Dipetalonema, Acanthocheilonema
(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 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 filarioids (without lips) living in subcutaneous, intermuscular, vascular or lymphatic systems of mammals. Two main families include the oviparous filariids (lay eggs) and the ovoviviparous onchocercids (eggs hatch internally releasing pre-larvae called microfilariae). Infections by the onchocercid genera *Dipetalonema* and *Acanthocheilonema* are transmitted by fleas and ticks (in which L3 develop). Various species live in the subcutaneous tissues in wild and companion animals, but usually not in association with clinical disease.

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:	Filarioidea (tissue-dwelling filarial parasites, lack lips)
Family:	Onchocercidae (adults loose in tissues or in nodules, viviparous (live birth of microfilariae))
Genus:	*Dipetalonema, Acanthocheilonema* (parasitic in connective tissues of dogs/camelids/humans)
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 (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)]
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.

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 spirurinid 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 Diplotriaenoidea (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 Filarioidea contains long thread-like nematodes which are predominantly tissue-dwelling parasites infecting the body cavities, subcutis, intermuscular tissues, blood vessels or lymphatic systems of terrestrial hosts. These worms are known colloquially as 'filariae', 'filarids' or 'filarioids' [Note: take care with terminology as the cognate family Filariidae (esp. genus *Filaria*) are known colloquially as 'filariids', and the unrelated metastrongyle (lungworm) family Filaroididae (genus *Filaroides*) are known colloquially as 'filaroids']. Adult filariae have a cylindroid pharynx with an anterior muscular portion and a posterior glandular portion. Males often have spirally-coiled tails, well-developed alae and dissimilar spicules. Females of most species are ovoviviparous (eggs hatch within body of parent) releasing pre-larval stages known as microfilariae (sometimes sheathed). Filariae have indirect life-cycles whereby microfilariae are taken up by blood-sucking or tissue-feeding invertebrates (arthropods, esp. mosquitoes) which act as intermediate hosts for the development of infective L3 larvae. Ten families are recognised: Filariidae and Onchocercidae infecting mammals, birds, reptiles and amphibians; Setariidae infecting mammals;

Aproctidae infecting birds; and Creagrocercidae, Drilonematidae, Homungellidae, Mesidionematidae, Scolecophilidae and Ungellidae infecting terrestrial annelids. Examples of filarioid genera covered in this resource are compared in the following table.

Genus	Definitive hosts	Adults (location)	Microfilariae (location)	Periodicity	Vectors	*Wolbachia* symbiotes
Family Onchocercidae						
Dipetalonema, Acanthocheilonema (57 spp.)	primates, carnivores, ungulates, rodents, cingulates, marsupials	1-7 cm (subcutis, serosa)	85-300 µm unsheathed (blood)	-	flies, fleas, lice, ticks	absent
Dirofilaria (34 spp.)	primates, carnivores, ungulates, rodents, lagomorphs, marsupials	4-31 cm (blood vessels)	180-385 µm unsheathed (blood)	-	mosquitoes, flies	present
Onchocerca (35 spp.)	primates, carnivores, ungulates, rodents	1.5-80 cm (subcutis, ligaments)	105-440 µm unsheathed (skin)	-	flies, midges	present
Mansonella (29 spp.)	primates, carnivores, ungulates, rodents	3-8 cm (subcutis, serosa)	170-300 µm unsheathed (blood/skin)	-	midges, flies, mosquitoes	present
Wuchereria (2 spp.)	primates	2.5-10 cm (lymphatics)	210-320 µm sheathed (blood)	nocturnal, subperiodic	mosquitoes	present
Brugia (10 spp.)	primates, carnivores, rodents	1-9 cm (lymphatics)	170-380 µm sheathed (blood)	nocturnal, subperiodic	mosquitoes	present
Loa (3 spp.)	primates, ungulates, rodents	2-7 cm (subcutis, eye)	250-300 µm sheathed (blood)	diurnal	flies	absent
Family Filariidae						
Parafilaria (4 spp.)	ungulates	2-7 cm (subcutis)	40-58 x 23-33 µm larvated eggs (skin)	diurnal	flies	absent
Stephanofilaria (7 spp.)	ungulates	0.2-1.4 cm (subcutis)	45-195 µm sheathed (skin)	-	flies	absent
Family Setariidae						
Setaria (42 spp.)	primates, ungulates, rodents, lagomorphs	4-19 cm (body cavities)	140-310 µm sheathed (blood)	-	mosquitoes	absent

Members of the family Onchocercidae form adult worms that live loose in body cavities or in tissue nodules. Female worms release microfilariae which disperse into the blood or dermal connective tissues (unlike filariids which live in the skin close to where they deposit eggs or larvae). Some 88 onchocercid genera are divided into 7 subfamilies: Onchocercinae and Dirofilariinae (syn. Loainae) mostly in mammals but some in birds and reptiles, Waltonellinae and Icosiellinae in amphibians, Oswaldofilariinae in reptiles, Splendidofilariinae and Lemdaninae in birds, reptiles and mammals (former subfamily Setariinae in large mammals recently elevated to family status as Setariidae). Members of the subfamily Onchocercinae are characterised as forming males with markedly dissimilar spicules and long tails lacking caudal alae (while members of the subfamily Dirofilariinae form males with highly developed caudal alae). Some 43 genera occur in the subfamily Onchocercinae: namely, *Acanthocheilonema, Ackertia*, *Agamofilaria*, *Andersonfilaria*, *Bisbalia*, *Breinlia* (incl. *Johnstonema*), *Brugia*, *Cercopithifilaria*, *Chabfilaria*, *Cherylia*, *Courduriella*, *Cruorifilaria*, *Cystofilaria*, *Deraiophoronema*, *Dessetfilaria*, *Dipetalonema*, *Elaeophora* (syn. *Cordophilus*, *Alcefilaria*), *Filarissima*, *Fuscicorpa*, *Josefilaria*, *Litomosa*, *Litomosoides* (syn. *Vestibulosetariam Finlaynema*), *Mansonella*,

Microfilaria, *Migonella*, *Molossinema*, *Monanema*, *Onchocerca* (syn. *Wehrdikmansia*, *Acanthospiculum*), *Paramadochotera*, *Paraochoterenella*, *Paraprocta*, *Paulianfilaria*, *Pseudolitomosa*, *Rumenfilaria*, *Sandnema, Serofilaria*, *Skrjabinofilaria* (syn. *Cortiamosoides*), *Sprattia, Strianema*, *Wuchereria* and *Yatesia* in mammals, *Struthiofilaria* in birds, and *Macdonaldius* (syn. *Saurofilaria*) in reptiles.

Adult *Dipetalonema* worms are long and slender with a thick transparent cuticle and a slightly bulbous head bearing 4 pairs of papillae and conspicuous amphids and a tail with 3-4 conical petals. Gravid females release unsheathed microfilaria into the blood and/or skin where they are taken up by a variety of haematophagous arthropod intermediate hosts (mosquitoes, flies, fleas, lice and ticks) in which larval stages develop mostly in the fat body. Many *Dipetalonema* spp. have previously been described, but almost half have been reassigned to other genera (notably *Breinlia* and *Sprattia* in Australian marsupials; *Skrjabinofilaria* in American marsupials; *Ackertia, Filarissima* and *Monanema* in rodents; *Macdonaldius* in American reptiles) and the remainder placed in several *Dipetalonema* subgenera (*D.* (*Orihelia*) and *D*. (*Dasypafilaria*) in cingulates; *D.* (*Molinema*) in rodents; *D.* (*Loxodontofilaria*) in African ungulates; *D.* (*Chenofilaria*) in Asiatic pholidotids and Australian marsupials; *D.* (*Dipetalonema*) and *D.* (*Yatesia* syn. *Alafilaria*) in primates and rodents; and *D.* (*Acanthocheilonema*) in insectivores, carnivores, pinnipeds and some rodents). Various authorities have elevated many of these subgenera to generic status causing considerable taxonomic confusion; which hopefully will be unravelled in the future by careful molecular and ultrastructural studies. Notwithstanding, most authorities now recognize *Acanthocheilonema* (syn. *Skrjabinaria*, *Monnigofilaria*, *Hepaticofilaria*) as a separate genus from *Dipetalonema*. In particular, the species *Acanthocheilonema reconditum* commonly found in dogs is often still reported under its older name *Dipetalonema reconditum* in many veterinary texts. While this species rarely causes clinical infections, its microfilariae may sometimes be confused with those of canine heartworm (*Dirofilaria immitis*). Another species in rodents, *Acanthocheilonema viteae* (previously *Dipetalonema viteae*), has often been used as a model to study human filarial infections.

Parasite species	Definitive Hosts (DH)	Location	Intermediate Hosts/Vectors (IH)	Distribution
***Dipetalonema* (*Dipetalonema*)** **[**cephalic extremity laterally expanded, oesophagus divided, gubernaculum present, microfilaria sheathed, parasitic in American primates]				
D. D. caudispina (syn. *D.* (*Alafilaria*))	Primates: atelid (Geoffroy's spider monkey, Guiana spider monkey, southern muriqui, brown woolly monkey, Venezuelan red howler), cebid (white-fronted capuchin, black-capped squirrel monkey, common squirrel monkey), aotid (Spix's night monkey), callitrichid (golden lion tamarin)	abdominal and thoracic cavities	Diptera: ceratopogonid (*Culicoides hollensis*)	South America
D. D. freitasi	Primates: cebid (white-faced capuchin)			South America
D. D. gracile	Primates: atelid (Geoffroy's spider monkey, Guiana spider monkey, black-headed spider monkey, Peruvian spider monkey, brown woolly monkey, southern muriqui), callitrichid (common marmoset, moustached tamarin, pied tamarin, black mantled tamarin, black lion tamarin, golden lion tamarin), cebid (black-capped capuchin, Azarae's capuchin, white-faced capuchin, Humboldt's white-fronted capuchin, gracile capuchin, wedge-capped capuchin, common squirrel monkey, Central American squirrel monkey), aotid (gray-bellied night monkey)	abdominal cavity, microfilariae in blood	Diptera: culicid (*Aedes aegypti*), ceratopogonid (*Culicoides hollensis*)	Americas
D. D. graciliformis	Primates: callitrichid (red-handed tamarin, moustached tamarin)			South America
D. D. robini	Primates: cebid (common squirrel monkey, black-capped squirrel monkey)		Diptera: culicid (*Aedes aegypti*)	South America
D. D. yatesi	Primates: atelid (Peruvian spider monkey)			South America

***Dipetalonema* (*Orihelia*)** [cephalic shield laterally elongated, tail with 2 lappets, oesophagus divided, gubernaculum present, microfilaria sheathed, parasitic in cingulates]				
D. O. anticlava (syn. *Acanthocheilonema, A. tatusi*)	Cingulata: chlamyphorid (screaming hairy armadillo, six-banded armadillo, southern three-banded armadillo), dasypodid (southern long-nosed armadillo)	peritoneum		South America
***Dipetalonema* (*Molinema*)** [cepahlic extremity flat or concave in lateral view, oesophagus divided, gubernaculum absent, microfilaria unsheathed, parasitic in rodents]				
D. M. arbuta	Rodentia: erethizontid (North American porcupine); Primates: hominid (human)	peritoneal cavity	Diptera: culicid (*Aedes aegypti, canadensis, cinereus, euedes, excrucians, fitchii, stimulans, vexans, Taeniorhynchus perturbans*)	North America
D. M. bifida	Rodentia: echimyid (Atlantic bamboo rat)	body cavity		South America
D. M. dessatae	Rodentia: echimyid (Guyenne spiny rat)	abdominal cavity	Diptera: culicid (*Anopheles stephensi*)	South America
D. M. diacantha (syn. *Filaria, Acanthocheilonema*)	Rodentia: erethizontid (Rothschild's porcupine, Brazilian porcupine, Paraguayan hairy dwarf porcupine), echimyid (red-crested tree-rat)	body cavity		South America
D. M. proechimyis	Rodentia: echimyid (Guyenne spiny rat)	body cavity		South America
D. M. raposoensis	Rodentia: echimyid (Tome's spiny rat)	body cavity		Central America
D. M. sprenti	Rodentia: castorid (North American beaver); Primates: hominid (human)	peritoneal, pleural and pericardial cavities	Diptera: culicid (*Aedes abserratus, intrudens*)	North America
D. M. travassosi	Rodentia: echimyid (coypu)	body cavity		South America
M. algardneri	Rodentia: echimyid (Napo spiny rat)	body cavity		South America
M. barbarae	Rodentia: echimyid (Guyenne spiny rat)	body cavity		South America
M. peruviensis	Rodentia: echimyid (Steere's spiny rat)	body cavity		South America
M. nattereri	Rodentia: echimyid (Brazilian spiny tree rat)	body cavity		South America
***Dipetalonema* (*Loxodontofilaria*)** [oesophagus undivided, gubernaculum absent, microfilariae unsheathed, parasitic in African ungulates]				
D. L. asiatica	Proboscidea: elephantid (Indian elephant)	unknown		Burma
D. L. caprini	Artiodactyla: bovid (Japanese serow)			Japan
D. L. faini	Artiodactyla: bovid (black-fronted duiker)	abdomen		Africa
D. L. gossi	Proboscidea: elephantid (African bush elephant)	portal veins		Africa
D. L. hippopotami	Artiodactyla: hippopotamid (hippopotamus)	abdominal cavity		Africa
D. L. loxodontis	Proboscidea: elephantid (African elephant)			Africa
D. L. okapiae sp. inq.	Artiodactyla: giraffid (okapi)			Africa
D. L. ruandae	Artiodactyla: bovid (cattle)	oesophageal connective tissue		Africa
***Dipetalonema* (*Chenofilaria*)**				

[body slightly expanded laterally behind cephalic extremity, oesophagus divided or undivided, gubernaculum absent, microfilaria unsheathed, parasitic in Asiatic pholidotids and Australian marsupials]				
D. C. filaria (syn. *D. fausti, Acanthocheilonema*)	Pholidota: manid (Chinese pangolin)	cystic pockets of intrahepatic portal system		China
D. C. johnstoni (syn. *Breinlia*, *D. lutreoli*) (now possibly *Cercopithifilaria*?)	Rodentia: murid (bush rat, Australian swamp rat, giant white-tailed rat); Peramelemorphia: peramelid (eastern barred bandicoot, long-nosed bandicoot, northern brown bandicoot, southern brown bandicoot); Diprotodontia: pseudocheirid (greater glider); Dasyuromorphia: dasyurid (Tasmanian devil)	subcutaneous and intermuscular connective tissues, mf in skin, lymphatics, occasionally in blood (unsheathed)	Ixodida: ixodid (*Ixodes trichosura, facialis, holocyclus, tasmani*)	Australia
D. C. japonica	Carnivora: ursid (Japanese black bear)	subcutaneous tissue		Japan
D. C. pearsoni (now possibly *Cercopithifilaria*?)	Peramelemorphia: peramelid (northern brown bandicoot)	subcutaneous connective tissue		Australia
***Dipetalonema* (*Dasypafilaria*)** [cephalic shield laterally elongated, tail with 2 lappets, oesophagus divided, gubernaculum absent, sheathed microfilariae, parasitic in armadillo]				
D. D. averyi	Cingulata: dasypodid (nine-banded armadillo)	omentum		North America
***Dipetalonema* (*Yatesia = Alafilaria*)** [cephalic shield rectangular, divided oesophagus, gubernaculum absent, microfilaria unsheathed, parasitic in capybara]				
D. Y. hydrochoerus	Rodentia: caviid (capybara)	skeletal muscle fascia	Ixodida: ixodid (*Amblyomma americanum, cajennense*)	South America
Acanthocheilonema, sometimes reported as ***Dipetalonema* (*Acanthocheilonema*)** [cephalic extremity flat or convex in lateral view, oesophagus divided, gubernaculum absent, microfilaria unsheathed, parasitic in insectivores, carnivores, pinnipeds and some rodents]				
A. didelphis (syn. *Dipetalonema, Cercopithifilaria*)	Didelphimorphia: didelphid (common opossum, Virginia opossum)	subcutaneous and perioesophageal tissues		Americas
A. delicata	Carnivora: mustelid (Japanese badger)	subcutaneous tissues		Japan
A. dracunculoides (syn. *Dipetalonema*)	Carnivora: canid (dog, red fox), hyaenid (spotted hyaena, aardwolf)	peritoneal cavity, microfilariae in blood (unsheathed)	Diptera: hippoboscid (*Hippobosca longipennis*); Ixodida: ixodid (*Rhipicephalus sanguineus*)	Eurasia, Africa
A. finlayi (syn. *Dipetalonema, Ackertia*)	Rodentia: chinchillid (northern viscacha)	peritoneal cavity		South America
A. mansonbahri (syn. *Dipetalonema*)	Rodentia: petetid (East African springhare)	subcutaneous tissue and fascia	Siphonaptera: pulicid (*Delopsylla crassipes, Ctenocephalides felis, Xenopsylla cheopis*)	Africa
A. mephitis (syn. *Dipetalonema*)	Carnivora: mephitid (striped skunk)			North America
A. odendhali (syn. *Dipetalonema*)	Carnivora: phocid (harbour seal), otariid (California sea lion, northern fur seal)	intermuscular fascia		North America
A. pachycephalum (syn. *Dipetalonema*)	Carnivora: mustelid (African striped weasel)			Africa
A. pricei (syn. *Dipetalonema, Skrjabinofilaria*)	Didelphimorphia: didelphid (big-eared opossum, Virginia opossum)	subcutaneous tissues		Americas
A. procyonis	Carnivora: procyonid (raccoon)	subcutaneous tissues		North America
A. reconditum	Carnivora: canid (dog, red fox,	subcutaneous	Siphonaptera: pulicid	Africa,

(syn. *Dipetalonema*)	jackal), hyaenid (hyaena); Artiodactyla: bovid (blackbuck)	connective tissue, body cavity, microfilariae in blood subcutaneous tissues, body cavity, kidneys	(*Ctenocephalides canis*, *felis, Pulex irritans, simulans, Echidnophaga gallinacea*); Phthiraptera: boopid (*Heterodoxus spiniger*), haematopinid (*Haematopinus*), lonognathid (*Linognathus setosus*); Ixodida: ixodid (*Rhipicephalus sanguineus*); Diptera: culicid (*Culex*)	Europe, Americas
A. sabanicolae	Cingulata: dasypodid (Llanos long-nosed armadillo)	subcutaneous tissue		South America
A. setariosa (syn. *Dipetalonema setariosum*)	Rodentia: murid (Libyan jird); Carnivora: herpestid (mongoose)	pleural cavity		North and East Africa
A. spirocauda (seal heartworm) (syn. *Dipetalonema*)	Carnivora: phocid (hooded seal, harp seal, bearded seal, ringed seal, common seal, ribbon seal, spotted seal, harbour seal), odobenid (walrus)	heart (right ventricle), pulmonary arteries	Phthiraptera: echinophthiriid (*Echinophthirius horridus*)	Northern Hemisphere
A. viteae (syn. *Dipetalonema*)	Rodentia: murid (wood mouse, brown spiny mouse, southern multimammate mouse, Natal multimammate mouse, striped field mouse, Libyan jird, Shaw's jird, Mongolian gerbil, soft-furred rat), cricetid (golden hamster, Campbell's dwarf hamster), dipodid (greater Egyptian jerboa)	subcutaneous tissues, fascia, body cavities	Ixodida: argasid (*Ornithodoros moubata, O. tartakovskyi*)	Asia, Africa
A. weissi (syn. *Dipetalonema*)	Macroscelidea: macroscelid (North African elephant-shrew)	peritoneum, subcutaneous tissues	Ixodida: argasid (*Ornithodoros erraticus*)	North Africa
Other reports				
D. boltoni (now *Breinlia*)	Diprotodontia: macropodid (agile wallaby)	peritoneal cavity		Australia
D. capilliforme (syn. *Breinlia*) (now *Sprattia*)	Dasyuromorphia: dasyurid (northern quoll)	hepatic venous spaces, mesenteric and portal veins		Australia
D. cephalophi (now *Cercopithifilaria*)	Artiodactyla: bovid (bay duiker)	subcutaneous tissue		Africa
D. dasyuri (now *Breinlia*)	Dasyuromorphia: dasyurid (eastern quoll, tiger quoll)	peritoneal cavity		Australia
D. degraaffi (now *Cercopithifilaria*)	Primates: cercopithecid (Chacma baboon)	subcutaneous tissue		Africa
D. dendrolagi (syn. *Breinlia*)	Diprotodontia: macropodid (grizzled tree-kangaroo)	peritoneal cavity		New Guinea
D. dentonensis (now *Breinlia*)	Diprotodontia: macropodid (eastern grey kangaroo, red kangaroo)	subcutaneous connective tissue		Australia
D. dermicola	Artiodactyla: bovid (cattle)	skin		Africa
D. evansi (syn. *D. cameli*) (now *Deraiophoronema*)	Artiodactyla: camelid (camel, dromedary); Perissodactyla: equid (horse)	pulmonary and testicular arteries, lymph spaces and nodes, microfilariae in blood (sheathed)	Diptera: culicid (*Aedes caspius*)	North Africa, Eastern Russia, Asia, Australia
D. freitaslenti (syn. *Bostrichodera, Deraiophoronema*)	Pilosa: myrmecophagid (giant anteater)	mesentery		South America
D. gabonensis	Rodentia: hystricid (African brush-	subcutaneous tissue		Africa

(now *Cercopithifilaria*)	tailed porcupine)			
D. grassi sp. inq. (syn. *Acanthocheilonema*) (now *Cercopithifilaria*)	Carnivora: canid (dog)	subcutaneous tissues	Ixodida: ixodid (*Rhipicephalus sanguineus*)	Southern Europe, Africa
D. herpestis	Carnivora: herpestid (mongoose)	peritoneal cavity		India
D. interstitium	Rodentia: sciurid (Sherman's fox squirrel, eastern gray squirrel)	subcutaneous tissue		North America
D. kenyensis (now *Cercopithifilaria*)	Primates: cercopithecid (olive baboon)	subcutaneous tissue		Africa
D. laemmleri	Rodentia: sciurid (Hodgson's giant flying squirrel)			India
D. macropi (now *Breinlia*)	Diprotodontia: macropodid (quokka)	peritoneal cavity		Australia
D. marmosetae (now *Mansonella* (*Tetrapetalonema*))	Primates: callitrichid (white-footed tamarin)			South America
D. mundayi (now *Breinlia*)	Diprotodontia: macropodid (red-necked wallaby)	pericardium		Australia
D. petteri sp. inq.	Primates: lemurid (black lemur)			Madagascar
D. pseudocheiri (now *Breinlia*)	Diprotodontia: pseudocheirid (common ringtail possum)	peritoneal cavity		Australia
D. rarum	Diprotodontia: macropodid (bridled nail-tail wallaby)	subcutaneous tissues		Australia
D. robertsi (syn. *D. australiense, D. tenue, Breinlia tenuis*)	Diprotodontia: macropodid (common wallaroo, eastern grey kangaroo, red kangaroo)	peritoneal cavity		Australia
D. rugosicauda (syn. *D.* (*Orihelia*), *Wehrdikmansia*) (now *Cercopithifilaria*)	Artiodactyla: cervid (roe deer)	microfilariae in subcutis (sheathed)	Ixodida: ixodid (*Ixodes ricinus*)	Europe, America
D. schneideri (now *Elaeophora*)	Artiodactyla: cervid (mule deer, black-tailed deer, elk/wapiti, moose, sika deer), bovid (sheep, goat)	arteries, cornea (migrating larvae may cause neurological signs), microfilariae in skin and capillary beds	Diptera: tabanid (*Hybomitra aatos, laticornis, osburni, phaenops, procyon, rupestris, tetrica, Tabanus abditus, eurycerus, gilanus, lineola, monsensis, nigrovittatus, punctifer, subsimilis, stoni, Silvius quadrivittatus*)	North America
D. spelaea (syn. *D. australe, Filaria, F. australis, Setaria, Acanthocheilonema*) (now *Breinlia*)	Diprotodontia: macropodid (brush-tailed rock-wallaby, Bennett's tree-kangaroo?)	peritoneal cavity		Australia
D. spiralis (syn. *D. spirale, Deraiophoronema*) (now *Bostrichodera*)	Pilosa: choloepodid (Linnaeus's two-toed sloth)			South America
D. thylogali (syn. *Breinlia*)	Diprotodontia: macropodid (red-legged pademelon, Tasmanian pademelon)	peritoneal and pleural cavities		Australia
D. trichosuri (syn. *Filaria,*	Diprotodontia: phalangerid (common brushtail possum)	peritoneal cavity		Australia

Acanthocheilonema australe) (now *Breinlia*)				
D. venacavincola (now *Sprattia*)	Diprotodontia: phalangerid (short-eared possum)	vena cava and hepatic veins, microfilariae in blood (sheathed)		Australia
Species assigned to *Johnstonema* (now considered to be a subgenus in the genus *Breinlia*)				
J. andersoni (now *Breinlia*)	Diprotodontia: macropodid (red kangaroo, eastern grey kangaroo, common wallaroo, swamp wallaby)	subcutaneous connective tissue		Australia
J. annulipapillatum (syn. *Dipetalonema*) (now *Breinlia*)	Diprotodontia: macropodid (black-striped wallaby, bridled nail-tail wallaby, swamp wallaby)	subcutaneous tissue, knee joint, body cavity?		Australia
J. woerlei (now *Breinlia*)	Diprotodontia: macropodid (short-eared rock-wallaby)	heart		Australia

Parasite morphology: These filarial worms produce 3 different morphological stages in their developmental cycles: adult worms; pre-larvae (microfilariae); and 4 consecutive larval stages (termed L1-4). Female worms produce and release unsheathed microfilariae which make their way into the vertebrate host circulation. The microfilariae are elongate and range considerably in size (85-300 x 4-6 µm) depending on species: most being moderate ranging from 250-300 µm in length (e.g. *Acanthocheilonema reconditum, A. mansonbahri, A. spirocauda, Dipetalonema dracunculoides, D. schneideri*); several being smaller ranging from 170-205 µm (e.g. *A. viteae*); and a few being comparatively tiny ranging from 85-130 µm (e.g. *D. gracile*). Microfilariae have a blunt-to-conical conical anterior end, most bearing a cephalic hook, and they often have attenuated pointed tails (e.g. *A. mansonbahri*), sometimes blunt (e.g. *D. schneideri*), often hooked (e.g. *A. reconditum*), sometimes straight (e.g. *D. dracunculoides*). [In comparison, *Dirofilaria* microfilariae are slightly larger (260-330 µm) and have straight, pointed filamentous tails.] *Dipetalonema* and *Acanthocheilonema* spp. form 3 larval stages in their arthropod vectors: first-stage larvae (L1) measuring 350-400 µm in length; second-stage-larvae (L2) 400-700 µm; and third-stage larvae (L3) growing up to 5.9 mm in length and distinguished by tails with a terminal cone-shaped structure flanked by 2 small dorsoventral projections. Adult worms are slender and elongate measuring up to 40 mm in length and are surrounded by a thick white-to-transparent cuticle, sometimes with striations. Adults have a slightly bulbous head bearing 4 pairs of papillae and conspicuous amphids, a small buccal capsule (buccal ring), an oesophagus with a well-developed glandular portion, and tails with 10 pairs of caudal papillae and 3 caudal lappets. Mature worms are sexually dimorphic, with female worms being larger than males (e.g. *A. reconditum* females 20-36 mm x 70-205 µm, males 9-17 mm x 70-133 µm; *A. dracunculoides* females 30-60 mm x 100-370 µm, males 13-31 mm x 100-310 µm; *A. sabanicolae* females 25-31 mm x 61-78 µm, males 11-15 mm x 42-44 µm; *A. vitae* females 49-72 mm x 230-350 µm, male 38-41 mm x 150-170 µm). Males have a long spiral tail with caudal alae and less than 5 large pedunculate precloacal papillae (cf. *Dirofilaria* which have short tails with 5 or more large pedunculate precloacal papillae). Mature males have 2 unequal dissimilar copulatory spicules: in *Acanthocheilonema* the right spicule is stout and curved and the left spicule has a slender and pointed distal third, while in *Dipetalonema* the right spicule is long and slender and the long left spicule has a slender distal half. Female worms have 2 ovaries with oviducts and uteri terminating in a common vagina opening into a vulva (located anteriorly around the oesophageal level but posterior to the nerve ring). Gravid females are ovoviviparous and release live young (microfilaria).

Site of infection: Adult worms live in the subcutaneous tissues or body cavities of their mammalian (definitive) hosts and their unsheathed microfilariae are found in peripheral blood. Larval developmental stages occur mainly in the fat body and sometimes the muscles of their arthropod (intermediate) hosts).

Pathogenesis: Infections are generally asymptomatic and rarely cause clinical disease. However, heavy infections by adult *A. reconditum* have been associated with subcutaneous nodule formation, pruritus, alopecia and dermal abrasions in dogs, adult *D. evansi* with arteriosclerosis, cardiac insufficiency and emaciation in camels, adult *D. johnstoni* with skin and ocular lesions in Australian marsupials, and migrating larvae of *D. schneideri* may cause neurological signs, allergic responses, vascular lesions, dermatitis, ischaemia necrosis and blindness in deer. It is often difficult to determine the pathogenicity of *Dipetalonema* and *Acanthocheilonema* infections as concurrent infections with other parasites generally occur. To date, no endosymbiotic *Wolbachia* bacteria have been found in these filarial worms, but molecular studies have detected *Wolbachia*-like sequences in their genomes suggesting prior acquisition and subsequent loss.

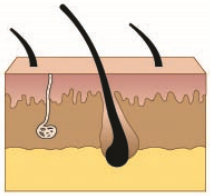
Developmental cycle and mode of transmission: *Dipetalonema* and *Acanthocheilonema* spp. have indirect heteroxenous life-cycles involving the development of adult worms in mammalian definitive hosts and larval stages in arthropod intermediate hosts. Transmission occurs when the arthropods feed on mammalian blood: vectors becoming infected when they ingest microfilariae with their blood meals; and mammals becoming infected when infective larvae are introduced during vector feeding. Unlike other filarial

worms, a broad range of haematophagous vectors may act as intermediate hosts, including insects (flies, mosquitoes, fleas, lice) and acari (ticks). Ingested microfilariae penetrate the gut and invade the fat body, sometimes the muscles, where they moult twice over 7-10 days to form third-stage larvae (L3) which are found in the haemocoel 15-20 days after infection. Larval development took longer in ticks and in vectors held at lower ambient temperatures (e.g. 54-67 days at 20°C). Mammals become infected when the relatively large L3 escape from the vector mouthparts during feeding and invade the bite site (contaminative transmission rather than inoculative salivary transmission). The larvae moult twice and form adults in the subcutaneous tissues and/or body cavities where they mature and mate. The prepatent period (time from infection to first detection of microfilariae) ranges from 45-126 days depending on species. Adult worms of *A. viteae* were found to live for up to 2 years, but it was noted that frequent matings were required to maintain continuous fertility.

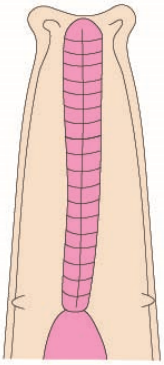
Differential diagnosis: Most infections are diagnosed serendipitously when unsheathed microfilariae are detected microscopically in blood samples, either in wet preparations coloured with methylene blue or cresyl blue, fixed thick or thin blood smears stained with Giemsa or haematoxylin, or in concentrates obtained by membrane filtration (5 µm pore size) or centrifugation (following saponin or formalin erythrolysis). The microfilariae are distinguished from those of other filarial worms by their moderate size, curved bodies with blunt heads and often hooked tails and by their progressive movement in wet preparations (in contrast, *Dirofilaria immitis* microfilariae have larger straight bodies with tapered heads and pointed tails and they exhibit nonprogressive (stationary) movement in wet preparations). Nonetheless, microscopic differentiation of microfilariae can sometimes be difficult due to morphological variation, especially in mixed infections. Occasionally, adult worms, or fragments thereof, may be detected in biopsies of skin nodules or incidentally during surgery or necropsy. No immunoserological tests have been developed to specifically detect *Dipetalonema/Acanthocheilonema* infections, even though little cross-reactivity was observed in tests for *Dirofilaria immitis* in dogs. More recently, molecular biological techniques have been used to detect parasite DNA in clinical samples following the polymerase chain reaction (PCR) amplification of specific gene sequences, notably internal transcribed spacer (ITS) regions of ribosomal RNA.

Treatment and control: A range of anthelmintic drugs have been used to treat the small number of symptomatic infections detected in mammalian hosts, mostly carnivores with cutaneous manifestations due to adult worms or herbivores with neurological complications due to migrating larvae. Treatment with diethylenediamine (diethylcarbamazine), macrocyclic lactones (ivermectin, doramectin, selamectin, moxidectin) and benzimidazole-methylcarbamates (mebendazole) have been found to be effective against microfilariae. While it is not known whether such treatment killed adult worms, in many cases they were effectively sterilized and no longer produced microfilariae. The prevention of infections centres around vector control, with various insecticides and acaricides used to reduce vector populations, improved sanitation and environmental hygiene used to eliminate breeding sites, and physical and chemical barriers used to protect hosts from vector bites.

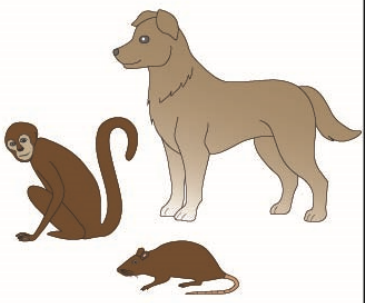
Dipetalonema, Acanthocheilonema



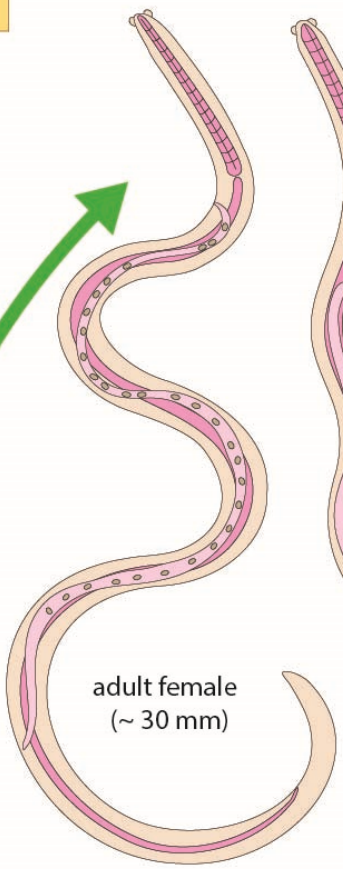
subcutis, serosa
(inflammation,
oedema,
macules)



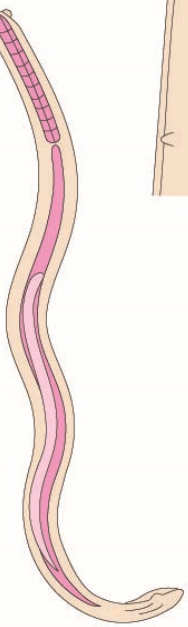
head



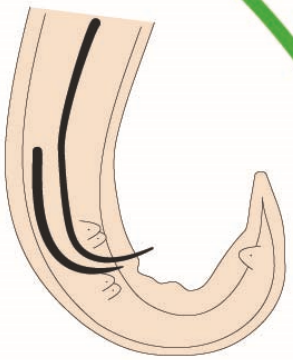
Definitive Hosts
(primates, carnivores,
ungulates, rodents,
marsupuials)



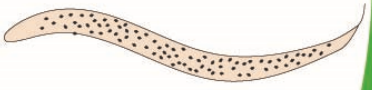
adult female
(~ 30 mm)



adult male
(~ 10 mm)



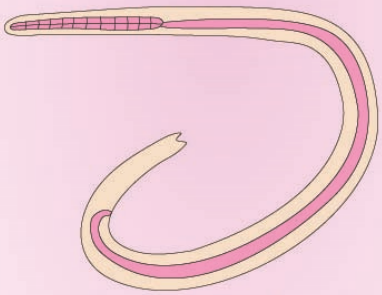
male tail (lateral)



microfilariae (mf) (~ 250 µm)
(released into blood)

L3
deposited
on skin

mf
ingested

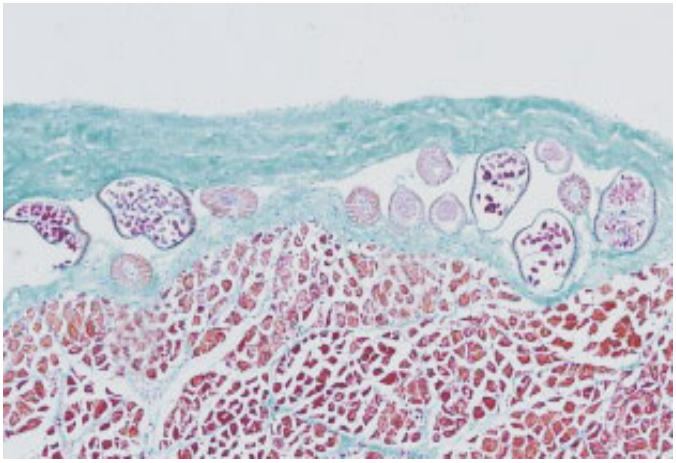


third-stage larvae
(L3) (~ 4 mm)

Intermediate Hosts (IH)
(fleas, ticks, mosquitoes)
(fat bodies, muscles, then mouthparts)

vector-borne transmission

Dipetalonema adult worms



Dipetalonema in section through skin

Dipetalonema microfilaria