

Elaphostrongylus

(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 spirurids, 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 *Elaphostrongylus* in intermuscular connective tissues or brain meninges produce eggs and larvae which travel to the lungs in the bloodstream, 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 connective/nervous tissues and develop into adult worms. Infections by *Elaphostrongylus cervi* cause acute neurological signs and illthrift in deer in Europe.

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, Phasmeida) (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: *Elaphostrongylus* (parasitic in muscles of cervids)
Species: various species cause neurological signs in cervids

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)]
<i>Incertae sedis</i> 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 clasp 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
Dictyocaulidae (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 <i>per os</i>)	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); Skrjabinogylidae (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					
<i>Elaphostrongylus</i> (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
<i>Parelaphostrongylus</i> (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
<i>Protostrongylus</i> (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
<i>Muellerius</i> (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*, *Neoststrongylus*, *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, Neoststrongylinae, 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 *Elaphostrongylus* comprises worms whose males have a bursa not divided into lobes by a terminal cleft and a mound-like dorsal ray with 2-3 branches, a gubernaculum with a boat-shaped corpus but no crura or capitulum, short stout spicules, and L1 with a dorsal spine on the tail. Three species have been described in the muscles and central nervous systems of cervids, mainly from Europe.

<i>Elaphostrongylus</i> species	Definitive hosts	Location [Clinical signs]	Intermediate hosts	Distribution
<i>E. alces</i> (syn. <i>Varestrongylus</i>) (brain worm)	Artiodactyla: cervid (moose, reindeer), bovid (sheep, goat); Rodentia: caviid (guinea pig)	lungs, central nervous system, intermuscular connective tissue [neurological disease]	Gastropoda: arionid (<i>Arion subfuscus</i>), helioid (<i>Arianta arbustorum</i>), gastrodontid (<i>Zonitoides nitidus</i>), succineid (<i>Succinea</i>), vitrinid (<i>Vitrina pellucida</i>); agriolimacid (<i>Deroceras agreste, reticulatum</i>), limacid (<i>Limax cinereoniger</i>)	Europe
<i>E. cervi</i> (<i>Protostrongyloides</i> , <i>E. panticola</i>) (tissue worm)	Artiodactyla: cervid (reindeer, Greenland reindeer, boreal woodland caribou, elk, red deer, Central European red deer, Norwegian red deer, Iberian red deer, Siberian red deer (maral), wapiti, sika deer, roe deer, fallow deer, mule deer, moose), bovid (sheep, goat); Rodentia: cricetid (golden hamster), caviid (guinea pig); Anura: ranid (edible frog)	lungs, central nervous system, intermuscular connective tissue [verminous pneumonia, acute neurological disease, chronic illthrift]	Gastropoda: agriolimacid (<i>Deroceras reticulatum</i>), bradybaenid (<i>Bradybaena fruticum</i>), helioid (<i>Arianta arbustorum</i> , <i>Cepaea hortensis, vindobonensis, Helix pomatia</i>), hygromioid (<i>Euomphalia strigella</i> , <i>Perforatella bidentata</i> , <i>Zenobiella nordenskioldi</i>), lymnaeid (<i>Lymnaea stagnalis, Radix ovata</i>), polygyrid (<i>Triodopsis multilinata</i>), succineid (<i>Succinea altaica, putris</i>)	Eurasia, New Zealand

<i>E. rangiferi</i> (syn. <i>E. cervi rangiferi</i>) (brain worm, meningeal worm)	Artiodactyla: cervid (reindeer, Greenland reindeer, boreal woodland caribou, moose, fallow deer), bovid (sheep, goat, muskox, cattle)	lungs, central nervous system, intermuscular connective tissue [verminous pneumonia, staggers, ataxia, stiff-neck]	Gastropoda: agriolimacid (<i>Deroceras laeve</i>), arionid (<i>Arion subfuscus</i>), euconulid (<i>Euconulus fulvus</i>), helioid (<i>Arianta arbustorum</i>), lymnaeid (<i>Lymnaea stagnalis</i> , <i>Galba trunculata</i>), succineid (<i>Oxyloma pfeifferi</i>)	Eurasia, North America
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Parasite morphology: *Elaphostrongylus* spp. form 3 distinct morphological stages during their development: eggs; larvae (4 consecutive stages designated L1-L4); and adult worms. Female worms lay eggs in blood vessels to be carried to the lungs where they embryonate and hatch. Eggs initially appear as indistinct round stages 40-50 µm in diameter, but develop to become ovoid measuring 55-67 x 46-63 µm with a central unsegmented morula clearly separated from the surrounding delicate smooth eggshell. L1 are elongate stages, measuring 288-490 x 15-24 µm depending on species, and they have conical heads, lateral alae, flask-shaped oesophagi, and curved tapering pointed tails (26-53 µm long) with a subterminal kink and a triangular cuticular dorsal spine (dorsal-spined L1 characteristic for non-protostongyline). L2 are similar in morphology to L1, but are larger and have non-spined tails. L3 vary in size according to species (*E. alces* 675-756 x 34-43 µm; *E. rangifer* 937-1,041 x 42-49 µm; *E. cervi* 687-1,291 x 33-73 µm) and have rounded heads, flask-shaped oesophagi, and rounded tails (33-80 µm long). L4 are temporary parasitic developmental stages that have begun to show adult worm morphological characteristics, particularly in developing genitalia (male bursa and female vulva). Adults are thin slender yellow-brown worms measuring 26-70 mm in length and having round anterior mouths without lips but with 6 peribuccal ridges bearing labial papillae and amphids (perityls or non-movable lips are present in *Parelaphostrongylus*). Adults have thin cuticles with longitudinal ridges (synlophe), excretory glands opening subapically and small short buccal capsules leading to a thick stout muscular oesophagus (bottle-shaped in *E. alces*, club-shaped in *E. rangiferi*, and cylindrical in *E. cervi*). Adult worms are sexually dimorphic, with males being shorter than females (*E. rangiferi* males 26-39 x 0.19-0.25 mm, females 33-55 x 0.20-0.28 mm; *E. cervi* males 29-45 x 0.15-0.28 mm, females 49-62 x 0.20-0.24 mm; *E. alces* males 29-47 x 0.15-0.24 mm, females 60-70 x 0.29-0.32 mm). Mature males have a well-developed copulatory bursa that is not divided into distinct lobes but appears circular (*E. rangiferi* 140-160 µm, *E. cervi* 180-190 µm) or oval (*E. alces* 180-215 x 130-150 µm). The supporting ventral and lateral rays are short and blunt, the externodorsal rays are isolated, and the dorsal ray is mound-like with 2-3 branches. Males also have a highly developed gubernaculum with a boat-shaped corpus measuring 47-110 µm (but without a crura or capitulum), a genital cone with a prominent medial region, and 2 short stout spicules (200-235 µm) with alae. Mature females are didelphic with 2 ovaries and uteri connected to an ovejector (with a strong sphincter split anteriorly) opening into a common vulva on the short rounded tail.

Site of infection: Adult worms infect the intermuscular connective tissues, either beneath the epimysium or in the fasciae between muscle bundles, of their vertebrate hosts (mainly cervids). *Elaphostrongylus* spp. exhibit variable site specificity: with *E. cervi* locating preferentially in the shoulders, chest, back and fore-limbs; *E. rangiferi* in the shoulders, chest, belly and hind-limbs; and *E. alces* in the thorax and thighs. Some worms may also infect the central nervous system and spinal cord (subdural and subarachnoid spaces and occasionally ventricles). Infective larvae of each species develop in the internal tissues of their invertebrate intermediate hosts (gastropods).

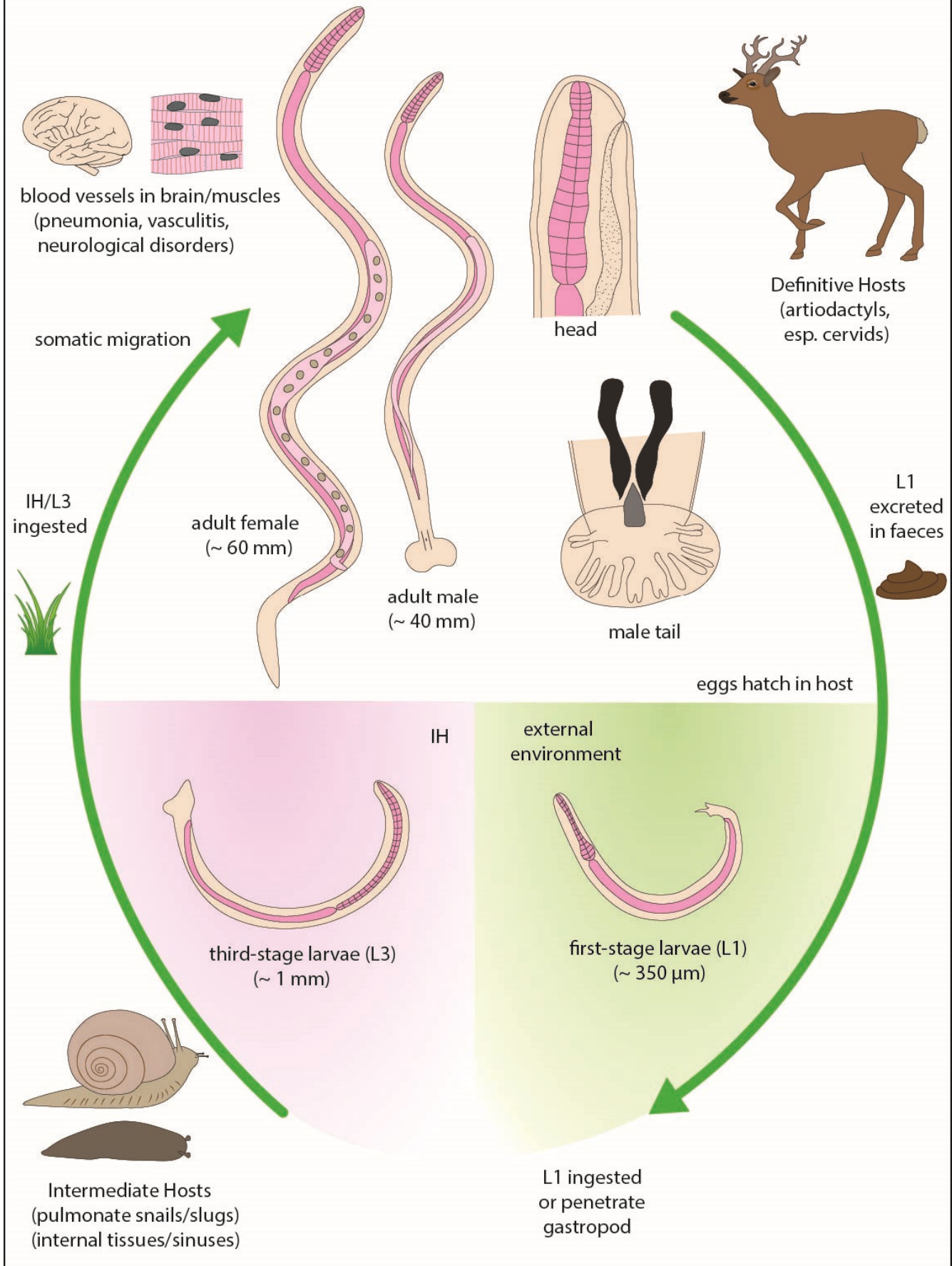
Pathogenesis: The clinical consequences of infection by individual *Elaphostrongylus* spp. varies greatly depending on the host species. Most infections are asymptomatic and subclinical in their normal permissive hosts, but infections in aberrant (abnormal) hosts may cause clinical disease, including periodic epizootics of neurological disorders in semi-domesticated and wild cervids, usually following unusually warm summers. Disease may be caused during the prepatent period when developing larvae (L3, L4) and young adults (L5) are migrating through host tissues, or during the patent period when mature adults produce eggs which are deposited in tissues releasing L1 to migrate through the lungs. Infections have been associated with both subacute respiratory diseases and debilitating neurological diseases, predominantly in young animals (< 1 year old). The former is more common and manifests as verminous interstitial pneumonia due to petechial haemorrhages, cellular infiltrates, alveolar fibrosis, focal emphysema, and eosinophilic granulomas with giant cells surrounding eggs/larvae. Clinical signs include dyspnoea (sometimes coughing), restlessness, weakness and poor condition. Yearlings may sometimes die of inanition (exhaustion caused by lack of nourishment) in winter and early spring. Neurological disease is sporadic in occurrence and severity, ranging from mild oedema and yellowish discolouration of the leptomeninges to firm adhesions between the dura and pia mater scattered over the brain, cellular infiltrates (lymphocytes, plasma cells, eosinophils), scattered axon demyelination, and small haemorrhagic foci in the muscles with green caseous plaques along fascial sheets and chronic granulomatous nodules encapsulating degenerating worms. Clinical signs include sensory and motor deficits and a range of behavioural changes, such as reduced vision (sometimes blindness), head tilting, ataxia, circling, weakness, unsteady gait, lameness, hindlimb incoordination and paralysis, recumbency, mental confusion, fearlessness, somnolence, poor growth, unthriftiness, emaciation, and death. The presence of parasites and inflammatory infiltrates in the host musculature may also produce unsightly discoloured lesions that require trimming, down-grading or condemning carcasses at meat inspection.

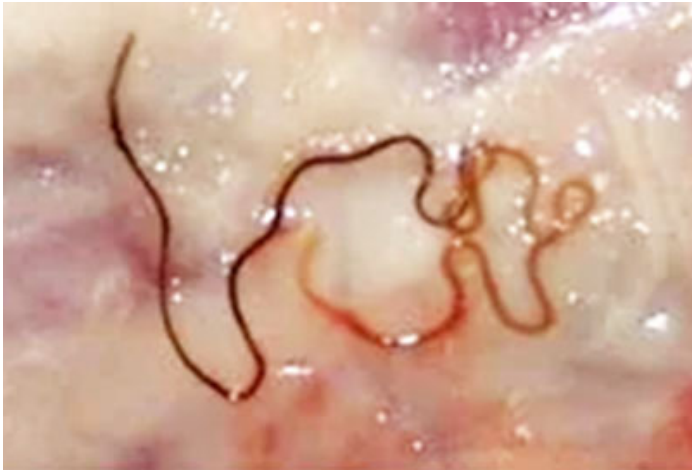
Developmental cycle and mode of transmission: *Elaphostrongylus* spp. have indirect heteroxenous life-cycles involving cyclic transmission between invertebrate intermediate hosts (harbouring infective larvae) and vertebrate definitive hosts (harbouring adult worms). The life-cycle is also unusual as the adult worms live in blood vessels (rather than the gastrointestinal tract) and produce eggs which are carried to the lungs to develop. The eggs hatch releasing L1 which invade alveoli and ascend the respiratory tree to the trachea where they are swallowed and excreted with host faeces. In the external environment, L1 survive well in cool moist conditions (up to 18 months), and even tolerate low temperatures but not freezing. They exhibit horizontal migration (dispersal) out of faecal pellets onto pastures, particularly after rainfall. The larvae infect a range of terrestrial and aquatic gastropods (agriolimacid, arionid and limacid slugs, and bradybaenid, euconulid, gastrodontid, helioid, hygromiid, lymnaeid, polygyrid, succineid and vitrinid snails) which act as obligate intermediate hosts. L1 penetrate foot tissues and moult to L2 and then L3 within 27-50 days, or longer at lower temperatures (but no development below 10°C). L3 survive for long periods in gastropods (up to 2 years), even those species which undergo aestivation. Definitive hosts become infected when they accidentally consume infected gastropods with vegetation when grazing pastures. L3 released in the gastrointestinal tract penetrate the gut wall and then migrate to the central nervous system either by haematogenous spread or by penetrating the peritoneal/pleural cavities and migrating along lateral nerves. The larvae undergo development to L4 and then young adults (L5) in the nervous system before migrating out to settle in the skeletal muscles. *E. rangiferi* and *E. cervi* develop in the meninges (subarachnoid and subdural spaces) and sometimes the spinal canal, ventricles or neural parenchyma, while *E. alces* does not penetrate beneath the dura mater but develops epidurally near lateral nerves and surrounding fat and connective tissues within the vertebral canal. Adult worms mature in blood vessels in the intermuscular connective tissues and gravid females begin egg production. The prepatent period (time from infection to first excretion of L1) varies according to species: ranging from 39-73 days for *E. alces*, 110-206 days for *E. cervi*, and 84-252 days for *E. rangiferi*. Adult worms may live for up to 2-6 years and larval production exhibits a seasonal cycle, peaking over winter (especially in young animals) and declining over summer. Infections also tend to be more prevalent and intense in young male cervids than in females.

Differential diagnosis: Infections are difficult to diagnose on the basis of symptomatology as clinical signs (pneumonia and neurological disorders) may be broad, vague, transient, intermittent or attributable to a range of conditions. Patent infections are usually diagnosed by the microscopic detection of L1 in faecal samples, usually following their recovery by soaking faecal packets in water or less successfully, by Baermann filtration. However, the dorsal-spined larvae cannot be reliably differentiated from those of other protostrongylids. Infections may be diagnosed at post-mortem by the detection of adult worms in musculature or nervous tissue, but considerable dissection may be required to find coiled worms in lesions. More recently, several immunoserological techniques (indirect fluorescent-antibody tests, enzyme immunoassays, immunoelectrophoresis, Western blotting) have been developed to detect host serum antibodies against larval cuticular, somatic or excretory/secretory (ES) products, but the results have demonstrated variable levels of sensitivity and cross-reactivity. Modern molecular biological techniques have been used to characterize larval and adult stages following the polymerase chain reaction (PCR) amplification and sequencing of nuclear genes (notably the internal transcribed spacer 2 or ribosomal RNA).

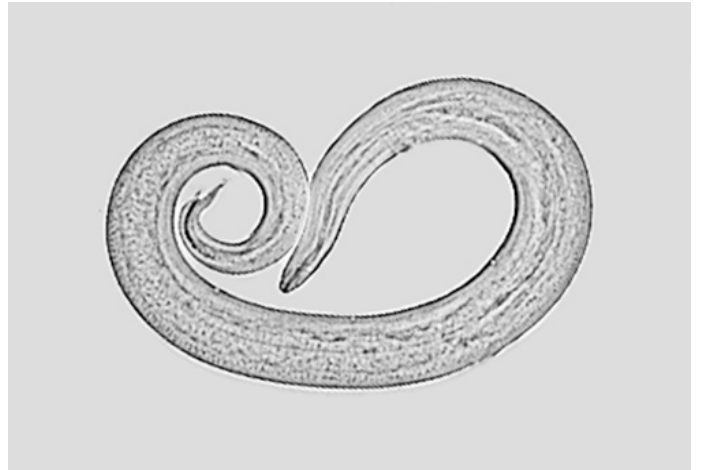
Treatment and control: The treatment of clinical infections using anthelmintic drugs has yielded conflicting results: with variable efficacies recorded depending on parasite species; host species and age; severity, stage and season of infection; and drug class, dose and route of administration. Infections may be difficult to treat as the parasites undergo extensive migrations in their life-cycles, they have developmental stages in privileged sites (behind the blood-brain barrier, and sometimes encapsulated by host reactions) and re-infections are commonplace on contaminated pastures. Nevertheless, some success has been reported in treating domestic livestock and wild animals with benzimidazoles (mebendazole, fenbendazole, oxfendazole, albendazole, thiabendazole), macrocyclic lactones (ivermectin) and heterocyclic thiazines (phenothiazine, now discontinued). Best results were obtained with repeated drenching, in-feed medications or subcutaneous injections, when drug levels could be sustained to access successive developmental stages. Mebendazole and ivermectin were most effective in reducing larval production, but not in eradicating infections. During treatment, some supportive therapy may be required with steroids and other anti-inflammatory agents to safeguard against adverse reactions to dying or dead parasites. Various preventive strategies have been developed to reduce transmission rates in managed stock, notably through pasture management (avoid seasonal grazing of same pastures, regular pasture rotation (3 year cycle), cultivating and/or draining pastures, chemical control of gastropod intermediate hosts) or stock management (quarantine new livestock, separate cohorts, discourage gregarious behaviours, selectively culling young males, excluding feral animals).

Elaphostrongylus





Elaphostrongylus adult worm



Elaphostrongylus larva