

Angiostrongylus
(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. Angiostrongyles have indirect life-cycles involving the development of L3 in invertebrate intermediate hosts, and their carriage in paratenic (transport) hosts. Adult *Angiostrongylus* in the pulmonary vessels of rodents and dogs produce eggs which hatch in the lungs releasing L1 that break through into alveoli to be swallowed and passed in faeces. L1 then penetrate the foot of a snail or slug and develop to L3. The larvae of some species may also persist in the tissues of small mollusc-eating animals, such as rodents and crustaceans (prawns and crabs). When definitive hosts eat intermediate or paratenic hosts, L3 migrate via the lymphatics to the lungs and develop into adult worms. Infections may cause pulmonary disease in dogs, and sometimes neurological disorders in humans.

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: Angiostrongylidae (no buccal cavity, infection of vertebrates by ingestion of earthworm/molluscan IH)
Genus: *Angiostrongylus* (parasitic in pulmonary artery of dogs)
Species: various species cause respiratory/neurological disease in dogs, rodents and humans

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 in bursate species, 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 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)				
Angiostrongylidae (lungworms)	no or reduced buccal cavity, short club-shaped oesophagus	carnivores, rodents	ingestion of IH or PH carrying L3	28
Metastrongylidae (lungworms)	small buccal capsule, 2 trilobed lips, bursa with reduced dorsal lobe	suids	ingestion of IH carrying L3	1
Protostrongylidae (lungworms)	small buccal capsule, bursa with large lobes, gubernaculum	artiodactyls	ingestion of IH carrying L3	17
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 <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).

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm larvae
Angiostrongylidae					
<i>Angiostrongylus</i> (lungworm)	15	carnivores, rodents	lungs, blood vessels	14-34 mm long, small buccal capsule dorsally hooked, indirect cycle, eggs laid in tissues travel to lungs, swallowed, L1 voided, L3 develop in snail IH, then small mollusc-eating PH	310-400 µm, long narrow buccal chamber
<i>Aelurostrongylus</i> (lungworm)	5	carnivores	lungs	4-10 mm long, small buccal capsule, short club-shaped oesophagus, indirect cycle, eggs laid in lungs, swallowed, L1 voided, L3 develop in snail IH, then in small mollusc-eating PH	300-400 µm, dorsal spine
<i>Parastrongylus</i> (lungworm)	12	rodents, primates	pulmonary arteries	10-42 mm long, vestigial buccal capsule, indirect cycle, eggs laid in vessels enter lungs, swallowed, L1 voided, L3 develop in snail IH, then small mollusc-eating PH	250-300 µm, sheathed

The family Angiostrongylidae contains 28 genera (*Aelurostrongylus*, *Andersonstrongylus*, *Angiocaulus*, *Angiostrongylus*, *Antechinostrongylus*, *Cercogylus*, *Chabaudstrongylus*, *Cosmostrongylus*, *Didelphostrongylus*, *Filostrongylus*, *Gallegostrongylus*, *Glirovyngylus*, *Gurltia*, *Heterostrongylus*, *Madafilaroides*, *Madangiostrongylus*, *Malayometastrongylus*, *Marsupostrongylus*, *Parastrongylus*, *Procyonostrongylus*, *Pulmostrongylus*, *Rauschivngylus*, *Rodentocaulus*, *Sobolevngylus*, *Stefanskostrongylus*, *Thaistrongylus*, *Trilobostrongylus*, *Viverrostrongylus*) parasitic in the respiratory and vascular systems of Australian and South American marsupials, insectivores, rodents, felids, mustelids, viverrids, canids and lemurs. The genus *Angiostrongylus* contains a variety of lungworms with a typical bursa and posterior vulva infecting the lungs and blood vessels of insectivores, rodents, felids and canids, and using gastropods as intermediate hosts for larval development. Two subgenera are recognised: *A.* (*Angiostrongylus*) syn. *Haemostrongylus*, *Cardionema*, and *Angiocaulus* (male worms with a bursal externolateral ray separate from the 2 other lateral rays); and *A.* (*Parastrongylus*) syn. *Pulmonema*, *Rattostrongylus* and *Morerastrostrongylus* (males with bursal externolateral ray joined with other lateral rays into a common stalk). The latter subgenus has been elevated to generic status by several workers although many reference texts still place species in the genus *Angiostrongylus* rather than *Parastrongylus*, especially those of considerable biomedical importance (*P. cantonensis* and *P. costaricensis*, both considered in the following separate section). The species *A. vasorum* is considered to be a newly emergent or re-emergent disease of dogs, particularly in southern Europe and isolated areas of Africa and North America.

<i>Angiostrongylus</i> species	Definitive hosts	Location [Clinical signs]	Intermediate hosts [plus Paratenic Hosts (PH)]	Distribution
<i>A. andersoni</i>	Rodentia: murid (Nigerian gerbil, Kemp's gerbil)	lungs [abscesses]	Gastropoda: helioid (<i>Helix aspersa</i>), lymnaeid (<i>Lymnea stagnalis</i>), planorbid (<i>Planorbarius corneus</i>)	Africa
<i>A. blarini</i>	Eulipotyphla: soricid (northern short-tailed shrew)			North America
<i>A. chabaudi</i>	Carnivora: felid (wild cat)	lungs		Europe
<i>A. daskalovi</i>	Carnivora: mustelid (beech marten, European pine marten, European badger)	pulmonary arteries		Europe
<i>A. felineus</i>	Carnivora: felid (<i>jaguarundi</i>)	pulmonary arteries		South America
<i>A. gubernaculatus</i>	Carnivora: mephitid (striped skunk), mustelid (American badger), canis (Island fox)	heart (right ventricle)		North America
<i>A. lenzii</i>	Rodentia: cricetid (montane grass mouse)	pulmonary arteries		South America
<i>A. michiganensis</i>	Eulipotyphla: soricid (common shrew, smoky shrew)			Eurasia
<i>A. minutus</i>	Eulipotyphla: talpid (Japanese shrew mole)			Asia
<i>A. morerai</i>	Rodentia: cricetid (dolorous grass mouse)	pulmonary arteries		South America

<i>A. ondatrae</i>	Rodentia: cricetid (musk rat)			Holarctic
<i>A. raillieti</i>	Carnivora: canid (dog, pampas fox, crab-eating fox), procyonid (South American coati)	pulmonary arteries		South America
<i>A. soricis</i>	Eulipotyphla: soricid (Laxmann's shrew, Eurasian pygmy shrew)			Eurasia
<i>A. ten incertae sedis</i>	Carnivora: mustelid (Japanese marten)	heart		Asia
<i>A. vasorum</i> (French heartworm)	Carnivora: canid (dog, wolf, coyote, jackal, hoary fox, red fox, Iberian fox, pampas fox, hoary fox, crab-eating fox, African desert fox), felid (cat), mustelid (European badger, tayra); Rodentia: murid (African grass rat)	pulmonary arteries, right ventricle [chronic cough, dyspnoea, exercise intolerance]	Gastropoda: achatinid (<i>Achitina fulica</i> , <i>Lissachatina fulica</i> , <i>Prosopoeas javanicum</i> , <i>Subulina octona</i>), agriolimacid (<i>Deroceras reticulatum</i>), arionid (<i>Arion ater</i> , <i>hortensis</i> , <i>rufus</i> , <i>vulgaris</i> (<i>lusitanicus</i>)), bradybaenid (<i>Bradybaena similis</i>), clausiliid (<i>Cochlodina laminata</i>), helacid (<i>Arianta arbustorum</i> , <i>Helix pomatia</i> , <i>Cepaea nemoralis</i> , <i>Cornu asperum</i>), limacid (<i>Limax flavus</i>), physid (<i>Physa</i>), planorbid (<i>Biomphalaria glabrata</i> , <i>pfeifferi</i> , <i>tenagophila</i>), succineid (<i>Omalonyx</i> , <i>Succinea putris</i>), veronicellid (<i>Laevicaulis alte</i>), unplaced (<i>Eceparypa physana</i>) [plus PH: Rodentia: murid (rat, mouse); Anura: ranid (European common frog); Galliformes: phasianid (chicken); Sauria (lizard?)]	worldwide (except North America)

Parasite morphology: *Angiostrongylus* spp. form 3 different types of morphological stages in their developmental cycles: eggs; larvae (4 stages designated L1-L4); and adult worms. The eggs are ellipsoidal thin-shelled stages measuring 63-67 x 37-42 µm and contain a developing embryo (morula). L1 are elongate cylindrical coiled stages measuring from 310-400 µm in length and they have rounded heads with a small cephalic button, a long narrow buccal chamber, a flask-shaped muscular oesophagus extending 33-50% of the body length, and a sharply-pointed wavy tail with a subterminal dorsal notch (kink) and a small ventral indentation. L2 are similar in morphology but slightly longer, while L3 are longer still measuring 425-524 x 23-34 µm and are characterised by the possession of an anterior rod-shaped structure, and a sharply-pointed tail. L4 are transient parasitic stages that have lost the anterior rod-shaped structure and have blunt tails. Adults are medium-sized white-pink worms measuring 14-34 mm long) and they have dorsally hooked mouths (similar to the hookworms), a round oral opening without adornments, a small rudimentary buccal capsule, and are surrounded by a cuticle with longitudinal ridges (synlophe). Adult worms are sexually dimorphic, with females being longer than males (15-34 x 0.28-0.56 mm cf. 14-25 x 0.25-0.42 mm). Mature females are didelphic with 2 ovaries and uteri in a prodelphic configuration (parallel and anteriorly directed) which appear as white tubules spirally twisted around the red gut (resembling a barber's pole). The oviducts connect to a common posterior vulva, sometimes equipped with a prominent sphincter. Mature males have a small caudal copulatory bursa with lateral lobes supported by 6 rays (2 partly fused ventral rays, 3 lateral rays, separate single externolateral ray) and a dorsal lobes supported by a stout dorsal ray (with stout terminal branches). [Note that differences in bursal ray structure have been used to differentiate *Angiostrongylus* (ventrolateral ray separated) from *Parastrongylus* (ventrolateral ray not separated) either as different genera or subgenera]. Males also possess a rudimentary gubernaculum and 2 elongate curved spicules.

Site of infection: Larval stages undergo extensive migrations through the tissues of their definitive hosts, moulting and developing into subadults along the way, before settling in their final predilection sites and maturing to fertile adult worms. Different species exhibit relatively strict tissue tropism, with larvae moulting either in the lungs (e.g. *A. andersoni*) or lymphatics (e.g. *A. vasorum*). Adult worms then mature in the lung parenchyma (e.g. *A. andersoni*) or in the pulmonary circulation (pulmonary arteries, right ventricle of heart, e.g. *A. vasorum*). Infective larvae (L3) develop in the tissues of various gastropods (aquatic and terrestrial snails and slugs), and they may also be carried in the tissues of various paratenic (transport) hosts, such as amphibians and rodents.

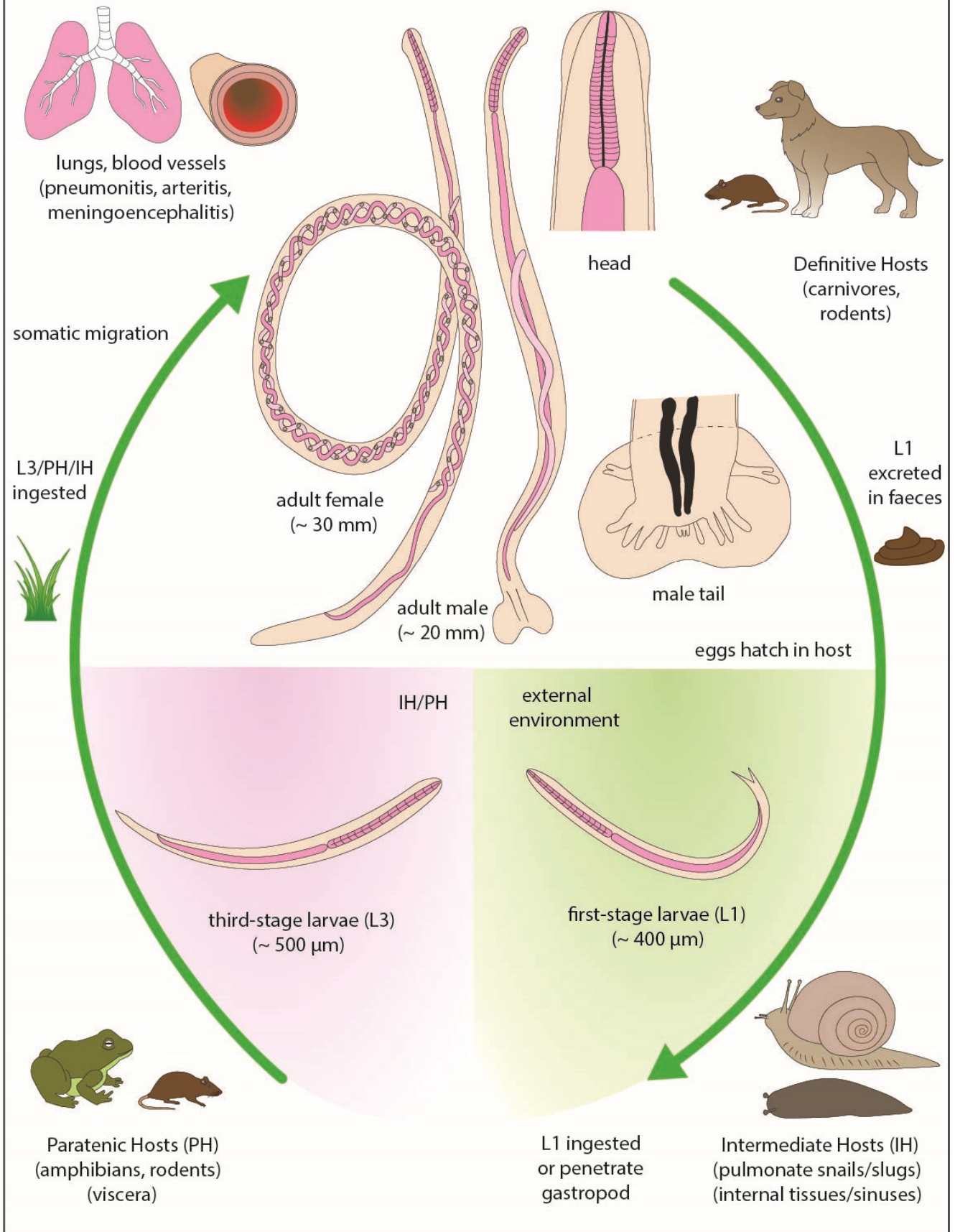
Pathogenesis: Many infections in definitive hosts have been detected fortuitously during post-mortem surveys of small carnivores or rodents, often without any indications of disease. Clinical infections, however, have been reported in wild and domestic carnivores, particularly canids. Canine angiostrongyliasis rarely presents as an acute disease (dyspnoea, violent cough, white-yellow occasionally bloody sputum), more often as a chronic condition developing over many months with widely varying clinical signs (respiratory, cardiovascular and neurological). Invading migrating larvae cause traumatic damage to host tissues, while adult worms and the eggs and larvae they produce elicit strong inflammatory host responses, all contributing to circulatory occlusions with downstream effects. Infections in the lungs may cause verminous interstitial pneumonia with pulmonary sclerosis and emphysema, while damage to blood vessels leads to arteritis, haemorrhagic conditions and coagulation abnormalities (including thrombotic endarteritis, periarteritis, petechial ecchymoses, bleeding in the abdominal and/or thoracic cavities, subcutaneous haematomas, with oedema, haemothorax, hydropericardium, and ascites). The clinical signs most commonly observed are coughing, exercise intolerance, weight loss and poor general body condition, but they may progress to include severe respiratory distress with dyspnoea, coughing, haemoptysis, gagging, vomiting, nasal discharge, melena, anorexia, depression and stunted growth. Animals may develop cardiac insufficiency and hypertrophy, and die due to congestive heart failure. Aberrant or erratic larval migrations and bleeding in the nervous system may also cause neurological signs, including meningitis, epileptic seizures, ataxia, paraplegia, cranial nerve deficits, vestibular signs, blindness and proprioceptive deficits.

Developmental cycle and mode of transmission: *Angiostrongylus* spp. have indirect heteroxenous life-cycles involving cyclic transmission between vertebrate definitive hosts (in which adult worms develop) and invertebrate intermediate hosts (in which infective larvae develop). Eggs laid by female worms in the bloodstream are carried to the lungs where they lodge to develop and hatch releasing larvae. The L1 penetrate into alveolar air-spaces and ascend the respiratory mucociliary escalator to the trachea where they are swallowed and excreted with host faeces. In the external environment, L1 infect gastropods either by ingestion (e.g. *A. andersoni*) or percutaneous penetration of the foot, or both (e.g. *A. vasorum*). A variety of terrestrial and aquatic gastropods (snails and slugs) act as obligate intermediate hosts in which L1 moult twice and form infective L3 in nodules in the connective tissues and muscles over 15-17 days (longer in cooler conditions). Infections are more prevalent in regions with wet mild climates that are favourable for gastropod development. Infective L3 of *A. vasorum* may also be carried in the tissues of various paratenic (transport) hosts (rodents, amphibians) which have consumed infected gastropods. Definitive hosts become infected when they consume L3 either in intermediate hosts or in paratenic hosts. The routes of infection and sites of development in definitive hosts varies depending on the parasite species: with larvae developing either in the lymphatics or lungs; and adults developing either in the lung parenchyma or in the pulmonary circulation (pulmonary arteries, right ventricle of heart). The simplest cycle is demonstrated by *A. andersoni* when L3 migrate from the gut via the hepatic portal system to the liver within 14 hours and then the lungs within 24-28 hours where they moult to L4 at 2-3 days and then L5 at 5-7 days. The prepatent period (time from infection to first excretion of L1) ranges from 24-31 days. The cycle of *A. vasorum* is more complex as L3 migrate from the gut to visceral lymph nodes where they moult twice in 4-5 days to subadults (L5) before migrating via the hepatic portal vein to the liver and then via the caudal vena cava to the right ventricle and pulmonary arteries by 9-10 days after infection. Here they mature to adult worms which produce eggs that hatch releasing L1 around 45 days (although the prepatent period is highly variable ranging from 28-108 days). It is thought animals may be infected for life with intermittent excretion of L1.

Differential diagnosis: While the occurrence of cardiovascular and pulmonary conditions may be indicative of infection, the clinical signs exhibited are highly variable and nonspecific. Similarly, medical imaging techniques (radiography, computed tomography) may reveal suspicious lesions, including diffuse peribronchial, interstitial and alveolar densities, multiple nodules in peripheral caudal lung lobes, and enlargement of the right heart and pulmonary artery, but other causes may be involved. Infections are therefore generally diagnosed by the microscopic detection of L1 in faecal samples, usually following their recovery by Baermann filtration. Multiple samples should be tested, however, as larval excretion is intermittent. L1 may also be detected in tracheal washes, bronchoalveolar lavages, fine needle lung aspirates and sometimes in urine. Infections may be diagnosed at post-mortem by the detection of lesions and parasites in respiratory tissues, although worms are difficult to remove from tissues. Several research studies have developed immunological tests (enzyme immunoassays and Western blots) to detect specific host antibodies against parasite antigens, but some problems were encountered with cross-reactivity. Molecular biological techniques have been used to characterize parasite species by polymerase chain reaction (PCR) amplification of parasite DNA, including nuclear genes (internal transcribed spacer region 2 of ribosomal RNA) and mitochondrial genes (cytochrome c oxidase subunit I).

Treatment and control: A variety of anthelmintic drugs have been used to treat clinical infections, including benzimidazoles (fenbendazole, albendazole, mebendazole), imidazothiazoles (levamisole) and macrocyclic lactones (ivermectin, moxidectin, milbemycin). Care was required during treatment to avoid exacerbating clinical signs, with corticosteroids, bronchodilators, expectorants and diuretics used to manage adverse reactions. On several occasions, lumbar puncture and analgesics were used to relieve signs of meningitis. Various preventive strategies may be applied in domestic and peri-domestic settings to reduce transmission rates to intermediate hosts (reduce faecal contamination through better sanitation), limit gastropod populations (using barriers or molluscicides), avoid transmission to paratenic hosts (vertebrate pest control, esp. rodents), and to minimise larval uptake by final hosts (improving hygiene, providing clean food and water, preventing hunting). Obviously, such interventions are impractical in larger non-domestic situations, so infections may persist in wild or feral animal populations.

Angiostrongylus

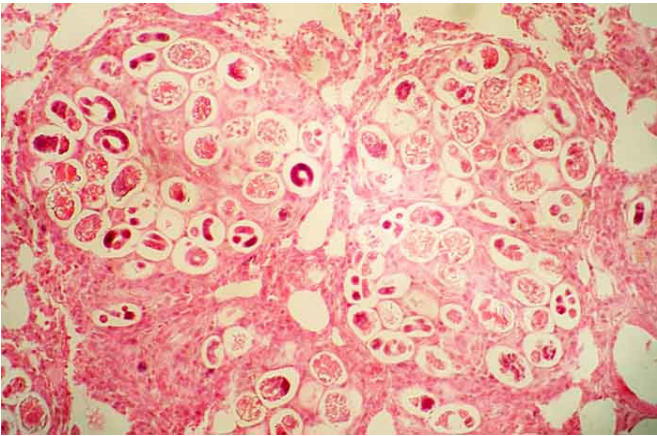




Angiostrongylus adult worms



Angiostrongylus adult worms



Angiostrongylus lung lesion



Angiostrongylus larva