Parastrongylus
(helminth: nematode)

Overview

Nematodes are triploblastic pseudocoelomate unsegmented worms that undergo protostomial embryonic cleavage and grow by cuticular moulting (ecdysis). Two groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Many phasmidian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including spirurinids, tylenchinids and rhabditinids. The latter contains the infraorder Rhabditomorpha which includes strongyloid nematodes characterised by an expansion of the tail of the male known as the copulatory bursa (clasper with one dorsal and two lateral lobes with muscular rays). Many families are recognised: including lungworms with small buccal capsules and reduced male bursae. Adult worms are found mostly in the lungs of their hosts, although some inhabit the pulmonary artery, meninges or connective tissues. Five main groups occur: dictyocaulids in ruminants and horses; metastrongyles in pigs; protostrongyles in ruminants; angiostrongyles in carnivores and rodents; and filaroids in dogs. Angiostrongyles have indirect life-cycles involving the development of L3 in invertebrate intermediate hosts, and their carriage in paratenic (transport) hosts. The genus *Parastrongylus* contains the rat lungworm *P. cantonensis* (formerly *Angiostrongylus cantonensis*). Adult worms in the pulmonary vessels of rodents 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 may also persist in the tissues of small mollusc-eating animals, such as 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 by migrating stages may cause eosinophilic meningoencephalitis 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:	*Parastrongylus* (parasitic in pulmonary artery of rats)
Species:	*P. cantonensis* (formerly *Angiostrongylus cantonensis*) causes eosinophilic meningoencephalitis in 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)]
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)				
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 *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).

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm larvae
Angiostrongylidae					
Parastrongylus (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
Angiostrongylus (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
Aelurostrongylus (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

The family Angiostrongylidae contains 28 genera (*Aelurostrongylus, Andersonstrongylus, Angiocaulus, Angiostrongylus, Antechinostrongylus, Cercogylus, Chabaudistrongylus, Cosmostrongylus, Didelpostrongylus, Filostrongylus, Gallegostrongylus, Glirovyngylus, Gurltia, Heterostrongylus, Madafilaroides, Madangiostrongylus, Malayometastrongylus, Marsupostrongylus, Parastrongylus, Procyonostrongylus, Pulmostrongylus, Rauschivyngylus, Rodentocaulus, Sobolevingylus, 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 *Morerastrongylus* (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, P. malaysiensis, P. costaricensis* and *P. mackerrasae*). Most species are primarily parasites of rodents and are transmitted by a range of gastropod intermediate hosts and some small vertebrate paratenic hosts. Humans may become accidentally infected when consuming infective L3 in snails, in paratenic hosts, or on contaminated vegetables. Larvae migrate through host tissues, some may moult and develop to sexual maturity producing eggs, but they eventually die. Nevertheless, they may cause severe clinical disease in humans, including eosinophilic meningoencephalitis in South-East Asia, and eosinophilic enteritis in Central and South America.

Parasite species	Definitive Hosts	Location [Clinical sign	Intermediate hosts [plus Paratenic Hosts (PH)]	Distribution
Parastrongylus cantonensis (formerly *Angiostrongylus*) [rat lungworm]	Rodentia: murid (black rat, brown rat, Philippine black rat, dusky field rat, yellow-breasted rat, white-bellied rat, Himalayan field rat, Turkestan rat, Ryukyu Island tree rat, lesser bandicoot rat, greater bandicoot rat, Bower's white-toothed rat, Polynesian rat, grassland mosaic-tailed rat, fawn-footed mosaic-tailed rat, house mouse), cricetid (eastern wood rat), capromyid (hutia); Eulipotyphla: soricid (Asian house shrew); Chiroptera: pteropodid (grey-headed flying fox, black flying fox); Perissodactyla: equid (horse); Artiodactyla: bovid (Barbary sheep), camelid (alpaca); Didelphimorphia: didelphid (Virginia opossum); Diprotodontia: macropodid	pulmonary arteries, right ventricle [eosinophilic meningoencephalitis, neurological lesions]	Gastropoda: achatinid (*Achatina fulica, Archachatina marginata, Subulina octona*), agriolimacid (*Deroceras laeve*, *reticulatum*), ampullariid (*Ampullaria canaliculata*, *Lanistes carinatus, Pila, Pomacea canaliculata, maculata, paludosa, poeyana*), ariophantid (*Macrochlamys indica, loana, Microparmarion malayanus, Parmarion martensi*), bradybaenid (*Acusta despecta, Bradybaena brevispira, circulus, ravida, similaris*), camaenid (*Camaena cicatricosa, Plectotrophis appanata, Satsuma mercatoria, Trichochloris hungertordiana, rufopila*), cepolid (*Jeanneretia bicincta, subtusulcata*), cyclophorid (*Cyclophorus*), discid (*Anguispira alternata*), helicarionid (*Helicarion*), helicid (*Emoda sagrayama, Helicina adspersa,*	Asia, Australia, India, Africa, Americas

	(red-necked wallaby, purple-necked rock wallaby, parma wallaby, western grey kangaroo), potoroid (rufous bettong), pseudocheirid (common ringtail possum), phalangerid (brushtail possum); Peramelemorphia: thylacomyid (greater bilby); Carnivora: canid (dog, fox); Primates: atelid (black howler), hylobatid (lar gibbon), lemurid (red-ruffed lemur), callitrichid (cotton-top tamarin), cebid (Guianan squirrel monkey), hominid (human); Psittaciformes: cacatuid (yellow-tailed black cockatoo, gang cockatoo); Caprimulgiformes: podargid (tawny frogmouth); Gruiformes: gruid (brolga); Cuculiformes: cuculid (channel-billed cuckoo)		*Viana regina*), helminthoglyptid (*Polymita muscarum, picta*), limacid (*Lehmannia poiureri, Limax flavus, maximus, Ambigolimax* (*Lehmannia*) *valentiana*), neocyclotid (*Poteria*), oleacinid (*Oleacina*), orthalicid (*Liguus fasciatus*), philomycid (*Philomycus bilineatus, carolinianus, Meghimatium bilineatum*), planorbid (*Biomphalaria glabrata, Gyraulus spirillus, Hippeutis umbilicalis*), pleurodontid (*Pleurodonte sagemon, Thelidomus aspera, Zachryia auricoma, guanensis*), polygyrid (*Mesodon thyroidus, Polygyra triodontoides*), sagdid (*Sagda*), spiraxid (*Euglandina rosea*), urocoptid (*Tetrentodon filiola*, *perdidoensis*), veronicellid *(Laevicaulis alte, Sarasinula plebeia, Vaginulus alte, ameghini, yuxjsjs, Veronicella alte, cubensis*), viviparid (*Cipangopaludina chinensis, Sinotaia* (*Bellamya*) *aeruginosa*, *quadrata*) [plus PH: Anura: hylid (golden bell frog), ranid (American bullfrog), dicroglossid (Asian grass frog), bufonid (Asian toad), rhacophorid (common tree frog); Sauria: varanid (Bengal monitor); Bivalvia: ostreid oysters (*Crassostrea rizophorae*, *virginica*), Decapoda: coenobitid crab (*Birgus latra*), palaemonid shrimp (*Macrobrachium lar*); Rhabditophora: geoplanid flatworm (*Platydemus manokwari*)]	
Parastrongylus costaricensis (formerly *Angiostrongylus*)	Rodentia: murid (brown rat, black rat, house mouse), cricetid (hispid cotton rat, short-tailed cane rat, Watson's climbing rat, Tome's rice rat, northern pygmy rice rat, black-footed pygmy rice rat, rat-headed rice rat, Costa Rican dusky rat, Mexican deer mouse), echimyid (Tome's spiny rat), heteromyid (Panamanian spiny pocket mouse, Salvin's spiny pocket mouse); Carnivora: procyonid (white-nosed coati, raccoon); Didelphimorphia: didelphid (Virginia opossum); Primates: atelid (black-handed spider monkey), aotid (Nancy Ma's night monkey), callitrichid (moustached tamarin),	mesenteric arteries [eosinophilic enteritis, necrotic gut lesions]	Gastropoda: achatinid (*Subulina octona*), ampullariid (*Pomacea flagellata*), bradybaenid (*Bradybaena similaris*), bulinid (*Bulinus*), helicid (*Helix aspersa*), limacid (*Limax flavus*, *maximus*), lymnaeid (*Lymnaea*), planorbid (*Biomphalaria glabrata*, *straminea*, *Helisoma trivolvis*), strophocheilid (*Megalobulinus abbreviatus*), succineid (*Succinea*), veronicellid (*Belocaulus angustipes*, *Phyllocaulis soleiformis*, *variegatus*, *Sarasinula marginata*, *plebeia*, *Vaginulus plebeius*) [plus PH: Anura: ranid (frog); Malacostraca: palaemonid (freshwater prawn)]	Americas

	hylobatid (siamang), hominid (human)			
P. dujardini	Rodentia: murid (wood mouse, yellow-necked mouse, house mouse), cricetid (European pine vole, bank vole, hamster)	pulmonary arteries, heart	Gastropoda: planorbid (*Biomphalaria glabrata*)	Europe
P. mackerrasae	Rodentia: murid (brown rat, bush rat, Australian swamp rat); Chiroptera: pteropodid (black flying fox); Primates: hominid (human)	pulmonary arteries, right ventricle, lungs	Gastropoda: agriolimacid (*Deroceras laeve*), helicarionid (*Helicarion*)	Australia
P. malaysiensis	Rodentia: murid (Malayan field rat, Polynesian rat, brown rat, black rat, Malayan house rat, ricefield rat, Muller's giant Sunda rat, Bower's white-toothed rat, long-tailed giant rat, Annandale's rat, red spiny rat, Whitehead's spiny rat, dark-tailed tree rat); Eulipotyphla: soricid (Asian house shrew); Scandentia: tupaiid (common treeshrew); Primates: cercopithecid (Taiwanese macaque), hominid (human)	pulmonary arteries, right ventricle, lungs	Gastropoda: achatinid (*Achatina fulica*, *Allopeas javanicum*, *Rumina decollata*), ampullariid (*Pila sututu*), ariophantid (*Macrochlamys resplendens*, *Microparmarion malayanus*, *Girasia peguensia*), lymnaeid (*Lymnea rubiginosa*), planorbid (*Biomphalaria glabrata*, *Indoplanorbus exustus*), veronicellid (*Laevicaulis alte*), viviparid (*Bellamyia ingalisiana*)	Asia
P. petrovi	Rodentia: glirid (forest dormouse)	heart, bronchi		Russia
P. ryjikovi	Rodentia: cricetid (northern red-backed vole)	pulmonary arteries		Russia
P. sandarsae	Rodentia: murid (Natal multimammate mouse, Indian gerbil)	pulmonary arteries		Africa
P. schmidti	Rodentia: cricetid (marsh rice rat, hispid cotton rat, white-footed mouse, golden hamster), murid (house mouse, brown rat, Mongolian gerbil)	pulmonary arteries	Gastropoda: planorbid (*Biomphalaria glabrata*), polygyrid (*Polygyra septemvolva*)	North America
P. sciuri	Rodentia: sciurid (red squirrel)	pulmonary arteries		Europe
P. siamensis	Rodentia: murid (house mouse, long-tailed giant rat, small white-toothed rat, black rat, red spiny rat, greater bandicoot rat, Savile's bandicoot rat, Mongolian gerbil), cricetid (hispid cotton rat); Primates: cercopithecid (crab-eating monkey)	mesenteric arteries	Gastropoda: planorbid (*Biomphalaria glabrata*)	Asia
P. tateronae	Rodentia: murid (eastern broad-toothed field mouse)	pulmonary arteries		Africa

Parasite morphology: *Parastrongylus* spp. form 3 different morphological stages in their developmental cycles: eggs; larvae (4 successive stages usually designated as L1-L4); and sexually dimorphic adult worms. Eggs are thin-shelled ovoid stages measuring 60-110 µm in longest diameter and they are partially embryonated containing a central multicellular morula. L1 are elongate cylindrical stages measuring 250-300 x 15 µm and covered by a transversely striated cuticle. They have an anterior triangular oral opening surrounded by six cephalic papillae, broad lateral alae extending along the body, and a sharply-pointed ventrally curved tail. L2 are slightly larger measuring 320-450 x 30 µm and have a distinct anterior structure with a keratinous cap. L3 measure 450-510 x 20 µm and the anterior structure has developed T-bar structures on the anterior tip. Both L2 and L3 may appear ensheathed if they retain the cuticle of the former stage, but the sheaths are shed during the infection process. L4 are transient parasitic stages measuring up to 1-2 mm x 40 µm and subadult stages (sometimes designated L5) measure 2-4 mm x 60 µm before maturing. growing up to 20-40 mm long as mature adults. Adults are slender elongate lungworms 10-42 mm long with filariform bodies tapering at both ends and bound by a tough cuticle with transverse striations (synlophe present). They have a small lipless mouth with a number of small hook-like teeth, a small buccal capsule, a stout oesophagus with a posterior valve leading to the elongate intestines terminating in a subterminal anus/cloaca. Adult worms are sexually dimorphic, with females generally larger than males (17-42 x 0.26-0.56 mm cf. 15-25 x 0.25-0.42 mm for *P. cantonensis,* 27-40 x 0.10-0.35 mm cf. 15-20 x 0.1-0.3 mm for *P. costaricensis*). Mature female worms are didelphic having 2 ovaries and uteri in a prodelphic configuration (parallel and anteriorly directed) and appearing as white tubules spirally wound around the red gut (resembling a barber's pole). The oviducts connect to a common posterior vulva, sometimes with a prominent sphincter or protective flap, and the tail is conical and slightly curved terminating in a small refringent spine. Mature males have a small but well-developed caudal copulatory bursa comprising 2 lateral lobes each supported by 6 rays (2 fused ventral rays, 4 lateral rays arising from common stalk) and a small dorsal lobe supported by a single dorsal ray (with a terminal branch). [Note that differences in bursal ray structure have been used to differentiate *Parastrongylus* (ventrolateral ray not separated) from *Angiostrongylus* (ventrolateral ray separated) either as different genera or subgenera]. Males also possess a weakly developed gubernaculum (0.01 mm) and 2 slender elongate striated spicules (0.3-1.3 mm) with blunt tips (pointed in *P. costaricensis*).

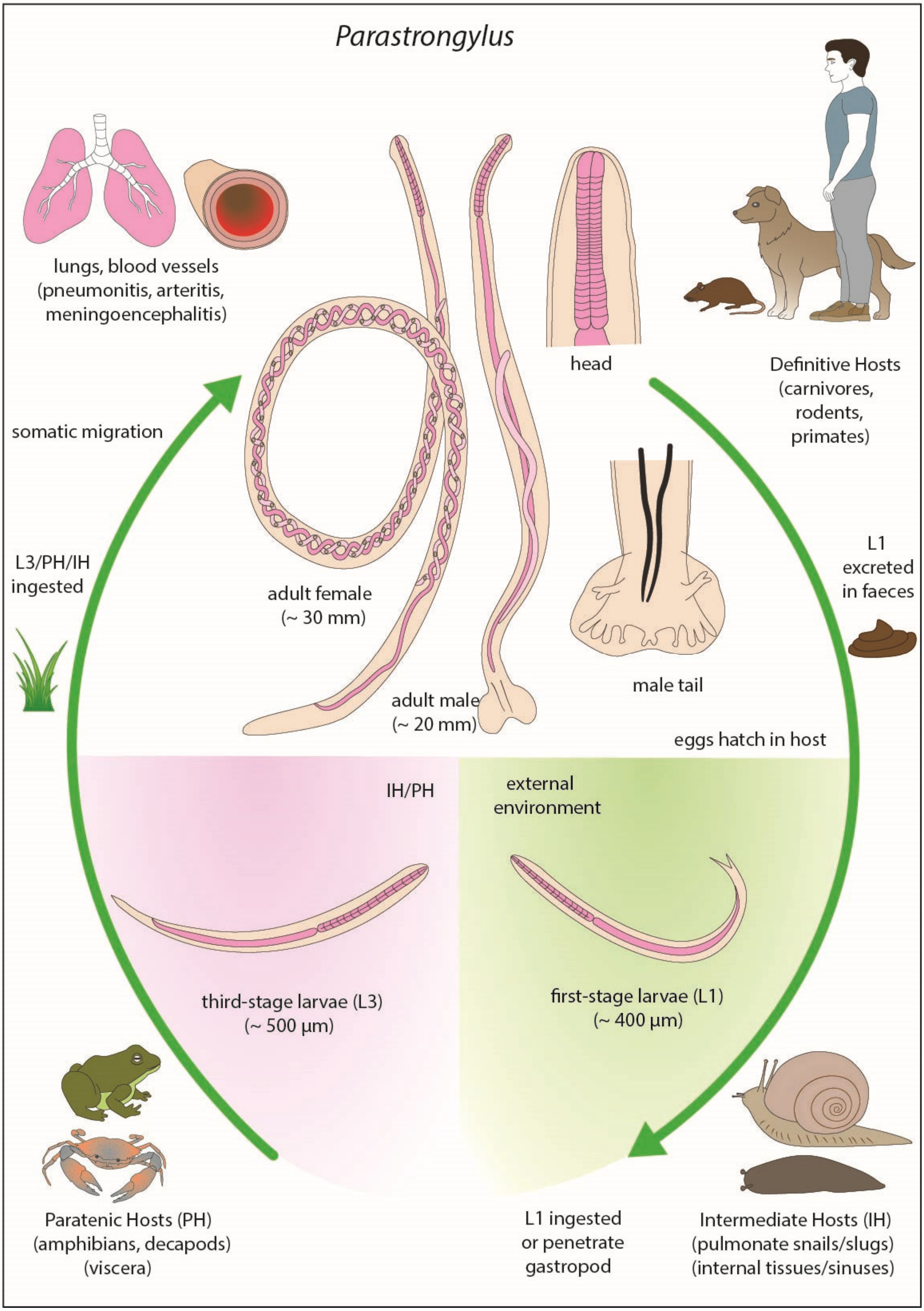
Site of infection: Different *Parastrongylus* spp. exhibit tissue tropism within their definitive hosts, with larvae and adults infecting specific tissues. Adult worms infect either the lung parenchyma (e.g. *P. dujardini, P. schmidti*), pulmonary circulation (pulmonary arteries, right ventricle of heart) (e.g. *P. cantonensis, P. mackerrasae, P. malaysiensis*) or the mesenteric circulation (mesenteric arteries (e.g. *P. siamensis*) or veins (e.g. *P. costaricensis*)). Pre-adult larval stages undergo extensive migrations through host tissues, moulting either in the lungs (e.g. *P. dujardini, P. schmidti*), lymphatics (e.g. *P. siamensis*), or circulation (e.g. *P. costaricensis*), sometimes becoming trapped in neural parenchyma (e.g. *P. cantonensis, P. mackerrasae, P. malaysiensis*). All species form infective third-stage larvae (L3) in the tissues of a variety of gastropods (aquatic and terrestrial snails and slugs). The infective L3 of *P. cantonensis, P. malaysiensis* and *P. costaricensis* may also be carried without further development in the tissues of various paratenic (transport) hosts, including crustacea (crabs, shrimps), molluscs (oysters), amphibians, lizards and planarians.

Pathogenesis: Most rat lungworm species appear to be well-adapted to their usual rodent hosts and infections generally do not produce any clinical disease although the parasite life-cycle involves obligate migration and development in host tissues before adults mature in the circulation and produce eggs. However, in accidental or aberrant hosts (including humans), parasites may not complete their development and migrating larvae and worms (alive and dead) elicit intense inflammatory reactions resulting in severe disease, notably eosinophilic meningoencephalitis due to *P. cantonensis* or eosinophilic enteritis due to *P. costaricensis*. Disease development and severity depends on parasites species (some being more virulent under certain conditions), host susceptibility (usual permissive (normal) host species versus unusual aberrant (abnormal) host species, young versus mature individuals, immunologically naive versus exposed individuals), intensity of infection (number of parasites), and stage of infection (prepatent period involving larval migrations, patent period involving worm and egg burdens). Infections by *P. cantonensis* are usually asymptomatic in rats even though larvae migrate and develop in the central nervous system before adults mature in the pulmonary arteries and right heart ventricle. Occasionally, heavy infections may form lesions in the meninges and lungs, with blockages of the pulmonary artery resulting in clinical signs involving coughing, sneezing, ataxia, paraplegia and death. However, in non-permissive hosts, the parasites do not complete their development but cause intense inflammation which may result in eosinophilic meningoencephalitis. Larvae migrate along peripheral nerves and nerve roots to the spinal cord, subsequently moving cranially within the parenchyma or via the subarachnoid space. The parasites cause traumatic damage to nervous tissue involving migratory tracts (sometimes abscesses) with petechial haemorrhages, nerve degeneration, inflammation and cellular infiltrates. Eosinophilia develops in peripheral blood and cerebrospinal fluid (100-2,000 cells/mm^3), the latter leading to high intra-cranial pressures sometimes with hydrocephaly. A range of neurological signs may be observed, including severe headache, neck stiffness, fever, vomiting, inappetence, diarrhoea, faecal incontinence, urinary incontinence, depression, convulsions, ataxia (incoordination), conscious proprioception deficits, paresis (impaired movement), paraesthesia (tingling), facial paralyses, paraplegia, coma, and eye involvement involving ocular pain, keratitis, ocular neuritis, retinal oedema, photophobia, visual impairment, diplopia and blindness. Many light infections are self-limiting with full recovery in a month, but heavier infections can lead to permanent neurological damage and death in domestic animals, wildlife and humans. Infections by *P. costaricensis* are usually nonpathogenic in rodents, even though parasites migrate through gut tissues and develop in the mesenteric circulation where they deposit eggs. However, in non-permissive hosts (including humans), parasites die and degenerate causing intense inflammatory and granulomatous reactions resulting in eosinophilic enteritis. The intestinal wall becomes thickened by granulomatous inflammation with massive infiltrates of eosinophils, sometimes producing palpable tumour-like masses (mimicking malignancy), and sometimes rupturing the intestines. Clinical signs include relapsing periods of severe abdominal pain (resembling acute appendicitis), fever, vomiting, diarrhoea, leucocytosis (esp. eosinophilia) and anorexia. In rare cases, parasites have been associated with testicular obstruction, arthritis, infarction, thrombosis, gastrointestinal haemorrhage, eosinophilic vasculitis and hepatic signs resembling visceral larval migrans.

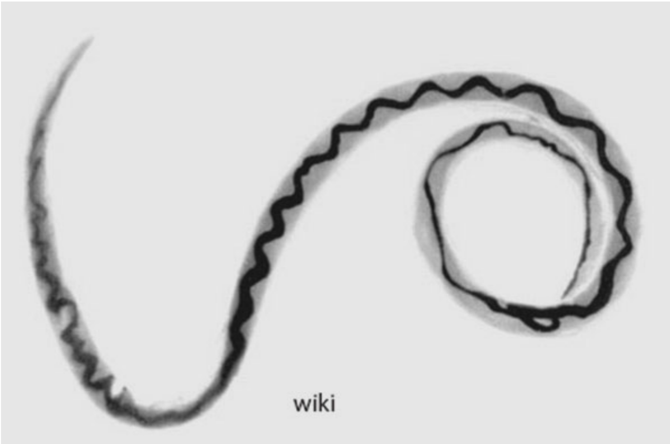
Developmental cycle and mode of transmission: *Parastrongylus* spp. have indirect heteroxenous life-cycles involving the formation of adult worms in vertebrate definitive hosts and the development of infective larvae in invertebrate intermediate hosts, and sometimes their carriage in paratenic (transport) hosts. Eggs laid by gravid female worms in the circulation are carried to the lungs where they develop and hatch releasing L1 which migrate up the respiratory tree to the trachea to be swallowed and excreted in host faeces. L1 infect a range of obligate intermediate hosts (aquatic and terrestrial snails and slugs) in which they moult twice forming L3 in 9-25 days. Infective L3 survive for long periods in gastropod tissues, and those of some species even survive for several days when shed in gastropod mucus trails. A range of animals (including frogs, shrimp, crabs, lizards and planarians) may also act as paratenic hosts for several species when they carry L3 in their internal tissues following the consumption of infected gastropods. Definitive hosts become infected by ingesting infective L3 which penetrate the gut wall and migrate through various host tissues moulting and maturing into adult worms. Several variations in this typical life-cycle have been observed for different *Parastrongylus* spp.; mainly in how gastropods become infected (L1 ingested or percutaneous penetration); how final hosts become infected (ingesting L3 shed in mucus or contained within gastropods or paratenic hosts); where larvae develop in final hosts (lungs, lymphatics, circulation or neural parenchyma); where adults mature in final hosts (lung parenchyma, pulmonary circulation or mesenteric circulation); and how L1 emerge from final hosts (via airways to the intestines or direct into the intestines). The most diverse cycles are exhibited by *P. cantonensis, P. mackerrasae* and *P. malaysiensis* whereby gastropods ingest L1, final hosts ingest L3 in mucus or in host tissues, larvae migrate from the stomach to the brain in 2-3 days (via an extensive migration through the lymphatics to the heart, the pulmonary circulation and then the arterial circulation), both moults occur in neural parenchyma over 1-2 weeks, young adults reside in the subarachnoid space for 2 weeks before entering the cerebral vein, adults develop in the right ventricle of the heart and in pulmonary arteries by 3-4 weeks, and eggs release L1 via the airways. The prepatent period (time from infection to first larval excretion) ranges from 32-45 days (*P. malaysiensis* 32 days, *P. mackerrasae* 40-42 days, *P. cantonensis* 42-45 days). Infections by *P. costaricensis* vary in their development in that L1 infect gastropods by ingestion or percutaneous penetration, final hosts ingest L3 in mucus trails or in gastropods, larvae undergo 2 migratory routes within 1-2 weeks moulting twice in the process (usually once in abdominal lymphatics and once in mesenteric arteries, but sometimes both in intrahepatic veins), adults mature in the mesenteric veins, eggs release L1 direct into the intestines, and the prepatent period ranges from 21-28 days. *P. siamensis* infects rodents by the ingestion of L3 in snails, larvae moult twice within a week in mesenteric lymph nodes and vessels, adults mature in mesenteric arteries, eggs release L1 into the intestines, and the prepatent period is 29-34 days. *P. dujardini* and *P. schmidti* infect rodents following the ingestion of L3 in snails, larvae moult twice within a week but in the lungs, adults mature in the lung parenchyma, eggs release L1 in the airways, and the prepatent period is 24-31 days. Humans become infected with *P. cantonensis* and *P. costaricensis* primarily when they consume infected intermediate or paratenic hosts, particularly in regions where shrimp and other crustaceans are traditionally eaten raw. People may also be infected when they consume salad vegetables contaminated with L3 in gastropod mucus trails, and children have been infected when consuming or playing with infected slugs or snails.

Differential diagnosis: Presumptive diagnosis may be made in humans on the basis of symptomatology (meningoencephalitis or enteritis) in individuals with a relevant history (travel to endemic regions, consumption of raw or partially cooked gastropods and/or crustaceans), but other infections may cause similar conditions (e.g. *Gnathostoma*, *Paragonimus*, *Taenia solium*). Infections are accompanied by a profound eosinophilia in the blood and cerebrospinal fluid, but other helminths also elicit eosinophilic responses. Occasionally, larvae or young worms may be detected microscopically in cerebrospinal fluid samples collected by lumbar puncture. Medical imaging techniques may reveal alterations commonly associated with infections, with computed tomography (CT) scans indicating cerebral oedema or ventricular dilatation in the absence of focal lesions, and magnetic resonance imaging (MRI) demonstrating multiple micronodular enhancements in the brain and spine. Regrettably, infections are generally confirmed in humans at necropsy by the detection of parasites (larvae, adults, eggs) in tissue samples. A range of immunological tests (enzyme immunoassays and Western blots) have been developed to detect specific host antibodies against crude, excretory/secretory (ES) or refined antigens from adults and larvae, but many demonstrated some cross-reactivity problems before the introduction of monoclonal antibody reagents. Modern molecular biological techniques have been used to characterize parasite species following the amplification (by polymerase chain reaction (PCR), real-time PCR, or loop-mediated isothermal amplification (LAMP)) of nuclear gene sequences (18S ribosomal RNA and internal transcribed spacer I) and mitochondrial genes (cytochrome c oxidase subunit I, 66 kDa protein).

Treatment and control: Despite the severity of clinical disease in humans, most infections are self-limiting and patients often recover spontaneously over 4-6 weeks, although an increasing number have protracted infections over several months with periodic relapses. Various attempts have been made to treat human infections with anthelmintic drugs, notably benzimidazoles (fenbendazole, albendazole, mebendazole), but such treatment is generally contraindicated as disease often worsens as worms die and degenerate leading to further adverse inflammatory reactions. A variety of supportive care options have been used to provide symptomatic relief, including corticosteroids (anti-inflammatories), lumbar puncture (to reduce intracranial pressure), analgesics and opioids (for pain relief), sedatives (for sensory hyperesthesia), intravenous fluid therapy (restoring fluid volumes), urinary catheterisation, passive physiotherapy and antibiotic treatment (for secondary infections). In exceptional circumstances, surgical intervention has been warranted to remove *P. cantonensis* from the eyes, and to remove inflamed intestinal tissue in *P. costaricensis* infections. A range of preventive measures have been applied in endemic areas in attempts to reduce cyclic transmission between hosts. Rodent control acts to reduce faecal contamination of the environment with parasite larvae as well as to reduce the number of natural final hosts that may acquire sylvatic infections. Controlling gastropod populations using molluscicides and barriers (especially around gardens) acts to reduce the number of infective larvae which may perpetuate infections. Attempts to control aquatic crustacean populations in waterways may help minimise the uptake of infective larvae into potential paratenic hosts. However, the greatest impact on reducing transmission involves changing people's behaviour with respect to food and personal hygiene. Fresh produce (salad and vegetables) should be thoroughly washed in clean water to remove gastropods and their mucus trails, both of which may contain infective larvae. Despite traditional culinary practices, molluscs and crustaceans should not be eaten raw, as cooking them effectively destroys any infective larvae present. Food handlers and cooks should practice strict personal hygiene by wearing gloves or washing hands and utensils in contact with potentially contaminated food items. Children should also be discouraged from playing with live gastropods and never to consume them even if dared to. Several countries have developed successful education campaigns to raise public awareness about infections and make recommendations to curb transmission rates.



Parastrongylus
lungs, blood vessels
(pneumonitis, arteritis,
meningoencephalitis)
head
Definitive Hosts
(carnivores,
rodents,
primates)
somatic migration
L3/PH/IH
ingested
adult female
(~ 30 mm)
adult male
(~ 20 mm)
male tail
L1
excreted
in faeces
eggs hatch in host
IH/PH
external
environment
third-stage larvae (L3)
(~ 500 μm)
first-stage larvae (L1)
(~ 400 μm)
Paratenic Hosts (PH)
(amphibians, decapods)
(viscera)
L1 ingested
or penetrate
gastropod
Intermediate Hosts (IH)
(pulmonate snails/slugs)
(internal tissues/sinuses)

 *Parastrongylus* adult worm	 *Parastrongylus* larva