

Filaroides

(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. Unlike most lungworms, filaroids have direct life-cycles where adults in the lungs produce eggs which hatch releasing L1 to be swallowed and passed in faeces. L1 are ingested by dogs or, more commonly, transferred to pups by maternal grooming or regurgitative feeding. L2 develop in the intestines and then migrate via the lymphatic-vascular route to the lungs and mature into adults. *Filaroides* spp. have been associated with respiratory distress in dogs worldwide.

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: Filaroididae (direct cycle, infection of carnivores by ingestion of L1)
Genus: *Filaroides* (parasitic in lungs of dogs/mustelids)
Species: various species cause subclinical infections in dogs

Parasite biodiversity and host range: Most Metazoa are multicellular triploblastic animals with differentiated tissues, many being bilaterally symmetrical with a body cavity. Most invertebrate animals are protostomes as their embryonic development involves spiral determinate cleavage. Those that moult their external cuticles during their life-cycles (process known as ecdysis) are grouped together in the unique clade Ecdysozoa, including the nematodes (roundworms), onychophorans (velvet worms), tardigrades (water bears) and arthropods (myriapods, chelicerates, crustaceans and hexapods, all with jointed limbs). Nematodes (roundworms) are unsegmented tubular worms with a fluid-filled body cavity (pseudocoelom) that acts as a hydrostatic skeleton. They have longitudinal muscles and typically exhibit a sideways thrashing motion. They have well developed digestive tracts with various partitions: the foregut comprising the mouth (often with lips and papillae), buccal capsule (sometimes with ridges, rods, plates, spears, stylets or teeth) and oesophagus (glandular, muscular or both); the midgut (nonmuscular absorptive section); and hindgut (rectum) emptying through a subterminal anus (cloaca in males). Most nematodes are dioecious and form separate sexes. Male worms have a single testis (sometimes 2), an elongate vas deferens often equipped with a seminal vesicle and ejaculatory duct (glandular and/or muscular), 1-2 copulatory spicules (sometimes with an accessory gubernaculum), and bursate species with elaborate posterior claspers. Female worms are usually didelphic with 2 ovaries (some monodelphic or polydelphic), 2 oviducts usually with spermatheca, 2 uteri opening into a common vagina and a vulva often equipped with a muscular ovejector. Female worms are oviparous or viviparous and produce numerous eggs or larvae, respectively. Larval stages undergo several moults (L1-L4) before maturing into adult worms. Some nematodes have direct life-cycles where eggs or larvae infect definitive hosts (per os or per cutaneous), but many have indirect cycles where larvae first develop in invertebrate intermediate hosts before infecting definitive hosts (by ingestion, injection or deposition). Many nematode species are free-living in terrestrial and aquatic habitats,

while some species from diverse groups have become plant or animal parasites. Two nematode groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Most Enoplia are free-living marine organisms but some are found in freshwater, and on land as plant parasites. The Dorylaimia comprise numerous freshwater and terrestrial species, including major groups of plant and animal parasites. The Chromadoria is represented by many marine groups as well as a terrestrial group of plant and animal parasites. The taxonomic ranks of many nematode assemblages vary considerably depending on which classification system has been followed. Molecular phylogenetic studies, however, have supported the separate classification of most groups, particularly at the level of superfamily. Collectively, species from at least 16 superfamilies are considered to pose serious threats to human and animal health as infectious diseases.

CLASSIFICATION* OF SUPERFAMILIES OF PARASITIC NEMATODES
Class: Enoplea (Aphasmidea, Adenophorea) (gland-bearers, cylindrical oesophagus, no phasmids, setae, two testes)
Subclass: Dorylaimia (five or more oesophageal glands, buccal stylet (odontostyle), free-living or parasitic)[clade I(2)]
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short anterior muscular and long posterior glandular portions)
Class: Chromadorea (spiral amphids, 3 oesophageal glands, usually annulated bodies, free-living and parasitic)
Order: Rhabditida (Secernentea, Phasmidea) (secretors, phasmids present, amphids anterior, bulbous oesophagus)
Suborder: Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)[clade V(9)]
Infraorder: Rhabditomorpha ('rod-shaped' buccal cavity)
Superfamily: Rhabditoidea (open tube stoma, excretory system with lateral canals)
Superfamily: Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Suborder: Spirurina (animal parasites, many use invertebrate intermediate hosts (IH))[clade III(8)]
<i>Incertae sedis</i> Superfamily: Dracunculoidea (elongate parasites of vertebrate tissues, freshwater crustacean IH)
Infraorder: Ascaridomorpha (large roundworms, three large lips, numerous caudal papillae)
Superfamily: Ascaridoidea (ascarids, eggs thick-shelled, larvae may undertake hepato-pulmonary migration)
Superfamily: Heterakoidea (preanal sucker anterior to cloaca in males, direct cycle, infection by egg ingestion)
Infraorder: Gnathostomatomorpha ('jaw-mouthed' due to unique bulbous armed heads)
Superfamily: Gnathostomatoidea (first IH copepod, often use paratenic hosts)
Infraorder: Oxyuridomorpha (pinworms, pointed tails, oesophagus with terminal bulb, males with single spicule)
Superfamily: Oxyuroidea (common in mammals, birds, reptiles, amphibians)
Infraorder: Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily: Acuarioidea (small parasites mostly of birds, with cephalic cordons, ptilina or serrated shields)
Superfamily: Camallanoidea (conspicuous phasmids, L1 with dorsal tooth, ovoviviparous, L1-L3 in copepod)
Superfamily: Filarioidea (tissue-dwelling filarial parasites, lack lips, infect tissues/vessels, arthropod IH)
Superfamily: Habronematoidea (unique head structures with small pseudolabia and median lips)
Superfamily: Physalopteroidea (stomach worms in mammals, insect IH)
Superfamily: Spiruroidea (pseudolabia, bipartite oesophagus, infect birds (crop/gizzard), arthropod IHs)
Superfamily: Thelazioidea (eye-worms of birds and mammals, transmitted by insects)
Suborder: Tylenchina (fungal, plant and animal parasites)[clade IV(10,11,12)]
Infraorder: Panagrolaimomorpha (free-living or parasitic (insects, reptiles, amphibians, mammals))
Superfamily: Strongyloidoidea (dauer stages, lip region without processes, striated cuticle)

*Contemporary genotypic classification schemes recognize strong monophyletic clades at the level of superfamily and infraorder, while previous phenotypic classification schemes had ranked many as separate orders.

The superfamily Strongyloidea comprises a range of worms often with prominent buccal capsules and specialised oral structures well-suited to their feeding habits on host tissues and/or fluids. Adults of most species are parasitic in the gastrointestinal tracts of mammals and some birds, while larval stages feed on bacteria in the external environment, although some larvae may infect invertebrates as intermediate or paratenic hosts. The adult worms are sexually dimorphic, the smaller males characterised by an expansion of the tail (bursa) which is used as a copulatory 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)				
Filaroididae (lungworms)	small buccal capsule, reduced male bursa, infective L1	carnivores	ingestion of L1	4
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
Angiostrongylidae (lungworms)	no or reduced buccal cavity, short club-shaped oesophagus	carnivores, rodents	ingestion of IH or PH carrying L3	28
Dictyocaulidae (lungworms)	small buccal capsule, bursa with large lobes, short stout spicules	ungulates, reptiles	ingestion of L3	5
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, sorcids and marsupials).

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm larvae
Filaroididae					
<i>Filaroides</i> (lungworm)	17	carnivores, primates	lungs	2-90 mm long, vestigial buccal capsule, bursa absent, L1 voided in faeces, vomitus or sputum, direct cycle (L1 transferred to young during grooming or regurgitative feeding) or indirect cycle (L1 infect gastropods and form infective L3)	220-325 µm, posterior kink
<i>Oslerus</i> (lungworm)	2	carnivores	trachea	4-64 mm long, small buccal capsule, bursa reduced, L1 voided in faeces, vomitus or sputum, direct cycle (L1 transferred to young during grooming or regurgitative feeding) or indirect cycle (L1 infect gastropods and form infective L3)	230-270 µm, S-shaped tail

The family Filaroididae contains 4 genera (*Filaroides*, *Filariopsis*, *Oslerus*) parasitic in the respiratory system of canids, mustelids, pinnipeds, primates and Australian marsupials. The family contains delicate lungworms which are difficult to remove from host tissues and study intact, but they have been separated from the family Angiostrongylidae in that the males are abursate and the females have a subterminal vulva. Their life-cycles are quite varied: some being direct; while others are indirect and use gastropods or fish as intermediate hosts. The genus *Filaroides* contains some 17 spp. classified in 2 subgenera: *F. (Filaroides)* (= *Pseudostrongylus*) (males with well-developed caudal papillae and spicules) parasitic in terrestrial carnivores, primates and Australian marsupials with direct cycles or indirect cycles involving gastropod intermediate hosts; and *F. (Parafilaroides)* (males lacking caudal papillae, with small spicules and a weakly developed gubernaculum) parasitic in the lung parenchyma of marine pinnipeds with indirect cycles involving coprophagous fishes.

<i>Filaroides</i> species	Definitive hosts	Location [Clinical signs]	Intermediate hosts (IH) [plus Paratenic Hosts (PH)]	Distribution
Subgenus <i>Filaroides</i>				
<i>F. (F.) athertonensis</i>	Diprotodontia: macropodid (red-legged pademelon)	Lungs		Australia
<i>F. (F.) bronchialis</i>	Carnivora: mustelid (sable)	Lungs		Asia
<i>F. (F.) canadensis</i>	Carnivora: mustelid (North American river otter)	Lungs		North America
<i>F. (F.) hirthi</i>	Carnivora: canid (dog)	Lungs	no IH (direct)	North America, Europe, Japan, Australia
<i>F. (F.) martis</i>	Carnivora: mustelid (American mink, American marten, beech marten, European pine marten, European polecat, sable, stoat, Japanese weasel, least weasel, ferret), mephitid (skunk), herpestid (Egyptian mongoose), canid (Iberian fox)	Lungs	Gatropoda: endodontid (<i>Anguispira alternata</i> , <i>Discus cronkhitei</i>), limacid (<i>Deroceras gracile</i>), physid (<i>Physa integra</i>), planorbid (<i>Gyraulus deflexus</i>), succineid (<i>Succinea ovalis</i>), zonitid (<i>Zonitoides arboreus</i>) [plus PH: Rodentia: murid (mouse)]	Eurasia, Americas
<i>F. (F.) mephitis</i>	Carnivora: mephitid (skunk)	Lungs		North America
<i>F. (F.) myonaxi</i>	Carnivora: herpestid (black-tipped mongoose, slender mongoose)	Lungs		Africa
<i>F. (F.) orientalis</i>	Carnivora: mustelid (stoat, least weasel, Siberian weasel)	Lungs		Eurasia

<i>F. (F.) pararostratus</i>	Carnivora: canid (dog)	Lungs		Americas
<i>F. (F.) pilbarensis</i>	Dasyuromorphia: dasyurid (little red kaluta)	Lungs		Australia
Subgenus <i>Parafilaroides</i>				
<i>F. (P.) decorus</i>	Carnivora: otariid (California sea lion, Steller sea lion, northern fur seal)	Lungs	Perciformes: kyphosid (opaleye fish)	North Pacific
<i>F. (P.) gymnurus</i> (syn. <i>Pseudalius</i> , <i>Halocercus</i> , <i>F. arcticus</i>)	Carnivora: phocid (hooded seal, harp seal, ringed seal, harbour seal, spotted seal, grey seal, bearded seal, Baikal seal)	lungs		Holarctic
<i>F. (P.) hispidus</i>	Carnivora: phocid (ringed seal, grey seal)	Lungs		western Arctic, western Atlantic
<i>F. (P.) hydrurgae</i>	Carnivora: phocid (leopard seal)	Lungs		Antarctic
<i>F. (P.) krascheninnikovi</i>	Carnivora: phocid (ringed seal, bearded seal, Baikal seal)	Lungs		Eurasia
<i>F. (P.) nanus</i>	Carnivora: otariid (Steller sea lion)	Lungs		North Pacific
<i>F. (P.) prolificus</i>	Carnivora: otariid (Steller sea lion)	Lungs		North Pacific
<i>Species inquirenda</i>				
<i>F. gordius sp. inq.</i>	Primates: cebid (common squirrel monkey)			South America
<i>F. kreisi sp. inq.</i>	Carnivora: canid (Cape hunting dog)			Africa
<i>F. (P.) caspicus sp. inq.</i>	Carnivora: phocid (Caspian seal)	Lungs		Caspian Sea
Re-assigned species				
<i>F. (F.) cebus</i> (syn. <i>Filariopsis arator</i> [now <i>Filariopsis barretoï</i>])	Primates: cebid (white-faced capuchin, common squirrel monkey), callitrichid (common marmoset)	Lungs		South America
<i>F. milksi</i> (now <i>Andersonstrongylus milksi</i> in family Angiostrongylidae as bursa present]	Carnivora: canid (dog)	Lungs		North America
<i>F. mustelarum</i> [now <i>Skrjabingylus nasicola</i>]	Carnivora: mustelid (stoat, weasel), mephitid (skunk)	frontal sinuses, lungs	Gastropoda: agriolimacid (<i>Deroceras reticulatum</i>) [plus PH; Eulipotyphla: soricid (common shrew); Rodentia: murid (field mouse), cricetid (bank vole)]	North America, Eurasia

Parasite morphology: These lungworms form 3 different types of morphological stages in their developmental cycles: eggs; larvae (4 successive stages encoded L1-L4); and adult worms. The eggs are thin-shelled transparent ellipsoidal stages measuring 49-80 x 39-50 µm and they are fully larvated when laid. L1 are elongate coiled stages measuring from 220-325 µm in length and they have annulated cuticles with lateral alae, rounded heads, narrow buccal capsules, rhabditiform (bulbed) oesophagus extending 33-50% the body length, and undulating tails with a subterminal dorsal indentation (but no dorsal spine) and a terminal lance-like tip. Few descriptions are available for subsequent larval stages for those species with direct cycles, while those with indirect cycles have been described from intermediate hosts, including gastropods (e.g. *F. martis*) and coprophagous fish (e.g. *F. decorus*). L2 measured 320-380 µm long and had cuticles with regular delicate transverse striations (apparently without alae) and blunt conical tails. L3 were more slender and serpentine measuring 318-362 µm and had striated cuticles with narrow lateral alae, well-developed cylindrical buccal capsules, and blunt conical tails, some with tiny digitiform appendages. L2 and L3 often appeared ensheathed as they retained the cuticles of their previous stages, but they were easily shed when larvae were disturbed. L4 were transient parasitic stages with developing male or female genitalia. Adults are small thin pale worms measuring 2-13 mm long (some species in the subgenus *F. (Parafilaroides)* measure up to 90 mm long) with inflated cuticles forming voluminous tegumental sheaths (outer cortical layer). They have small mouths surrounded by 4 mound-like excrescences, small buccal capsules, club-shaped oesophagi, intestines terminating in subterminal anus/cloaca, and short blunt rounded tails. Adult lungworms are sexually dimorphic, with females being slightly larger than males (5-90 cf. 2-37 mm long). Mature female worms are didelphic with 2 ovaries and uteri in a prodelphic configuration (parallel and anteriorly directed) connected to a common posterior subterminal vulva. Mature males are abursate and do not possess a distinct caudal copulatory bursa (the family Filaroididae was separated from the family Angiostrongylidae by the absence of a male bursa). The bursal rays are completely reduced to well-developed caudal papillae in members of the subgenus *F. (Filaroides)*, but they are absent in those of the subgenus *F. (Parafilaroides)*. Males also have a weakly developed gubernaculum and 2 stout arcuate spicules.

Site of infection: Adult worms infect the lung parenchyma of their carnivorous hosts, usually being tightly coiled up in alveoli and small bronchioles, particularly in diaphragmatic lobes, and sometimes forming granulomatous nodules in mucosa. In parasite species with direct life-cycles, larval stages also develop within the lungs, whereas those of species with indirect cycles develop within the viscera of intermediate hosts (gastropods or coprophagous fishes).

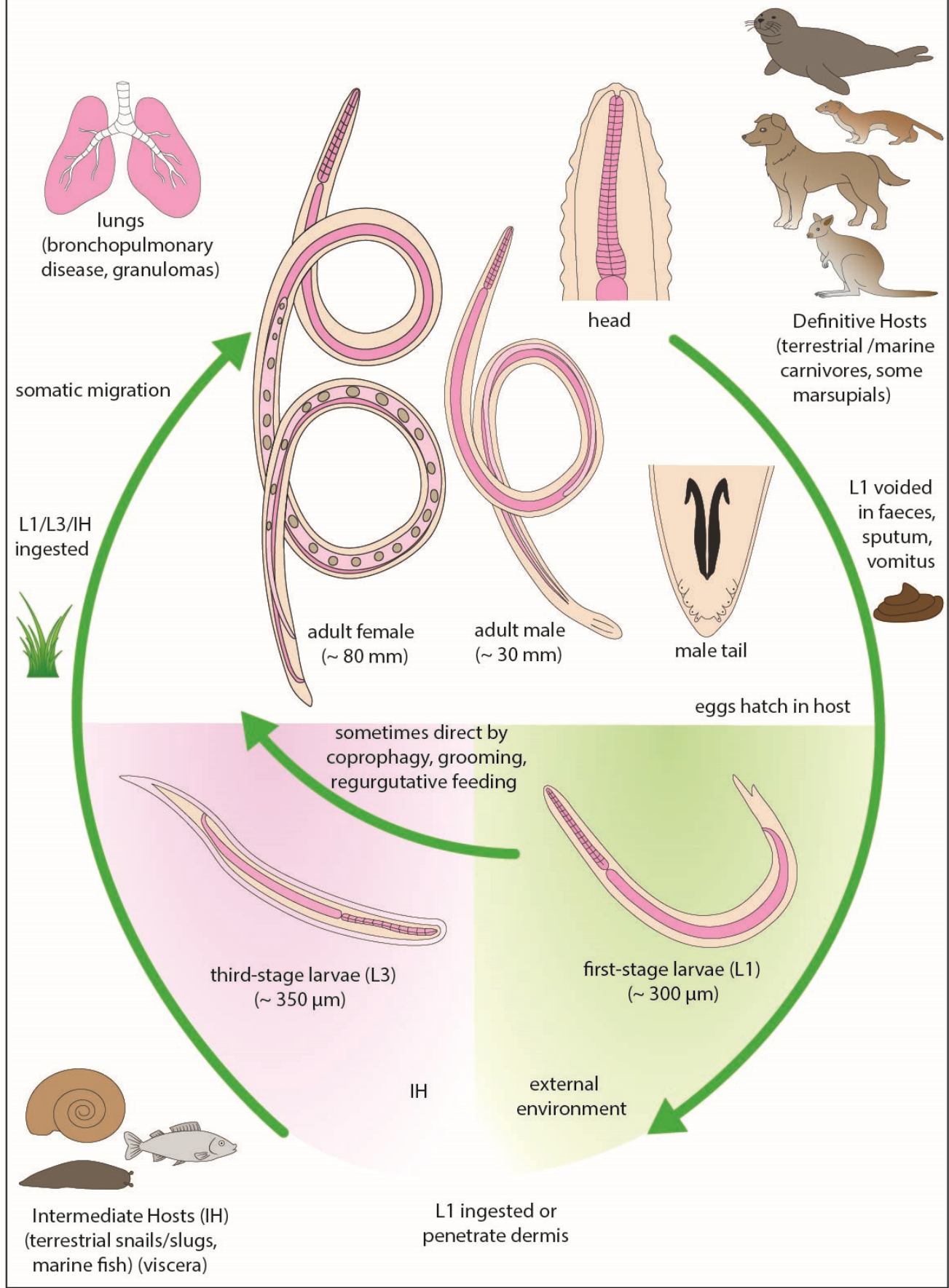
Pathogenesis: *Filaroides* infections are usually asymptomatic, often being detected incidentally during post-mortem examination of lung tissues from captive or wild animals dying of other causes. Heavy infections have been associated with bronchopulmonary disease (verminous pneumonia) in carnivores (mostly canids and pinnipeds) with sporadic chronic development over months, but overwhelming in animals that are immunologically compromised (young or immuno-suppressed individuals) or have complicating conditions (such as canine distemper, adrenal cortical carcinoma, or chronic post-operative stress). Parasites cause tissue destruction during migration and feeding and elicit strong local inflammatory responses. Worms coil into complex knots forming soft grey miliary nodular lesions distributed subpleurally and throughout the lung parenchyma. Four types of nodules may be formed: round subpleural foci 0.5-1.0 mm in diameter; round white raised foci 1-2 mm; irregular white foci 2-10 mm with grey centres; and confluent mottled white-red foci up to 14 mm. The progressively enlarging granulomatous nodules may coalesce and obstruct airflow causing nodular pneumonia with multifocal atelectasis (alveolar collapse) and emphysema as well as epithelial hyperplasia, squamous metaplasia, alveolitis, suppurative bronchiolitis, peribronchiolitis, perivasculitis, pulmonary oedema, and pleural and interstitial fibrosis. Clinical signs include spasmodic attacks of hard dry rasping coughing (precipitated by exercise or exposure to cold air), dyspnoea, tachypnoea, laboured breathing, sero-mucus nasal discharge, difficulty eating, anorexia, emaciation, malaise and death.

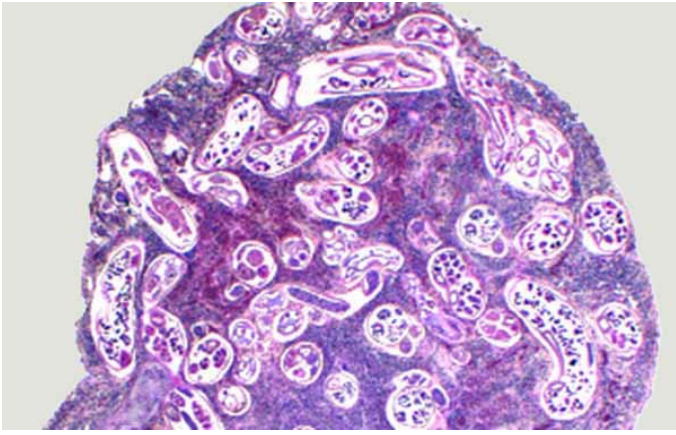
Developmental cycle and mode of transmission: These lungworms are unusual in that some have direct monoxenous life-cycles while others have indirect heteroxenous life-cycles involving intermediate hosts. Direct horizontal transmission occurs for some terrestrial species in the subgenus *F. (Filaroides)* (e.g., *F. (F.) hirthi*). Larvated eggs laid in lungs hatch releasing L1 which migrate up the respiratory tree via the mucociliary escalator and may be voided in faeces, vomitus or sputum. New final hosts become infected when they ingest infective L1 by eating fresh faeces (coprophagy) or vomitus, by regurgitative feeding (more common in some wild animals) or by their transfer in sputum during maternal grooming (licking) of pups. Ingested L1 penetrate the intestinal wall and migrate to the mesenteric lymph nodes where they moult to L2, L3 and then L4. Any of these larval stages may then migrate through the lymph nodes and liver to the lungs where they moult to subadults (often designated L5) which settle in the lung parenchyma to mature. The prepatent period (time from infection to first larval excretion) is 32-35 days, and heavy infections may develop in immuno-compromised hosts by autogenous re-infection when L1 are not excreted but re-invade tissues. In contrast, indirect cycles are exhibited by other terrestrial species in the subgenus *F. (Filaroides)* (e.g., *F. (F.) martis*) where L1 infect terrestrial and aquatic gastropods (snails and slugs) and develop to infective L3 which are consumed by mollusc-eating carnivores and become patent in 41-53 days. All species in marine pinnipeds in the subgenus *F. (Parafilaroides)* (e.g., *F. (P.) decorus*) are thought to have indirect cycles involving larval development in the mesenteries of coprophagous fishes which are subsequently eaten by piscivorous seals becoming patent after 3 weeks. Infections may remain patent for over 1 year and adult worms are thought to live for several years.

Differential diagnosis: While clinical respiratory signs (cough to pneumonia) may be suggestive of infection, they are relatively nonspecific and may be attributed to other conditions. Haematological changes often indicate neutrophilia and eosinophilia, but these are similarly nonspecific. Infections in live animals are usually diagnosed by the detection of larvae (rarely eggs) in faecal samples, often following their concentration by floatation rather than Baermann filtration as the larvae are not very active. Larvae and eggs may also be detected in sputum samples, tracheal washes or bronchial lavages. Bronchoscopy may be used to collect biopsy samples as well as to reveal nodular lesions. Thoracic radiography of verminous pneumonia often reveals diffuse infiltrates throughout the lungs, sometimes with bronchiolar nodules apparent as space-occupying masses. Infections are often diagnosed incidentally at post-mortem by the detection of worm fragments, eggs and larvae in association with nodular lesions in fresh, frozen or fixed lung tissues (sometimes in squeeze preparations from the cut surface of the lungs). Recovering intact worms by dissection is almost impossible as they are tightly knotted within host tissues. However, some success has been reported in recovering *F. Parafilaroides* lungworms in pinnipeds by mincing lung tissues in seawater and allow worms to migrate out. Molecular biological techniques have recently been used to characterize adult worms and larvae by polymerase chain reaction (PCR) amplification and sequencing of nuclear genes (18S, 5.8 S and 28S ribosomal RNA and internal transcribed spacers 1 and 2).

Treatment and control: Clinical infections in canids and pinnipeds have responded well to treatment with various anthelmintic drugs, including benzimidazoles (fenbendazole, oxfendazole, thiabendazole, albendazole), imidazothiazoles (levamisole) and macrocyclic lactones (ivermectin, doramectin), particularly when higher doses were used over extended periods. Preventive measures used in animal breeding or housing facilities include improved sanitation (regular removal of faeces), good hygiene (clean food and water), chemoprophylactic treatment (particularly pregnant and nursing bitches), quarantine and isolation (including separating pups from older infected animals, sometimes requiring hand-raising or foster-rearing), and excluding molluscs and wild animals from facilities (using chemical or physical barriers).

Filaroides





Filaroides nodule



Filaroides larva