Protostrongylus
(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. 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 *Protostrongylus* in the lungs release L1 which are swallowed and passed in faeces. L1 then penetrate the foot of a snail and develop to L3. When eaten by ruminants, larvae penetrate to the mesenteric lymph nodes and moult to L4 which then migrate via the lymphatic-vascular systems to form adults in the lungs. Infections by *Protostrongylus* spp. in sheep and goats are generally asymptomatic.

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:	*Protostrongylus* (parasitic in lungs of sheep/goats, snail intermediate host)
Species:	various species cause subclinical infections in sheep and goats

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					
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
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

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, indicating that several may be monophyletic, and even that the genus *Protostrongylus* may be paraphyletic grouping strongly with *Spiculocaulus* and *Orthostrongylus*. Clearly, further work needs to be conducted to differentiate protostrongylid species, genera and subfamilies. Members of the genus *Protostrongylus* are characterised by males with well-developed bursal rays, telamon with simple plates and arches, gubernaculum with capitulum, corpus and paired crura, short stout spicules, L1 with pointed tail and no dorsal spines. Some 27 species have been described around the world from the lungs of sheep, goats, chamois, antelope, cervids and lagomorphs. Three subgenera have been differentiated on the basis of morphological differences in reproductive organs: *P.* (*Protostrongylus*) (edges of gubernacular crura nodulated or toothed, provagina well-developed)*; P.* (*Davtianostrongylus*) (edges of gubernacular crura nodulated or toothed, provagina weakly-developed or absent); and *P.* (*Pulmostrongylus*) (edges of gubernacular crura smooth). Nonetheless, the subgeneric designation of most species remains undetermined as many descriptions are ambiguous or often incomplete. All protostrongylid lungworms have heteroxenous life-cycles with infective larvae developing in gastropod intermediate hosts. Infections in domestic livestock have been associated with respiratory disease (parasitic bronchitis and pneumonia), particularly in goats and sheep in countries with warm moist climates.

***Protostrongylus* species**	**Definitive hosts**	**Location [Clinical signs]**	**Intermediate hosts**	**Distribution**
P. andrejevi	Artiodactyla: bovid (Amur goral)			Russia
P. boughtoni (syn. *Synthetocaulus leporis*)	Lagomorpha: leporid (snowshoe hare, eastern cottontail, European rabbit)	Bronchi	Gastropoda: euconulid (*Euconolus fulvus*), vallonid (*Vallonia pulchella*), vertiginid (*Columella edentula*, *Vertigo gouldi*, *ovata*)	North America
P. brevispiculatum	Artiodactyla: bovid (sheep, chamois, goat)	Lungs		North America
P. caprae	Artiodactyla: bovid (Siberian ibex)			Russia
P. coburni	Artiodactyla: cervid (white-tailed deer)	Lungs		North America
P. cuniculorum (maybe a variety of *P. rufescens* specific for lagomorphs)	Lagomorpha: leporid (European rabbit, European hare)	Lungs		Europe
P. davtiani	Artiodactyla: bovid (sheep, argali, goat)	Lungs		North America
P. frosti	Artiodactyla: bovid (bighorn sheep)	Lungs		North America

P. hobmaieri	Artiodactyla: bovid (sheep, chamois, goat, alpine ibex)	Lungs		Asia
P. indicus	Artiodactyla: bovid (wild goat)			Eurasia
P. kamenskyi	Lagomorpha: leporid (mountain hare)			
P. kochi	Artiodactyla: cervid (roe deer, red deer), bovid (sheep, mouflon)			Europe
P. macrotis	Artiodactyla: cervid (moose)			North America
P. muraschkinzewi	Artiodactyla: bovid (sheep)		Gastropoda: geometrid (*Cochlicella barbara*), helicid (*Cepaea nemoralis*)	Russia
P. oryctolagi	Lagomorpha: leporid (European hare, European rabbit)	Lungs		Europe
P. ovis	Artiodactyla: bovid (sheep)			
P. pulmonalis (syn. *P. commutatus, terminalis*)	Lagomorpha: leporid (European hare, Cape hare, mountain hare, European rabbit)	Lungs		Europe, Africa
P. raillieti	Artiodactyla: bovid (goat, Siberian ibex, sheep, argali, chamois)			Eurasia
P. rufescens (red lungworm) (incl. subspp. *rufescens*, *boevi*)	Artiodactyla: bovid (water buffalo, sheep, argali, mouflon, goat, chamois, alpine ibex, Iberian ibex)	lungs (small bronchioles)	Gastropoda: chondrinid (*Abida*), enid (*Zebrina*), geometrid (*Cernuella arigonis*, *virgata*, *Cochlicella acuta*, *barbara*, *conoidea*), helicid (*Arianta, Capaea nemoralis, Theba*), hygromiid (*Helicella apicina*, *corderoi*, *itala*, *jamuzensis*, *madritensis*, *ordunensis*, *rugosiuscula*, *valdeona*, *zaratei*, *Perforatella incarnata*)	Africa, Europe, North America, Australia, New Zealand
P. rupicaprae	Artiodactyla: bovid (chamois, Pyrenean chamois)			Europe
P. rushi	Artiodactyla: bovid (sheep, bighorn sheep, goat)	Lungs		North America
P. shiozawai	Artiodactyla: bovid (Japanese serow)	Lungs		Asia
P. skrjabini	Artiodactyla: bovid (sheep, goat)	Lungs		Eurasia
P. stilesi	Artiodactyla: bovid (mountain goat, white-faced muskox, bighorn sheep, Dall sheep)	Lungs		North America
P. sylvilagi	Lagomorpha: leporid (cottontail rabbit, jackrabbit)	Lungs		North America
P. tauricus	Lagomorpha: leporid (European hare, brown hare, European rabbit)	Lungs		Europe
P. vsevolodovi	Artiodactyla: bovid (sheep, Siberian ibex)	Lungs		Russia

Parasite morphology: *Protostrongylus* spp. form 3 different morphological stages during their developmental cycles: eggs; larvae (4 consecutive stages designated L1-L4); and adult worms. Eggs are thin-walled elliptical stages measuring 50-90 x 35-60 µm and are partially embryonated when deposited in lung tissues where they hatch. First-stage larvae (L1) are elongate cylindrical forms ranging in length from 250-400 µm and are often half curled posteriorly. They have rounded heads, cuticles with fine transverse striations and well-developed lateral alae, a long rhabditiform (double-bulbed) oesophagus occupying the anterior 33-50% of the body, intestines without food granules, and a long tapering tail with a pointed terminus (lacking dorsal spines as is characteristic of protostrongylines). L2 are similar in morphology but are slightly larger (300-450 µm) and are often ensheathed in the L1 cuticle. L3 are larger still (400-750 µm) but have a strongyliform (flask-shaped) oesophagus and blunt rounded tails. L3 contained within snail tissues are ensheathed in both the L1 and L2 cuticles, which are shed when the infective L3 are released from host tissues. L4 are transient parasitic stages that have begun to adopt the morphological characteristics of adults, especially in mouth structures and developing genitalia. Adults are thin tubular red-brown worms measuring 13-80 mm in length and the cuticle bears small longitudinal ridges (synlophe). They have a small anterior mouth with 6 elevations or flat perityls that appear like small lips. The

buccal capsule is small and unarmed and leads to a stout oesophagus. Adult worms are sexually dimorphic, with females being larger than males (21-80 cf. 13-45 mm). Mature females are didelphic with 2 ovaries and uteri connected to a common posterior vulva where the body abruptly narrows to the conical tail. Most species have a well-developed provagina extending posterior to the vulva but anterior to the anus. Mature males have a small but well-developed copulatory bursa with large lateral lobes (each supported by 6 rays) and a prominent dorsal lobe (supported by a globular dorsal ray with 6 ventral papillae). They also have a highly developed gubernaculum (comprising capitulum, corpus and paired boot-shaped crura with nodulated or toothed edges) and telamon (with simple plates and arches) and 2 stout spicules (250–320 μm long) terminating in membranous alae. Some consider that the genera *Spiculocaulus* and *Orthostrongylus* should be synonymized with *Protostrongylus* as they were differentiated primarily on the basis of longer filiform spicules in *Spiculocaulus* and an elaborately developed telamon in *Orthostrongylus.*

Site of infection: Adult lungworms are found in the air passages of their definitive hosts, ranging from the alveoli and alveolar ducts to the bronchioles and small bronchi. Earlier developing larval stages migrate from the gut to the lungs via the lymphatics and/or circulation. Infective larvae develop in the tissues and sinuses of obligate gastropod intermediate hosts.

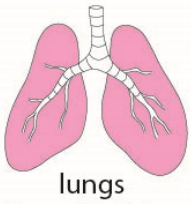
Pathogenesis: Infections by these lungworms cause characteristic discoloured lesions usually seen on the surface of dorsal lobules of the lungs at necropsy. The lesions in the lungs are more extensive than those caused by *Muellerius* infections, as occlusion of the small bronchioles leads to lesser branches filling with eggs, larvae and cellular debris. Occasionally, *Protostrongylus* infections may cause respiratory signs similar to dictyocaulosis, although not as severe and involving localised bronchiolitis and sometimes pneumonia (the latter frequently involving secondary bacterial infections). Worms in alveoli and small air passages cause local inflammation with epithelial desquamation, leucocyte infiltrations, exudate formation and connective tissue proliferation all contributing to occlusion, atelectasis, emphysema, peribronchitis, bronchitis, and small foci of lobular pneumonia with nodular or polygonal plaque-like lesions (up to 1 cm in diameter) appearing as red-gray to yellow discolourations, sometimes progressing to granuloma formation. Respiratory signs are rarely observed, but include dyspnoea (with crackles, crepitation and hypersonority on auscultation), cough (dry then productive), nasal discharge and weight loss, sometimes diarrhoea. Despite intense innate immune responses, hosts tend not to acquire any strong protective immunity, so infections accumulate with age (adults have more prevalent and intense infections). Nonetheless, these lungworm infections are not considered to represent serious health threats to domestic livestock.

Developmental cycle and mode of transmission: *Protostrongylus* spp. have indirect heteroxenous life-cycles involving the faecal contamination of pastures and the formation of infective larvae in obligate gastropod intermediate hosts and their transmission back to herbivorous definitive hosts when grazing. Female worms lay eggs in the airways where they complete embryonation and hatch releasing L1 which migrate up to the trachea via the mucociliary escalator and are swallowed to be passed in host faeces (previous suggestions that L1 moult in the airways with L2 being excreted have not been supported). In the external environment, L1 may survive for months in faecal pellets, eventually migrating outwards onto pastures and into soils, usually following rainfall or flooding. The L1 actively penetrate the foot of gastropods which are used as intermediate hosts in which infective L3 develop in body tissues and cavities over 12-14 days in optimal thermal conditions (20-26°C), but with development being inhibited in colder conditions and in aestivating snails. Infective L3 have been shown to survive in snail tissues for up to 2 years (easily over-wintering). Intermediate host specificity is poorly known but appears to be quite broad involving a range of aquatic and terrestrial snails and slugs. Definitive hosts become infected when they consume infected gastropods with herbage, although some reports suggested that they could also be infected by directly ingesting L3 released from gastropods onto pastures. Ingested L3 penetrate the intestinal wall and migrate to the mesenteric lymph nodes where they moult to L4 and then move to the lungs via the hepatic portal system and heart. The larvae moult to subadults (often designated L5) which settle in the alveoli and bronchioles and mature to adults. The prepatent period (time from infection to first excretion of L1) ranges from 19-54 days, and larval migration have been implicated in transplacental and transcolostral transmission for several species. Infections demonstrate a pronounced seasonality with clinical signs developing over winter and infections becoming more prevalent in spring when humidity and temperatures rise.

Differential diagnosis: Few infections become symptomatic and are easily confounded with other conditions, including dictyocaulosis, strongyloidosis, pulmonary hydatosis, and viral or bacterial bronchopneumonia. Most infections are diagnosed fortuitously by the detection of L1 in faecal samples usually by Baermann filtration. It should be noted that L1 often occur deep in the core of faecal pellets, so samples need to be wetted and thoroughly mixed. The L1 can be differentiated from those of *Dictyocaulus* by the absence of an anterior protoplasmic knob, and from other metastrongyles by the absence of a dorsal tail spine. Infections can be diagnosed at post-mortem by the detection of characteristic lesions on the dorsal surfaces of the lungs, but recovering intact worms from the lesions can be difficult. Recent molecular biological techniques have been used to characterize protostrongyle species by polymerase chain reaction (PCR) amplification and sequencing of nuclear genes (ribosomal RNA, especially internal transcribed spacer 2) and mitochondrial genes (esp. cytochrome c oxidase subunit 1).

Treatment and control: A range of broad-spectrum anthelmintic drugs have been used to treat infections, mostly benzimidazoles (laxabendazole, albendazole, oxfendazole, fenbendazole, flubendazole) and macrocyclic lactones (abamectin, moxidectin, eprinomectin, ivermectin) at higher doses or with repeated treatments. Care should be taken during treatment as clinical signs may initially worsen due to parasite death and host inflammation, so supportive therapy may be required with anti-inflammatory agents, and possibly antibiotics to prevent secondary bacterial pneumonia. Where possible, preventive measures should be taken to reduce faecal contamination of pastures (improved sanitation and hygiene) and limit transmission by controlling gastropod populations (improved drainage, or employing molluscicides), stock management (quarantining new livestock, reduced stocking rates, separating cohorts) and pasture management (rotational grazing, cultivation, spelling).

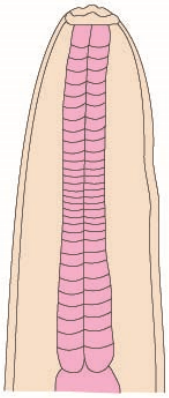
Protostrongylus



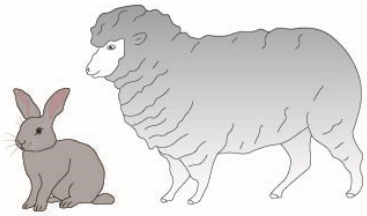
lungs
(bronchiolitis,
sometimes
pneumonia)

adult female
(~ 80 mm)

adult male
(~ 45 mm)



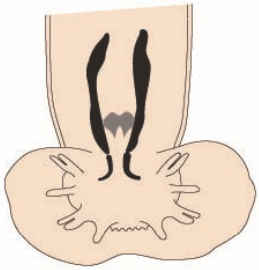
head



Definitive Hosts
(artiodactyls,
lagomorphs)

rarely vertical
transmission

IH/L3
ingested



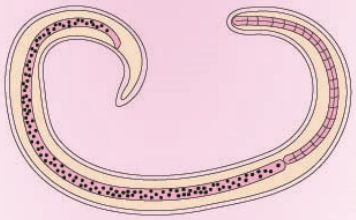
male tail

L1
excreted
in faeces

eggs hatch in host

IH

external
environment

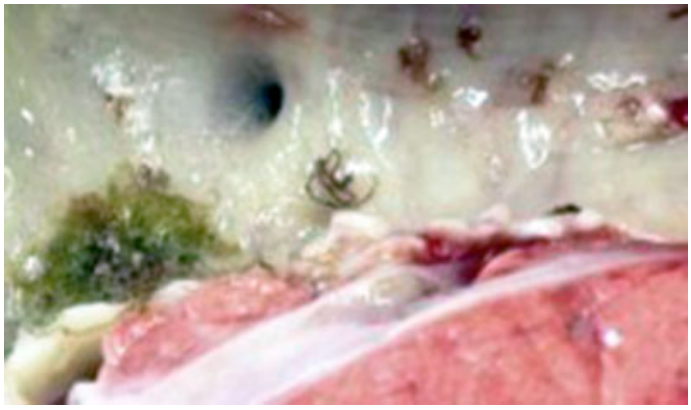


third-stage larvae (L3)
(~ 500 µm)

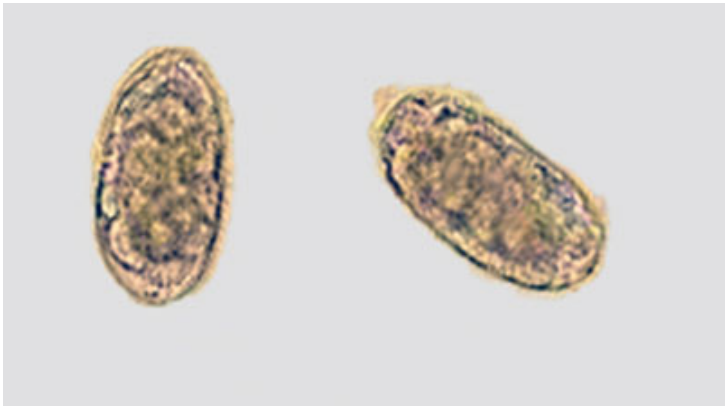
first-stage larvae (L1)
(~ 350 µm)

Intermediate Hosts
(geometrid snails)
(internal tissues/sinuses)

L1 penetrate
foot of snail



Protostrongylus adult worms in lung bronchi



Protostrongylus worm eggs

Protostrongylus larva