Parelaphostrongylus
(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 spirurinids, tylenchinids and rhabditinids. The latter contains the infraorder Rhabditomorpha which includes strongyloid nematodes characterised by an expansion of the tail of the male known as the copulatory bursa (clasper with one dorsal and two lateral lobes with muscular rays). Many families are recognised: including lungworms with small buccal capsules and reduced male bursae. Adult worms are found mostly in the lungs of their hosts, although some inhabit the pulmonary artery, meninges or connective tissues. Five main groups occur: dictyocaulids in ruminants and horses; metastrongyles in pigs; protostrongyles in ruminants; angiostrongyles in carnivores and rodents; and filaroids in dogs. Protostrongyles have indirect life-cycles involving the development of L3 in invertebrate intermediate hosts. Adult *Parelaphostrongylus* in the meninges release eggs into the bloodstream where they travel to the lungs, break through to alveoli and are passed in faeces. L1 then penetrate the foot of a snail or slug and develop to L3. When eaten by ruminants, larvae migrate to the central nervous system and develop into adult worms. Infections by *Parelaphostrongylus tenuis* cause neurological signs in deer and moose in North America.

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:	Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)
Infraorder:	Rhabditomorpha (‘rod-shaped’ buccal cavity)
Superfamily:	Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Family:	Protostrongylidae (infection of ruminants by ingestion of earthworm/molluscan IH carrying L3)
Genus:	*Parelaphostrongylus* (parasitic in brain of cervids)
Species:	*P. tenuis* causes neurological signs in deer and moose

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 with 2 ovaries (some monodelphic or polydelphic), 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 superfamily Strongyloidea comprises a range of worms often with prominent buccal capsules and specialised oral structures well-suited to their feeding habits on host tissues and/or fluids. Adults of most species are parasitic in the gastrointestinal tracts of mammals and some birds, while larval stages feed on bacteria in the external environment, although some larvae may infect invertebrates as intermediate or paratenic hosts. The adult worms are sexually dimorphic, the smaller males characterised by an expansion of the tail (bursa) which is used as a copulatory clasping organ. Many classification schemes group these 'bursate' nematodes into one or more superfamilies in the order Strongylida (with suborders containing the strongyles, trichostrongyles, hookworms and lungworms), although the families essentially remain the same. Many families are recognised on the basis of parasite morphology, biology, life-cycle, host specificity and tissue tropism; including the following which contain many notorious parasites of vertebrates.

Representative Strongyloidea (cf. Strongylida) [with bursate males]				
Family	**Characters**	**Definitive Hosts**	**Transmission***	**No. genera**
Metastrongylina (lungworms)				
Protostrongylidae (lungworms)	small buccal capsule, bursa with large lobes, gubernaculum	artiodactyls	ingestion of IH carrying L3	17
Metastrongylidae (lungworms)	small buccal capsule, 2 trilobed lips, bursa with reduced dorsal lobe	Suids	ingestion of IH carrying L3	1
Angiostrongylidae (lungworms)	no or reduced buccal cavity, short club-shaped oesophagus	carnivores, rodents	ingestion of IH or PH carrying L3	28
Dictylocaulidae (lungworms)	small buccal capsule, bursa with large lobes, short stout spicules	ungulates, reptiles	ingestion of L3	5
Filaroididae (lungworms)	small buccal capsule, reduced male bursa, infective L1	carnivores	ingestion of L1	4
Trichostrongylina (trichostrongyles)				
Trichostrongylidae (trichostrongyles)	reduced buccal capsule, ridged synlophe, oesophagus lacking bulb, thin-shelled eggs	artiodactyls, birds	ingestion of L3	50
Molineidae (stomach/intestinal worms)	reduced buccal capsule, cephalic vesicle, female tail with spine or cusps, oviparous/viviparous	mammals, birds, reptiles	ingestion of L3	61
Heligmonellidae (hookworm-like)	body coiled, cephalic vesicle, ridged synlophe, bursa asymmetrical	mammals, birds	transdermal penetration of L3	56
Strongylina (strongyles)				
Strongylidae (strongyles)	large buccal capsule often armed with teeth, leaf crown around mouth	mammals, reptiles, birds	ingestion of L3	32
Chabertiidae (nodule worms)	large buccal capsules, leaf crown of labial collar, L3 sheathed	artiodactyls, primates	ingestion of L3	22
Syngamidae (gapeworm)	cup-shaped buccal capsule, armed with teeth, male attached to female	birds, mammals	ingestion of L3 or invertebrate PH	7
Stephanurinae (kidneyworm)	buccal capsule armed with teeth, leaf crowns and external epaulettes	Suids	transdermal penetration or ingestion of L3 or PH	1
Ancylostomatina (hookworms)				
Ancylostomatidae (hookworms)	large buccal capsule bent dorsally, armed with teeth/cutting plates	primates, carnivores, artiodactyls	transdermal penetration of L3 (sometimes *per os*)	20

*IH = intermediate host, PH = paratenic (transport) host, L1 = first-stage larva, L3 = third-stage larva

Lungworms are characterised mostly by their unique location within the respiratory systems of their mammalian hosts, although some species also infect cardiovascular, nervous or intermuscular connective tissues. Adult worms have a small buccal capsule, often reduced to an annulus, and sometimes possessing lips. Male worms have a caudal bursa that is variable in structure (often with reduced lobes and/or rays), spicules and a gubernaculum and telamon that are often not highly developed. Female worms have a median or posterior vulva, sometimes with a sphincter, and they are oviparous (releasing eggs) or ovoviviparous (releasing larvae). Many species have direct cycles involving the ingestion of infective larvae, while others have indirect cycles involving the ingestion of larvae in invertebrate intermediate hosts, and sometimes paratenic hosts. Eight metastrongyline families are recognised: Metastrongylidae (mouth with 2 large lateral trilobed lips, bursa with large lateral lobes and reduced dorsal lobe, oviparous, indirect cycle, earthworms used as intermediate hosts, 1 genus in lungs of suids); Angiostrongylidae (mouth with or without lips, bursa well-developed, oviparous, ovoviviparous, indirect cycle, gastropods used as intermediate hosts, 28 genera in respiratory and vascular systems of marsupials, rodents, insectivores, lemurs, mustelids, viverrids, felids and canids); Dictyocaulidae (mouth small, bursa with large lateral lobes and large dorsal lobe (divided to base), ovoviviparous, direct cycle, 2 genera in airways of ruminants and horses); Filaroididae (mouth small, bursa absent or reduced (rays reduced to papillae), ovoviviparous, direct cycle, 4 genera in respiratory system of canids, mustelids, pinnipeds, primates, and marsupials); Protostrongylidae (mouth small, bursa with large lateral lobes and prominent dorsal lobe, highly developed gubernaculum and telamon, oviparous, indirect cycle, molluscs used as intermediate hosts, 17 genera in lungs of ruminants, felids, canids, leporids, and skeletal muscles and central nervous system of cervids); Pseudaliidae (mouth small, bursa reduced (rays fused but not reduced to papillae), ovoviviparous, direct cycle, 7 genera in respiratory, auditory, circulatory systems of delphinids, phocoenids, monodontids and mongoose); Skrjabingylidae (mouth small, bursa modified to form lateral fleshy lobes, ovoviviparous, direct cycle, 1 genus in nasal cavities of mustelids); and Crenosomatidae (mouth small, bursa with large lateral lobes and large dorsal lobe (not divided to base), ovoviviparous, direct cycle, 5 genera in respiratory system of canids, felids, pinnipeds, soricids and marsupials). Several protostrongylid genera of significance to livestock production are compared below:

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm larvae
Protostrongylidae					
Parelaphostrongylus (meningeal worm, brain worm)	3	artiodactyls	brain, lung	17-90 mm long, small buccal capsule, indirect cycle, eggs laid in meninges travel via blood to lungs, swallowed, L1 voided, L3 develop in snail IH	300-380 µm, dorsal spine
Elaphostrongylus (brain worm)	3	artiodactyls	muscles, brain, lung	26-70 mm long, small buccal capsule, indirect cycle, eggs laid in tissues travel to lungs via blood, swallowed, L1 voided, L3 develop in snail IH	288-490 µm, dorsal spine
Protostrongylus (lungworm)	27	artiodactyls, lagomorphs	respiratory tract	13-80 mm long, small buccal capsule, 6 lip-like elevations, indirect cycle, eggs laid in lungs swallowed, voided, L3 develop in snail IH	250-400 µm, fine striations
Muellerius (lungworm)	4	artiodactyls	respiratory tract	10-30 mm long, small buccal capsule, indirect cycle, eggs laid in lungs, swallowed, voided, L3 develop in snail IH	230-340 µm, dorsal spine, tail kink

The family Protostrongylidae contains 17 genera: *Cystocaulus, Dukerostrongylus, Elaphostrongylus* (syn. *Protostrongyloides*), *Imparispiculus, Mariostrongylus, Muellerius, Neostrongylus, Orthostrongylus, Paraelaphostrongylus* (syn. *Odocoileostrongylus, Neurofilaria*), *Pneumocaulus, Pneumostrongylus, Protostrongylus* (syn. *Gelanocaulus, Synthetocaulus*), *Pulmostrongylus, Skrjabinocaulus, Spiculocaulus, Umingmakstrongylus,* and *Varestrongylus.* Early works placed some of these genera into separate subfamilies (Elaphostrongylinae, Muelleriinae, Neostrongylinae, Protostrongylinae, Skrjabincaulinae, and Varestrongylinae) but recent molecular studies failed to support them, even indicating that several clustering together may be monophyletic. Clearly, further work needs to be conducted to differentiate protostrongylid species, genera and subfamilies. The genus *Parelaphostrongylus* comprises worms whose males have well-developed mound-like dorsal rays with 2-4 branches, a gubernaculum with a wedge-shaped corpus, a well-defined crura but no capitulum, short stout spicules, and L1 with a dorsal spine on the tail. Three species have been found as tissue parasites in the muscles and central nervous system of a range of cervids, notably in North America.

***Parelaphostrongylus* species**	**Definitive hosts**	**Location [Clinical signs]**	**Intermediate hosts**	**Distribution**
P. andersoni (muscle worm)	Artiodactyla: cervid (white-tailed deer, Greenland reindeer, boreal woodland caribou, barren ground caribou, moose, mule deer, fallow deer)	intermuscular blood vessels and connective tissues	Gastropoda: polygyrid (*Mesodon thyroidus*, *Triodopsis albolabris*, *multilineata*), agriolimacid (*Deroceras laeve*)	North America
P. odocoilei (syn *Elaphostrongylus*) (mule deer muscle worm)	Artiodactyla: cervid (mule deer, Columbian black-tailed deer, woodland caribou, moose, western moose), bovid (mountain goat, Dall sheep); Rodentia: caviid (guinea pig)	intermuscular blood vessels and connective tissues	Gastropoda: agriolimacid (*Agriolimax*, *Deroceras laeve*, *reticulatum*), discid (*Discus cronkhitei*, *shimeki*), euconulid (*Euconulus fulvus*), gastrodontid (*Zonitoides arboreus*, *nitidus*), helicid (*Helix aspersa*), monadeniid (*Epigramorpha* (*Monadenia*?) *arrosa*), polygyrid (*Trodopsis multilineata*), vitrinid (*Vitrina limpida*)	North America
P. tenuis (syn. *Odocoileostrongylus, Elaphostrongylus, Neurofilaria cornellensis*) (meningeal worm, brainworm)	Artiodactyla: cervid (white-tailed deer, northern white-tailed deer, Dakota white-tailed deer, Columbian black-tailed deer, mule deer, red deer, fallow deer, reindeer, boreal woodland caribou, wapiti, elk, moose), bovid (cattle, sheep, bighorn sheep, goat, common eland, sable	venous sinuses of cranial meninges [neurological signs] [moose sickness]	Gastropoda: agriolimacid (*Deroceras laeve*, *reticulatum*), arionid (*Arion circumscriptus*), cochliocopid (*Cochlicopa lubrica*), discid (*Anguispera alternata*, *Discus cronkhitei*, *patulus*), gastrodontid (*Striatura exigua*), haplotrematid (*Haplotrema concavum*), helicid (*Helicina*	Americas, Africa

	antelope, bongo antelope, scimitar-horned oryx, blackbuck), antilocaprid (pronghorn), camelid (llama, guanaco, alpaca, camel); Carnivora: mephitid (striped skunk); Lagomorpha: leporid (European rabbit); Rodentia: murid (brown rat), caviid (guinea pig)		*orbicula*, *orbiculata*), philomycid (*Pallifera dorsalis*, *Phylomycus carolinianus*), polygyrid (*Mesodon inflectus*, *sayanus, thyroidus*, *Polygyra dorenilliana*, *jacksoni*, *Stenotrema fraternum*, *strenotrema*, *Triodopsis albolabris*, *divesta*, *multilineata*, *notata, tridentata*), succineid (*Succinea ovalis*), strobilopsid (*Strobilops labyrithica*), zonitid (*Mesomphix cupreus*, *Ventridens collisella, intertextus*, *Zonitoides arboreus*, *nitidus*)	

Parasite morphology: *Parelaphostrongylus* spp. form 3 different morphological stages during their developmental cycles: eggs; larvae (4 consecutive stages encoded L1-L4); and adult worms. Female worms produce small delicate eggs which are laid in the blood to be carried to the lungs where they appear as round-ovoid stages 40-80 µm in diameter with a central unsegmented embryonic mass clearly separated from the thin surrounding eggshell. L1 are tubular elongate stages measuring 300-380 x 16-36 µm with conical heads, lateral alae, a flask-shaped oesophagus, and curled tails (30-40 µm long) with a subterminal kink and a distinctive triangular dorsal spine (characteristic of non-protostrongyline L1). L2 are similar in morphology but are slightly longer and have non-spined pointed tails. L3 are larger still, measuring from 624-1,323 x 33-52 µm depending on species, (*P. odocoilei* 624-977 µm; *P. andersoni* 911-1,200 µm; *P. tenuis* 900-1,323 µm), and have bullet-shaped heads, rounded lateral thickenings, and short rounded tails usually with a small dorsal swelling. L4 are transient parasitic stages that are beginning to show adult worm characteristics, especially with respect to head structures and developing genitalia (male bursa and female vulva). Adults are slender white worms (17-90 mm long) with thin cuticles bearing fine longitudinal striations, circular anterior mouths bounded by a cuticular ring and 6 inconspicuous perityls (non-movable lips, absent in *Elaphostrongylus*), small conical buccal capsules, a broad muscular club-shaped oesophagus, excretory glands opening subapically, and greenish-yellow to brown-black intestines extending to a subterminal anus (cloaca in males). Adult worms are sexually dimorphic, with females being larger than males (*P. odocoilei* females 40-56 mm, males 20-35 mm; *P. andersoni* females 23-36 mm, males 17-23 mm; *P. tenuis* females 60-90 mm, males 40-60 mm). Mature males have a well-developed copulatory bursa with 2 lateral lobes (each supported by 6 stout rays (2 ventrals partially united, 3 laterals partially united, separate externodorsal ray) and a prominent dorsal lobe (supported by a mound-like dorsal ray with 2-4 branches). Males also have a highly developed gubernaculum with a wedge-shaped bifurcate corpus and a well-defined crura (but no capitulum) and 2 short stout spicules (100-130 µm long) with alae. Mature females are didelphic with 2 ovaries and uteri connected to an ovejector and a common posterior vulva.

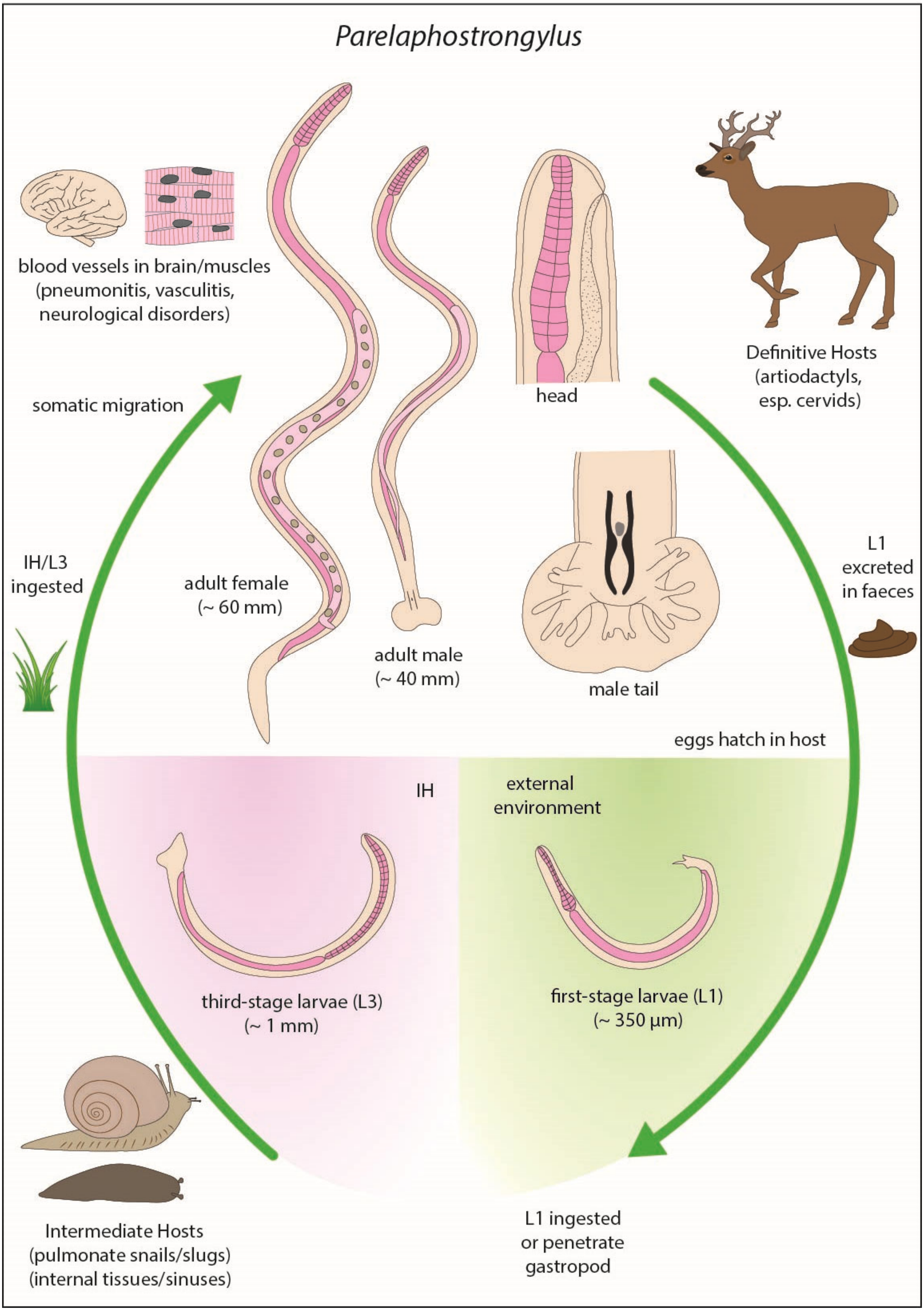
Site of infection: Adult worms infect blood vessels in the brains or muscles of their vertebrate hosts (mostly artiodactyls, especially cervids). *Parelaphostrongylus* spp. differ in their predilection sites: *P. tenuis* infecting veins and venous sinuses in the cranial meninges; *P. odocoilei* infecting veins in connective tissues between muscle bundles; and *P. andersoni* infecting blood vessels and connective tissues deep in the loin and thigh muscles. Infective larvae of each species develop in the tissues and sinuses of invertebrate intermediate hosts (gastropods).

Pathogenesis: Most infections by *Parelaphostrongylus* spp. are relatively nonpathogenic in their normal host species, but when parasites infect aberrant (abnormal) host species they may cause severe neurological diseases. For example, infections by the meningeal worm *P. tenuis* have little effect in most domestic livestock (bovids appear to have innate resistance) and white-tailed deer (which rapidly acquire protective immunity and usually support light infections). However, infections in other cervid species (moose, wapiti (elk), caribou, reindeer, mule deer, black-tailed deer) may lead to debilitating cerebrospinal disease when parasites invade neurological tissues as well as the meninges. Adult worms are frequently associated with space-occupying lesions near cranial nerves causing tissue compression, perineuritis, myelin sheath degeneration, and disruption of axis cylinders. Worms also become embedded in the dura mater over the brain and spinal cord causing minute haemorrhages, perivasculitis with cuffing and infiltrates by lymphocytes, plasma cells and eosinophils, yellowish exudates and meningoencephalitis within weeks of infection. Clinical signs are highly variable in onset, duration and nature involving motor and sensory deficits and numerous behavioural changes, including rapid eye movements (nystagmus), reduced vision (sometimes blindness), torticollis (head tilting), circling, general or hindlimb ataxia (incoordination) with weakness, stiffness, lameness, swaying, difficulty standing, recumbency, paresis (muscle weakening), paraparesis (partial paralysis), paraplegia (paralysis), fearlessness, depression, unthriftiness, anorexia and weight loss. Neurological disease is generally progressive and often fatal, although there may be short periods of remission when animal appear normal. Infections may also cause respiratory signs when worm eggs released in host blood vessels disseminate and accumulate in the lungs where they release larval stages that migrate through tissues causing petechial haemorrhages, fibrosis, atelectasis (alveolar collapse), congestion and pneumonia. Infections by *P. andersoni* and *P. odocoilei* appear to be less pathogenic but have been associated with transient verminous pneumonia, bronchiolitis, bronchitis and vasculitis (esp. arteritis) in the lungs. Adult worms of both species develop in the skeletal muscles and experimental infections in cervids have resulted in disturbances in posture and gait with weakness and recumbency due to petechial haemorrhages and focal necrosis, often with few cellular responses but sometimes with granuloma formation around parasites and their subsequent calcification.

Developmental cycle and mode of transmission: These parasites have indirect heteroxenous life-cycles, involving the development of infective larvae in invertebrate intermediate hosts (gastropods) which are then consumed by vertebrate definitive hosts (usually ruminants). The life-cycles are also unusual in that adult worms live in the host vasculature (rather than the gastrointestinal tract) and produce eggs which are carried to the lungs where they lodge in alveolar capillaries to develop and hatch releasing L1. Adult worms of *P. tenuis* living in subdural spaces may also deposit eggs on the dura mater where they develop and hatch releasing L1 which penetrate small blood vessels and are carried to the lungs. Migrating L1 penetrate into alveolar airspaces and ascend the mucociliary escalator to the trachea to be swallowed and excreted with host faeces. These larvae are often found in the mucus coating faecal pellets and they may survive for several months in cold moist conditions (including subzero temperatures beneath snow, but not repeated freezing and thawing). A range of terrestrial pulmonate gastropods (agriolimacid, arionid and philomycid slugs, and cochliocopid, discid, gastrodontid, haplotrematid, helicid, polygyrid, succineid, strobilopsid and zonitid snails) then act as obligate intermediate hosts. They become infected either when L1 actively penetrate the foot or when L1 in mucus are ingested during feeding. The larvae moult in internal tissues to L2 and then to L3 in 3-4 weeks (longer at lower temperatures), but their development may be arrested in aestivating snails. Most infected gastropods have been found to contain only a few infective L3 (mean 2-6) which may remain viable for the life of the host. Definitive hosts become infected when they consume infected gastropods on vegetation. L3 released in the gastrointestinal tract penetrate the gut wall into the peritoneal cavity. The larvae of each *Parelaphostrongylus* spp. then migrate to their different predilection sites to moult twice and mature into adult worms. Those of *P. andersoni* and *P. odocoilei* penetrate the musculature and move to veins in the intermuscular connective tissues, while those of *P. tenuis* migrate directly to the central nervous system following lateral spinal nerves (mostly lumbar) to the spinal cord (dorsal horns of grey matter) before moving anteriorly in subdural spaces to reach cranial venous sinuses. The prepatent periods (time from infection to first excretion of L1) varies from 49-75 days for *P. andersoni*, 45-62 days for *P. odocoilei*, and 82-137 days for *P. tenuis.*

Differential diagnosis: While neurological signs may be suggestive of clinical *Parelaphostrongylus* infections, they are often nonspecific (variable and/or vague) and could be caused by other infectious organisms or toxicological disturbances. Evaluation of various haematological and biochemical parameters proved unfruitful, although an eosinophilic pleocytosis was often detected in cerebrospinal fluid. Most infections are diagnosed during patency when L1 may be detected in faecal samples, usually following their recovery by submerging faecal packets in water (Baermann filtration has been found to be unreliable). Regrettably, the dorsal-spined larvae cannot readily be differentiated from those of other protostrongylids (including *Elaphostrongylus* and *Muellerius*). Infections can be diagnosed at post-mortem by the detection of adult worms in smears or sections of host neural tissues or the detection of worm eggs/larvae in washings (particularly of cranial meninges). Several attempts at xeno-diagnosis have been made whereby laboratory snails have been infected with L1 from faeces and then examined later for L3 which assume a characteristic C- or J-shape when heat-relaxed, but larval dimensions within and between genera vary considerably. Several immunological techniques have been developed to detect specific host antibodies in serum or cerebrospinal fluid by enzyme immunoassays or to detect specific parasite antigens by immunoblot analyses, but the tests demonstrated some cross-reactivity with other nematodes. More recently, modern molecular biological techniques have been used to characterize larvae and adult worms by polymerase chain reaction (PCR) amplification of nuclear gene sequences (especially internal transcribed spacer region 2 of ribosomal RNA).

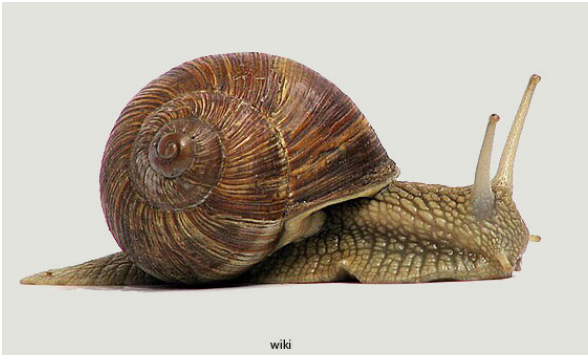
Treatment and control: Clinical infections in domestic livestock or managed free-range herds have been treated with various anthelmintic drugs, including benzimidazoles (albendazole, fenbendazole), imidazothiazoles (levamisole), diethylenediamines (diethylcarbamazine) and macrocyclic lactones (ivermectin), but with variable efficacy. Most treatments reduced larval excretion, bit it often resumed later without repeated treatment. Parasites appear to be difficult to treat due to their slow development (long prepatent and patent periods), their highly migratory nature within host tissues, their development behind the blood-brain barrier, their encapsulation by host responses, and their swift re-infection on contaminated pastures. Animals may also require supportive treatment with steroids and anti-inflammatory agents to prevent adverse reactions to numerous dying or dead parasites. A range of interventions have also been utilized in attempts to prevent or reduce infections in intensive and extensive farming situations, and even in feral and wild populations as appropriate. Most efforts have involved reducing faecal contamination (through improved sanitation), limiting gastropod populations (by applying molluscicides, building gravel or paved barriers, draining wet pastures), controlling stock (isolation and quarantine of new animals, separate cohorts, exclude wild animals through better fencing or culling by hunting) or pasture management (rotational grazing, cultivating and/or spelling pastures).


Parelaphostrongylus
blood vessels in brain/muscles
(pneumonitis, vasculitis,
neurological disorders)
somatic migration
head
Definitive Hosts
(artiodactyls,
esp. cervids)
IH/L3
ingested
adult female
(~ 60 mm)
adult male
(~ 40 mm)
male tail
L1
excreted
in faeces
eggs hatch in host
IH
external
environment
third-stage larvae (L3)
(~ 1 mm)
first-stage larvae (L1)
(~ 350 μm)
Intermediate Hosts
(pulmonate snails/slugs)
(internal tissues/sinuses)
L1 ingested
or penetrate
gastropod

Parelaphostrongylus adult worms

Parelaphostrongylus larva

Parelaphostrongylus vector, agriolimacid slug



Parelaphostrongylus vector, helicid snail