pathogenesis of infections is frequently complicated by concomitant infections by *Toxocara* spp. but transplacental and transmammary transmission does not occur and the prolonged prepatent period of ~8 weeks in dogs and ~13 weeks in cats makes it unlikely to observe infections in animals < 2-3 months of age. Felids exhibit some age resistance with infections being more pronounced in kittens than in adult cats, but no age resistance is observed in canids and parasites may be found in puppies and adult dogs. Humans may occasionally become infected with larvae which wander throughout the body causing traumatic damage and inflammation (condition known as visceral larval migrans) but they are unable to complete their development.

Developmental cycle and mode of transmission: *Toxascaris* spp. are unusual in that their life-cycles may be direct (involving faecal-oral transmission) or indirect (involving predator-prey transmission), the infective stages are usually larvated eggs containing L2, and parasite development takes place exclusively within the small intestines. Gravid female worms lay unembryonated eggs in the intestines and they are excreted with host faeces into the external environment. The eggs embryonate over several days depending on environmental conditions (3-5 days at 25-30°C, 6-10 days at 17-22°C) producing L1 which moult within the eggshell to form ensheathed L2. The eggs are very resistant to harsh conditions and disinfectants and may survive for several years. Carnivorous definitive hosts become infected when they ingest larvated eggs with contaminated food or water (direct cycle), or by eating encysted larvae in the tissues of small prey animals (indirect cycle). Ingested eggs hatch in the duodenum releasing the infective L2 which moult to L3 and penetrate the mucosa undergoing local migration and histotrophic development to L4 before re-emerging into the lumen 9-14 days later (some larvae have also been observed to develop directly in the lumen). The L4 moult to subadult stages (often referred to as L5) which mature to sexually reproductive adults in the intestines. If larvated eggs are ingested by some small vertebrate animals (rodents, lagomorphs), they may hatch releasing L2 which penetrate the gut wall, migrate via the mesenteries to the musculature over 6-7 days, and then encyst over 9-29 days. Reports differ as to what larval stage becomes encysted: many consider them to still be L2 (which makes the animals paratenic (transport) hosts in which parasites do not further develop); while some consider them to have moulted to L3 (which makes the animals intermediate hosts as they support parasite development). The encysted larvae have been shown experimentally to survive for up to 5 months in mice. Once they are consumed by carnivorous final hosts, the encysted larvae resume development in the intestines eventually maturing to adult worms. The prepatent period (time from infection to first egg excretion) ranges from 42-74 days, and adult worms are thought to live for up to 1.5 years.

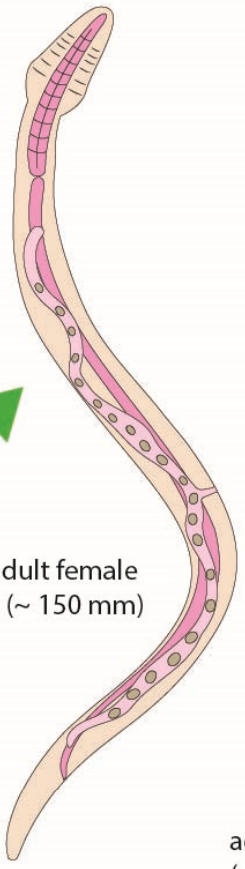
Differential diagnosis: Infections are not diagnosed on the basis of symptomatology as most are subclinical and even when clinical signs are present they are vague and nonspecific. Patent infections are conventionally diagnosed by the microscopic detection of characteristic worm eggs in faecal samples, usually following their concentration by sedimentation in water and floatation in saturated sugar or salt solutions. Large white adult worms may also be detected occasionally in vomitus or faecal samples. On necropsy, adult worms may be detected in the small intestinal lumen on dissection. The worms have a characteristic appearance with long narrow spear-like cervical alae (as opposed to the short wide arrowhead-like cervical alae of *Toxocara* spp.). Molecular biological techniques have been used to characterize parasite species by the polymerase chain reaction (PCR) amplification and sequencing of nuclear genes (ribosomal RNA) or mitochondrial genomes. Parasites were also detected by DNA analyses in puma coprolites dated back to the Pleistocene in South America.

Treatment and control: A wide range of anthelmintic drugs has proven effective in the treatment of infections in cats and dogs, particularly the benzimidazoles (oxibendazole, mebendazole, fenbendazole) and prebenzimidazoles (febantel), but also including macrocyclic lactones (selamectin, milbemycin, moxidectin, ivermectin), imidazothiazoles (levamisole), tetrahydropyrimidines (pyrantel), isoquinolines (praziquantel), depsipeptides (emodepside), isothiocyanates (nitroscanate) and diethylenediamines (piperazine). Treated animals may be promptly re-infected if returned to the same contaminated facilities. Veterinary authorities recommend regular treatment of kittens and puppies monthly until 6 months of age and then selectively as needed. A range of preventive measures may be used to reduce parasite transmission, mostly involving improved sanitation and hygiene (removing faeces, disinfecting pens/cages using steam or bleaches, avoiding grassy shaded runs, providing clean food and water) but also involving animal control (avoid over-crowding, quarantine and isolation, excluding rodents, preventing hunting/foraging).

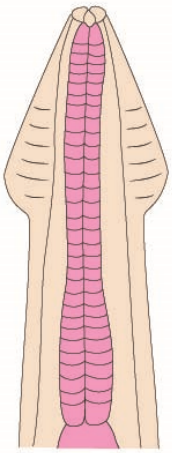
Toxascaris



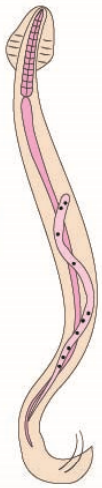
intestines
(illthrift,
ocassionally
diarrhoea)



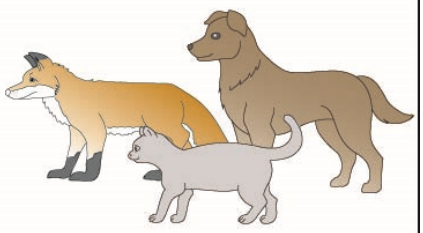
adult female
(~ 150 mm)



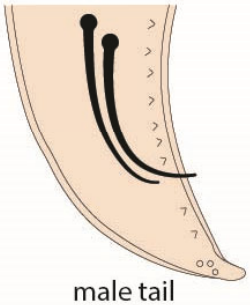
head



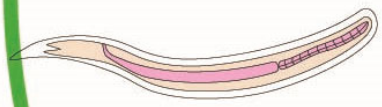
adult male
(~ 50 mm)



Definitive Hosts
(carnivores)



male tail
(lateral)



third-stage larvae (L3)
(~ 650 µm)

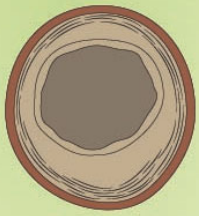
eggs,
L2/L3
ingested

some L2 carried in PH,
or develop to L3 in IH

external
environment

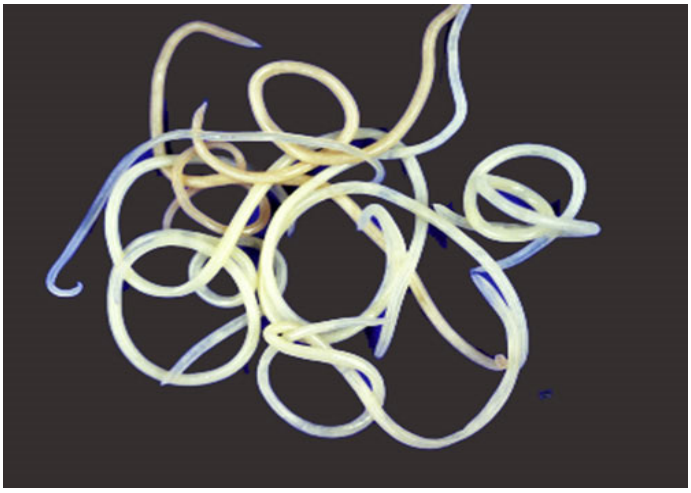
eggs
excreted
in faeces

L2 develop
within eggs



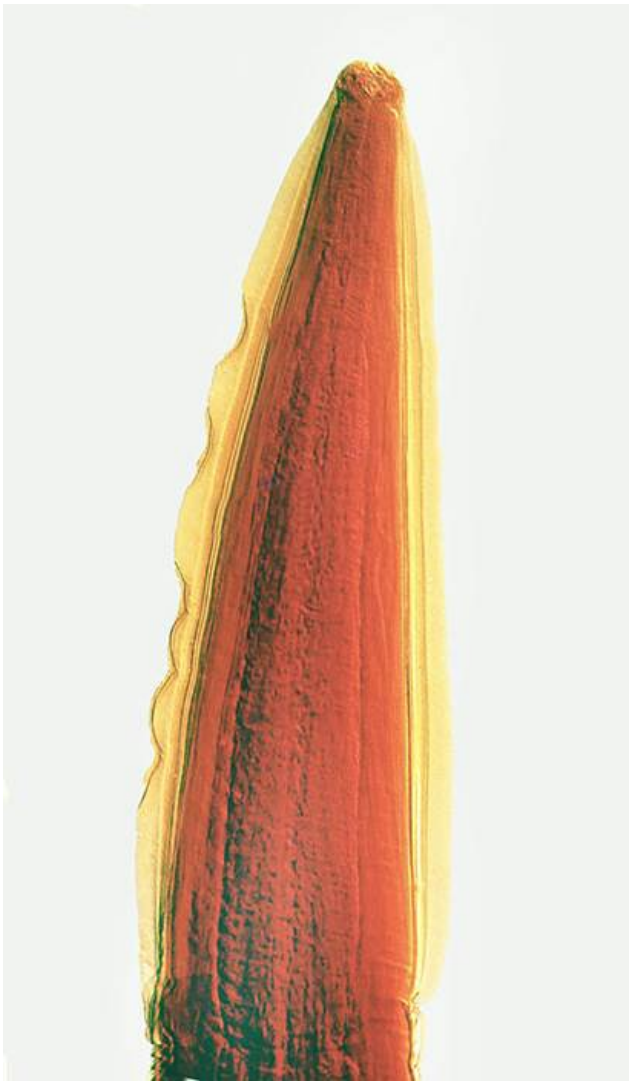
eggs
(~ 80 µm)

Paratenic/Intermediate Hosts
(PH/IH) (rodents)
(muscles)



Toxascaris adult worms

Toxascaris worm eggs



Toxascaris adult worm, head