

Cylicospirura/Cyathospirura
(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 phasmodian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including tylenchinids, rhabditinids and spirurinids. The latter contains the infraorder Spiruromorpha: an enigmatic clade linked by molecular characters, but all having indirect life-cycles involving one or more intermediate hosts, the first invariably being an arthropod. Most possess two trilobed lips (sometimes greatly reduced), a bipartite oesophagus (anterior muscular, posterior glandular) and non-bursate males with coiled tails and two dissimilar spicules. Several superfamilies are recognised: including spiroroids (with prominent lips) containing spirocercids found in the stomachs of wild carnivores and thought to be transmitted by coprophagous beetles. Infections by *Cylicospirura* and *Cyathospirura spp.* have been associated with nodular lesions in cats, dingoes, foxes and carnivorous marsupials.

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: Spirurina (mostly parasitic in vertebrate hosts)
Infraorder: Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily: Spiuroidea (two trilobed lips, oesophagus never with bulb, coiled tail in males, two unequal spicules)
Family: Spirocercidae (stout pink-red worm, well-developed buccal capsule, with 6 rudimentary lips)
Genus: *Cylicospirura* (parasitic in stomach of cats/foxes/dasyurids)
Genus: *Cyathospirura* (parasitic in stomach of cats/foxes/dasyurids)
Species: various species cause subclinical infections in carnivores

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 (some monodelphic or polydelphic) with 2 ovaries, 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.

Molecular phylogenetic studies have grouped a variety of superfamilies into the infraorder Spiruromorpha whose members are parasites of vertebrates with indirect life-cycles involving larval development within invertebrate intermediate hosts. Most members were previously classified within the order Spirurida: either within the suborder Camallanina (worms with conspicuous phasmids, uninucleate oesophageal glands, larvae without cephalic hooks, usually with copepodid intermediate hosts); or the suborder Spirurina (worms with inconspicuous phasmids, multinucleate oesophageal glands, larvae with cephalic hooks or spines, usually with non-copepodid intermediate hosts). Ten spirurid superfamilies are recognised: Gnathostomatoidea and Physalopteroidea (buccal cavity weakly cuticularized, 2 large lateral pseudolabia); Habronematoidea and Acuarioidea (buccal cavity well cuticularized, 2 large lateral pseudolabia); Filarioidea, Rictularioidea, Aproctoidea and Diplostriaenoidea (buccal cavity well cuticularized, without pseudolabia); Thelazioidea (long cylindrical buccal cavity well cuticularized, body without caudal alae); and Spiruroidea (short buccal cavity well cuticularized, body with caudal alae).

The superfamily Spiruroidea comprises worms with simple non-ornamented heads infecting the stomach (sometimes oesophagus) of mammals and birds and using arthropods as intermediate hosts for the development of distinctive larvae with conspicuous buccal capsules with a left cephalic hook and a rasp of tiny spines. Four families are recognised: Gongylonematidae (body covered with large verruciform thickenings, pseudolabia absent, oral opening octagonal with median lobes, parasites of birds and mammals); Spiruridae (body without verruciform thickenings, reduced pseudolabia, oral opening elongated with lateral elevations, buccal cavity without teeth, parasites of mammals, rarely birds); Spirocercidae (body without verruciform thickenings, reduced pseudolabia, oral opening hexagonal, buccal cavity with teeth, parasites of mammals, rarely birds); and Hartertiidae (body without verruciform thickenings, large pseudolabia subdivided into lobes, parasites of birds). The family Spirocercidae contains 3 subfamilies: Spirocercinae (lips poorly developed, not prominently raised above oral opening, pharynx without rugose or annular thickenings, parasites of mammals and birds); Ascaropsinae (lips poorly developed, not prominently raised above oral opening, pharynx with rugose or annular thickenings, parasites of mammals); and Mastophorinae (lips highly-developed forming 6

denticulate labial lobes, separate over oral opening, parasites of rodents). The subfamily Spirocercinae contains 8 genera (*Cyathospirura*, *Cylicospirura* (syn. *Petrowospirura*), *Didelphonema*, *Mazzia*, *Paraspiralatus*, *Spiralatus*, *Spirocerca* and *Vigisospirura*) which are differentiated primarily on the basis of differences in adult morphology (cephalic, cuticular and genital structures), larval morphology (anatomy and ornamentation), host occurrence/specificity, geographic distribution and transmission patterns (predation, parateny). Genera of veterinary and medical significance are tabulated below:

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Eggs	Transmission
Family: Spirocercidae (stout pink-red worm, well-developed buccal capsule, with 6 rudimentary lips)						
Subfamily: Spirocercinae (weakly-developed lips)						
<i>Cylicospirura</i> (red worm)	10	mammals	stomach	20-30 mm long, buccal capsule with 6 longitudinal ribs ending in bifid knobs, 6 teeth, bipartite oesophagus	30-40 x 15-25 µm, elongate, thick-shelled	indirect (L3 in insect IH)
<i>Cyathospirura</i> (red worm)	5	mammals	stomach	6-12 mm long, buccal capsule with 6 longitudinal ribs ending in single knob, 8 teeth, bipartite oesophagus	29-38 x 13-22 µm, ovoid, thick-shelled	indirect (L3 in insect IH)
<i>Spirocerca</i>	5	carnivores	stomach, aorta	3-8 cm long, body pink-red, buccal capsule with thick wall, 2 prominent trilobed lips, bipartite oesophagus	22-38 x 8-15 µm, elongate, thick-shelled	indirect (L3 in insect IH) [sometimes rodent, bird, reptile PH]
Subfamily: Ascaropsinae (buccal cavity with rugose or annular thickenings)						
<i>Ascarops</i> (thick stomach worm)	10	artiodactyls, rodents	stomach	10-25 mm long, oblique annuli in buccal capsule, 2 prominent trilobed lips, bipartite oesophagus	34-51 x 20-26 µm, oval, thick-shelled	indirect (L3 in insect IH) [sometimes amphibian or avian PH]
<i>Physocephalus</i> (thick stomach worm)	10	artiodactyls, rodents	stomach	6-22 mm long, transverse annuli in buccal capsule, 2 prominent trilobed lips, bipartite oesophagus	31-39 x 15-17 µm, ellipsoidal, thick-shelled	indirect (L3 in insect IH) [sometimes amphibian or avian PH]
Family: Gongylonematidae (anterior cuticle covered with large bosses or irregular scutes arranged in 8 rows)						
<i>Gongylonema</i>	46	mammals, birds	oesophagus, stomach	2-15 cm long, numerous anterior bosses, 2 prominent trilobed lips, bipartite oesophagus	40-70 x 22-35 µm, ovoid, thick-shelled	indirect (L3 in insect IH)

The genus *Cyathospirura* comprises worms whose buccal cavities have 8 teeth and 2 lobes (one ventral and one dorsal) while those of the genus *Cylicospirura* have 6 teeth but lack median lobes. Early studies recognised 3 *Cylicospirura* subgenera: namely, *C. (Cylicospirura)* (females with median vulva, males with 6 pairs of pedunculate caudal papillae (4 precloacal and 2 postcloacal) and 4 pairs of sessile papillae near tail tip, caudal end of male without spines, parasites of carnivores); *C. (Gastronodus)* (females with anterior vulva, males with 9-10 pairs of pedunculate caudal papillae (6-7 precloacal and 3 postcloacal) and 3 pairs of sessile papillae near tail tip, caudal end of male with 1 pair of spines, parasites of insectivores); and *C. (Skrjabinocercina)* (females with vulva near anus, males with 6 pairs of pedunculate caudal papillae (4 precloacal and 2 postcloacal) and 2 pairs of sessile papillae (one precloacal and one near tail tip), parasites of rodents). More recent studies, however, have elevated the latter 2 subgenera to the rank of genus, and reclassified the genus *Petrowospirura* as a subgenus of *Cylicospirura* (females with anterior vulva, males with 6 pairs of pedunculate caudal papillae (4 precloacal and 2 postcloacal), parasites of felids). Worms of both genera infect the stomach walls of carnivores (particularly canids and felids) and they are commonly found in wild animals around the world and only occasionally in domestic pets. The life-cycles of most species are not known, but are thought to involve arthropods as intermediate hosts, and possibly small vertebrates as paratenic hosts.

Parasite species	Definitive Hosts	Location [Clinical signs]	Intermediate hosts [plus Paratenic Hosts (PH)]	Distribution
Cylicospirura				
<i>C. C. advena</i>	Carnivora: felid (cat)	stomach		New Zealand
<i>C. P. barusi</i>	Carnivora: felid (cat)	stomach		India
<i>C. crocutae</i>	Carnivora: hyaenid (spotted hyena)			Africa
<i>C. felineus</i>	Carnivora: felid (cat, wildcat, bobcat, Canada lynx, leopard cat, tiger), canid (dog, Arctic fox, red fox)	stomach		worldwide
<i>C. C. heydoni</i> (syn. <i>Spirocerca</i>)	Dasyuromorphia: dasyurid (tiger quoll, eastern quoll, northern quoll, New Guinean quoll); Peramelemorphia: peramelid (northern brown bandicoot); Diprotodontia: macropodid (red-necked wallaby, red-bellied pademelon); Carnivora: felid (cat)	stomach, intestines, peritoneal cavity		Australasia
<i>C. P. lyncis</i>	Carnivora: felid (Eurasian lynx, Pallas's cat)	stomach		Russia
<i>C. pardalis</i>	Carnivora: felid (leopard)	oesophagus		Africa
<i>C. petrowi</i> (ex Matschulsky, 1952) (= <i>Skrjabinocercina</i>)	Rodentia: dipodid (Mongolian five-toed jerboa)			Russia
<i>C. P. petrowi</i> (ex Sadykhov, 1957)	Carnivora: felid (jungle cat)	stomach		Eurasia
<i>C. skrjabini</i>	Carnivora: canid (red fox, Arctic fox)	stomach		Eurasia
<i>C. G. stresseni</i> (= <i>Gastronodus</i>)	Eulipotyphla: soricid (Asian house shrew)	stomach		Asia
<i>C. subaequalis</i> (syn. <i>Spiroptera</i>)	Carnivora: felid (cougar, jaguarundi, cat, jungle cat, African wild cat, lynx, Canada lynx, leopard cat, leopard, Bengal tiger, lion), viverrid small Indian civet), canid (red fox), hyaenid (spotted hyena)	stomach		worldwide
Cyathospirura				
<i>C. chabaudi</i>	Carnivora: canid (dog)	stomach	[PH: Sauria: gekkonid (yellow-belly gecko)]	India
<i>C. chevreuxi</i>	Carnivora: felid (African wild cat, ocelot)			Africa
<i>C. grimaldiae</i>	Carnivora: canid (Atlas fox)			Africa
<i>C. noveli</i>	Carnivora: viverrid (genet)			Africa
<i>C. seurati</i> (<i>seurata</i>) (syn. <i>C. dasyuridis</i>)	Carnivora: canid (fennec fox, red fox, dog, dingo), felid (cat), viverrid (common genet), mustelid (beech marten); Dasyuromorphia: dasyurid (eastern quoll, tiger quoll, New Guinean quoll, Tasmanian devil); Rodentia: murid (black rat), cricetid (Gambian pouched rat), glirid (garden dormouse)	stomach		worldwide

Parasite morphology: Members of the genera *Cylicospirura* and *Cyathospirura* each form 3 different morphological stages during their developmental cycles: namely, eggs, larvae, and adult worms. The eggs are small thick-shelled oval-elliptical stages measuring 29-38 x 13-25 µm and are fully embryonated when laid. Larvae moult through 4 consecutive stages (designated L1 to L4) before forming adult worms. L1 are formed within worm eggs, L2 appear transiently within invertebrate intermediate hosts, L3 become encysted within the same intermediate hosts and are possibly transferred to small vertebrate paratenic hosts, while L4 appear transiently in definitive hosts prior to moulting to subadult worms. Few detailed studies have been conducted on the development of

these larval stages, so their morphometrics are relatively unknown. The L3 of some species have been described as elongate cylindrical stages measuring 1.4-1.5 mm long with weakly developed genital primordia and tapering tails terminating in groups of spines. Adults are bright red cylindrical worms measuring 6-30 mm in length with rounded heads, sometimes with small lateral alae, and short rounded tails without spines. They have thick-walled buccal capsules with rudimentary non-protruding lips and longitudinal supporting ribs terminating anteriorly in tooth-like structures with rounded knobs or pointed bifid or trifid projections. *Cyathospirura* spp. have 2 median lobes (one ventral and one dorsal) and 8 buccal teeth, while *Cylicospirura* spp. lack median lobes and have 6 buccal teeth (2 lateral and 4 submedian). Both genera possess a short pharynx without rugose or annular thickenings (which are present in the genera *Physocephalus* and *Ascarops* in the sister subfamily *Ascaropsinae*). Adult worms are sexually dimorphic, with females being larger than males (30 cf. 22 mm long). Mature female worms are didelphic with 2 ovaries and uteri connected to a common vulva located near the oesophageal-intestinal junction. Mature males possess a single testis connected to a posterior cloaca, narrow caudal alae bearing 6 pairs of pedunculate papillae (4 precloacal and 2 postcloacal) and 4 pairs of sessile papillae, a gubernaculum and 2 dissimilar spicules (left spicule 2 mm long, right spicule 0.5 mm long).

Site of infection: Adult worms infect the stomach (sometimes oesophagus) of their vertebrate hosts, often being found in fibrous nodules in the mucosa, but sometimes free in the lumen. Larval stages are thought to develop in invertebrate intermediate hosts, and encapsulated L3 have been found in the internal organs of lizards presumably acting as paratenic hosts.

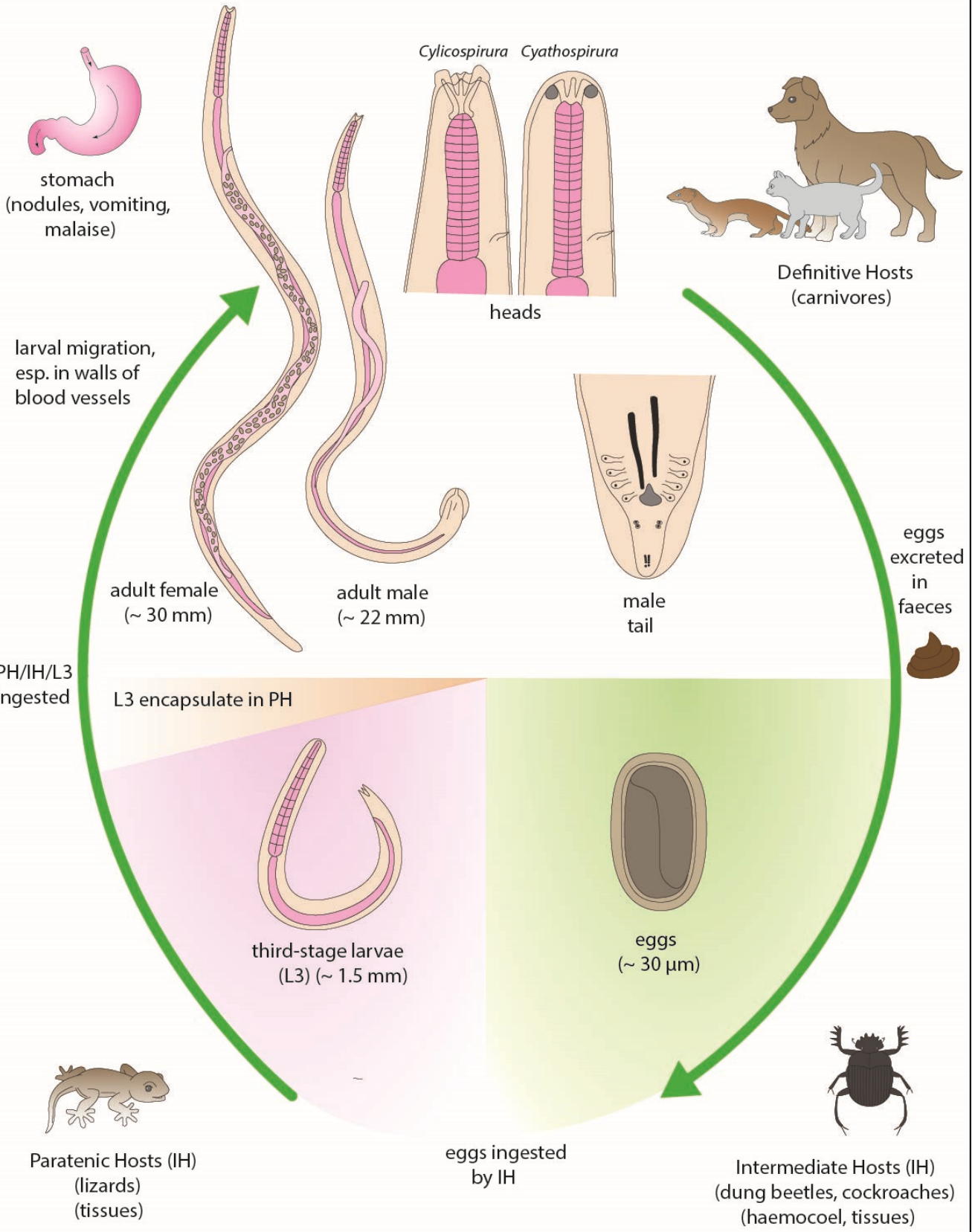
Pathogenesis: Most infections remain subclinical as either few parasites are involved or they are not highly invasive. Some species form adult worms which stay within the stomach lumen while those of other species are found coiled together within granulomatous tumour-like nodules deep in the mucosa or submucosa of the stomach, particularly along the greater curvature. The nodules ranged in size from 4-30 mm in diameter and contained up to 45 worms. Most nodules have a small central orifice from which the posterior ends of some worms protrude. Other small nodules were observed to be filled with firm yellowish caseous material. Infections have been associated with general malaise in cats, with intermittent vomiting, anorexia and weight loss, and occasionally with purulent cysts and melena, and rarely with gut perforation and septicaemia. The unique fibrous stromal reaction involved in nodule formation may cause a condition known as verminous alimentary sclerosing fibroplasia, which may be misdiagnosed as sclerosing mast cell tumours or extraneous osteosarcomas, but *Cylicospirura* nodules have not been shown to progress to neoplasms (unlike those of *Spirocerca lupi*).

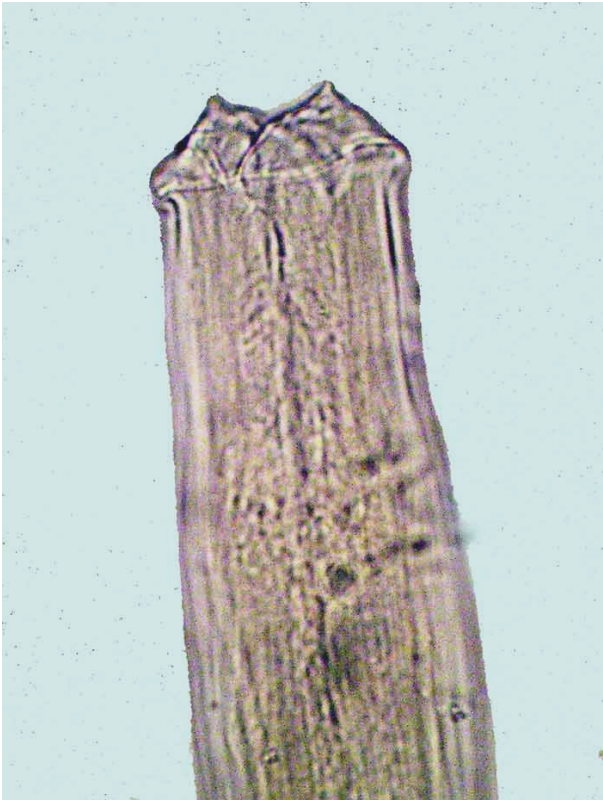
Developmental cycle and mode of transmission: While detailed life-cycle studies are lacking, these worms, like other spirocerid nematodes, are thought to have indirect heteroxenous cycles involving larval development in invertebrate intermediate hosts, and possibly larval transport in small vertebrate paratenic hosts. Gravid female worms lay embryonated eggs in the stomach of their vertebrate hosts, either directly into the lumen or through the central orifice in mucosal nodules. The eggs pass posteriad and are excreted with host faeces. It is then thought that the eggs are ingested by terrestrial insects (such as cockroaches, ground beetles and crickets) which act as intermediate hosts supporting further parasite development. Typically, eggs hatch in the arthropods releasing L1 which invade tissues and develop through 2 moults to infective L3. Paratenic transport hosts may now be involved in some cycles, as studies have found L3 encapsulated in the gut tissues of insectivorous lizards were infective to dogs resulting in the development of adult worms in 24 days. It has been speculated that a range of paratenic hosts (e.g. lizards, snakes, frogs and even small mammals such as rodents) may be involved in various cycles. The final hosts (carnivorous eutherian and metatherian mammals) become infected when they consume infective L3 contained within the tissues of intermediate or paratenic hosts. Ingested L3 do not undertake any somatic or extra-intestinal migration but develop through 2 moults to adult worms directly within the gut. The prepatent period (time from infection to first egg excretion) has been variously reported to range from 75-156 days.

Differential diagnosis: Infections are most often diagnosed by the detection of worm eggs in faecal samples, usually following their concentration by floatation in sugar or salt solutions with high specific gravities. Gastroscopy has been used to detect suspect nodular lesions in the stomach mucosa, sometimes with slender red worms extending through the central orifice. Infections may also be diagnosed at post-mortem by the detection of adult worms in the stomach lumen or mucosa. More recently, molecular biological techniques have been used to characterize parasite species by polymerase chain reaction (PCR) amplification and sequencing of mitochondrial genes (cytochrome c oxidase subunit 1).

Treatment and control: Broad-spectrum anthelmintics have been used with some success to treat infections mainly in felids, but those species in which adult worms are contained within large fibrous nodules were more resistant to treatment. Therapeutic courses of benzimidazoles (fenbendazole) and macrocyclic lactones (selamectin) were most effective, particularly when dosages were maintained by repeated or sustained applications. Various preventive strategies may be applied in peri-domestic situations (involving indoor holding facilities) to reduce contamination and transmission rates by improving sanitation and hygiene (regular removal of faeces, cleaning cages, providing clean food and water) and limiting contact with potential intermediate and paratenic hosts (reducing insect vector populations using chemicals and/or barriers, and preventing final hosts from scavenging and hunting).

Cylicospirura, Cyathospirura





Cylicospirura adult worm, head



Cylicospirura worm eggs