Setaria
(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 genus *Setaria* are transmitted by mosquitoes and cause asymptomatic infections of the body cavities of cattle and deer, but neurological signs when ectopic.

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:	*Setaria* (parasitic in peritoneum/eye/scrotum of sheep/cattle/horses, mosquito IH)
Species:	various species cause neurological signs in cattle

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 Setariidae						
Setaria (42 spp.)	primates, ungulates, rodents, lagomorphs	4-19 cm (body cavities)	140-310 µm sheathed (blood)	-	mosquitoes	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 Onchocercidae						
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
Dirofilaria (34 spp.)	primates, carnivores, ungulates, rodents, lagomorphs, marsupials	4-31 cm (blood vessels)	180-385 µm unsheathed (blood)	-	mosquitoes, flies	present
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
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

Members of the family Setariidae (formerly classified as the subfamily Setariinae in the family Onchocercidae) typically form medium to large worms in the abdominal cavities of mammals. Three genera are recognised: *Chabfilaria* in edentates, *Setaria* (syn. *Hyraconema*, *Artionema*) in ungulates and hyracoids, and *Papillosetaria* in ungulates. Adult worms have complex cephalic structures (spines, ridges or shield-like thickenings), sclerotized buccal capsules with thin peribuccal rings, and tails with conspicuous conical lappets. Females have a complex vagina and an anterior vulva through which they birth sheathed microfilariae which are transmitted by mosquitoes. Over 40 *Setaria* spp. have been described throughout the world from domestic and wild artiodactyls (mostly bovids and cervids) and perissodactyls (mainly equids). Heavy infections by larvae may cause cerebrospinal filariasis with neurological disorders, resulting in considerable economic losses to some livestock industries.

***Setaria* species**	**Definitive Hosts (DH)**	**Location**	**Vectors/Intermediate Hosts (IH)**	**Distribution**
S. africana	Perissodactyla: rhinocerotid (black rhinoceros); Artiodactyla: bovid (African buffalo, great eland, greater kudu, harnessed bushbuck, common duiker, grey duiker)			Africa
S. bernardi	Artiodactyla: suid (pig)			?
S. bicoronata	Artiodactyla: bovid (Soemmering's gazelle, waterbuck, lechwe, southern reedbuck, African buffalo)			Africa
S. bidentata (syn. *Artionema*)	Artiodactyla: cervid (red brocket)			South America
S. boulengeri	Artiodactyla: bovid (waterbuck, lechwe, Bohor reedbuck, mountain reedbuck)			Africa
S. capreoli	Artiodactyla: cervid (moose, roe deer)			North America
S. castroi	Artiodactyla: suid (desert warthog, bushpig)	peritoneal cavity		Africa
S. cervi (syn. *S. altaica*, *indica*)	Artiodactyla: bovid (cattle, zebu, yak, Asian buffalo, water buffalo, sheep, goat, blackbuck), cervid (moose, roe deer, wapiti, chital, fallow deer, red deer, sika deer, sambar deer, Indian muntjac, black-tailed deer, white-tailed deer, reindeer); Perissodactyla: equid (horse); Rodentia: murid (brown rat)	abdominal and thoracic cavities, mf in blood (sheathed), (larvae may cause neurological signs in aberrant hosts)	Diptera: muscid (*Haematobia stimulans, Haematobosca stimulans, Stomoxys calcitrans*), hippoboscid (*Hippobosca maculata*), tabanid (*Tabanus brunnipenis*), culicid (*Aedes aegypti, albopictus, scatophagoides, Anopheles peditaeniatus, stephensi, subpictus, Armigeres obturbans, Culex fatigans, vishnui, fuscanus*); Ixodida: ixodid (*Boophilus microplus, Haemaphysalis bispinosa*)	Eurasia
S. congolensis	Artiodactyla: suid (warthog, desert warthog)	peritoneum, pleural cavity	mosquito	Africa
S. cornuta	Artiodactyla: bovid (red forest duiker, black-fronted duiker, bushbuck, suni)			Africa
S. digitata (kumri)	Artiodactyla: bovid (cattle, zebu, gayal, buffalo, sheep, goat), cervid (Reeve's muntjac); Perissodactyla: equid (horse); Rodentia: murid (southern multimammate mouse); Lagomorpha: leporid (European rabbit); Primates: cercopithecid (rhesus macaque)	peritoneum, pleural cavity, (larvae may cause neurological or ocular signs in aberrant hosts)	Diptera: culicid (*Aedes togoi, vittatus*, *Armigeres obturbans, Anopheles sinensis, nigerrimus, Culex tritaeniorhynchus*)	Asia, Mauritius
S. dipetalonematoides	Artiodactyla: bovid (duiker)			Africa
S. dubosti	Artiodactyla: bovid (duiker, Peter's duiker)			Africa
S. effilaria	Artiodactyla: tragulid (Java mouse-deer)			Asia
S. equina (syn. *S. lymphatica*) (abdominal worm)	Perissodactyla: equid (horse, Przewalski's horse, donkey, mule, onager, quagga, plains zebra);	peritoneum, pleural cavity, (ectopic	Diptera: muscid (*Haematobia stimulans*), culicid	worldwide

	Artiodactyla: bovid (cattle), camelid (dromedary): Primates: hominid (human)	infections may cause neurological signs)	(*Aedes aegypti, pembaensis, communis, maculatus*)	
S. gagarini	Artiodactyla: bovid (European bison)			Europe
S. gaillardi	Artiodactyla: bovid (oribi, common duiker)			Africa
S. graberi	Artiodactyla: bovid (southern reedbuck, Bohor reedbuck)	abdominal cavity		Africa
S. hornbyi	Artiodactyla: bovid (roan antelope, sable antelope, common eland, waterbuck, lechwe, steenbok, southern reedbuck, common duiker)			Africa
S. javensis	Artiodactyla: tragulid (mouse-deer)		Diptera: culicid (*Aedes togoi*)	Malaysia
S. kabarga	Artiodactyla: moschid (Siberian musk deer)			Europe
S. labiatopapillosa	Artiodactyla: bovid (cattle, zebu, American bison, European bison, water buffalo, African buffalo, yak, goat, sheep, argali, Cyprus mouflon, alpine ibex, nilgai, southern reedbuck, Cape bushbuck), cervid (moose, roe deer, red deer, sambar deer, Indian muntjac, sika deer), camelid (camel), suid (pig); Perissodactyla: equid (horse); Primates: hominid (human)	peritoneum, pleural cavity (ectopic infections may cause neurological or ocular signs)	Diptera: culicid (*Aedes aegypti, albopictus, caspius, togoi, vexans, Anopheles claviger, hyrcanus, maculopennis, Armigeres obturbans, Culex nilgiricus, Mansonia*?), muscid (*Haematobia stimulans*)	worldwide
S. lamyfortensis	Artiodactyla: bovid (Bohor reedbuck)			Africa
S. longicauda	Artiodactyla: bovid (kob)			Africa
S. loveridgei (syn. *S. hyracis*)	Hyracoidea: procaviid (tree hyrax, yellow-spotted rock hyrax)			Africa
S. machadoi	Artiodactyla: bovid (duiker)			Africa
S. marshalli	Artiodactyla: bovid (cattle, water buffalo); Perissodactyla: equid (horse)	peritoneal cavity, mf in blood, parasites in foetuses, prenatal infection?		Asia
S. pillersi	Artiodactyla: bovid (kob, southern reedbuck, Cape bushbuck)			Africa
S. poultoni	Artiodactyla: bovid (hartebeest, tiang)			Africa
S. rodhaini	Artiodactyla: suid (red river hog)			Africa
S. saegeri	Artiodactyla: bovid (common duiker)			Africa
S. sandersoni	Artiodactyla: bovid (bay duiker)			Africa
S. scalprum	Artiodactyla: bovid (impala, red forest duiker, common duiker, bushbuck, oribi, steenbok, southern reedbuck)			Africa
S. shohoi	Artiodactyla: suid bushpig)			Africa
S. southwelli	Artiodactyla: bovid (duiker)			Africa
S. thomasi	Artiodactyla: suid (pig)	peritoneal cavity		South-East Asia
S. thwaitei	Artiodactyla: bovid (roan antelope, waterbuck, bluebuck)			Africa
S. transcaucasica	Artiodactyla: cervid (moose, roe deer, white-tailed deer)			Eurasia
S. transversata	Artiodactyla: bovid (blue duiker, yellow-backed duiker, bushbuck)			Africa

S. tundra (syn. *S. hartwichi*)	Artiodactyla: cervid (reindeer, roe deer, white-tailed deer, moose)		Diptera: culicid (*Aedes vexans*)	Holarctic
S. yehi	Artiodactyla: cervid (moose, mule deer, white-tailed deer, reindeer, woodland caribou, barren-ground caribou)			Eurasia
S. yorkei	Artiodactyla: bovid (impala, bushbuck)			Africa

Parasite morphology: *Setaria* spp. form 3 distinct morphological stages: adult worms, live young (microfilariae) and a series of larval developmental stages (designated L1-4). Mature female worms in mammalian definitive hosts produce and release microfilariae (pre-larvae) that range in size from 140-310 x 5-8 µm depending on species. The microfilariae are sheathed and surrounded closely by vitelline eggshell membranes with some free space observed anteriorly and posteriorly. They have rounded heads and straight tapering tails and the nuclear column formed by the primordia of internal organs does not extend to the tip of the tail. In dipteran intermediate hosts, the microfilariae exsheath and moult twice to form infective third-stage larvae (L3) measuring from 1.5-2.6 mm in length and characterised by tails with a terminal papilla and 2 small lateral subterminal papillae. Back in the definitive host, the larvae moult twice to form thin slender adult worms measuring up to 190 mm long. Adults are covered by a tough flexible cuticle with a milky translucent appearance. They have elaborate heads, sometimes with spines, and a chitinous cuticular ring surrounding the mouth forming 4 lip-like structures. They have a tubular digestive system with a well-sclerotized buccal capsule (thin peribuccal ring present) and an oesophagus with a well-developed glandular portion. Adults have tapering curved tails with conspicuous conical lappets. Mature worms demonstrate marked sexual dimorphism, with females being larger than males (measuring 60-190 x 1.0-1.2 mm cf. 40-80 x 0.4-0.6 mm). Males have 2 unequal dissimilar copulatory spicules (left spicule 370-660 µm long, right spicule 120-210 µm long sometimes ending in a claw). Females may have a spiny knob or a few large conical projections on the tail, 2 large ovaries with oviducts and uteri opening into an anterior vulva with a muscular ovejector. Mature female worms are ovoviviparous and produce embryonated eggs which develop internally to release sheathed microfilariae. Different *Setaria* spp. are distinguished primarily on the basis of morphotypic differences in the peribuccal crown (projections, lips, mouth shape) and tail (size, shape, appendages).

Site of infection: Adult *Setaria* worms commonly infect the abdominal (peritoneal) cavity of domesticated and wild mammals, mainly artiodactyls and perissodactyls, and microfilariae occur in the peripheral circulation. Occasionally, pre-adult larval stages (L4) or sub-adults (L5) may invade the central nervous system or eyes of their hosts, or localize under the serosal surfaces of internal organs (liver, spleen, lungs, heart). Larval development (L1-3) occurs in the thoracic muscles or fat bodies of their dipteran insect vectors.

Pathogenesis: Infections are mostly asymptomatic as the adult worms cause little damage in the body cavities of their mammalian hosts, although they may cause focal fibrosis and occasionally mild focal peritonitis. Infections by microfilariae has been associated with systemic clinical signs in horses, involving fever, depression, stiff gait and poor body condition. Immature developmental stages may sometimes invade the central nervous system of unusual (atypical?) susceptible hosts (mainly horses, sheep and goats, particularly the young) causing traumatic damage to nerve tracts and the neuropil (especially in the spinal cord), resulting in neurological manifestations (verminous meningoencephalomyelitis) including muscular weakness, ataxia, conscious proprioceptive deficits, uncoordinated movements of the hindlimbs or all four limbs, atonic tail and bladder, paralysis and death. Disease may appear overnight and rapidly worsen within days to become life-threatening. Occasionally, infections by larvae or adult worms may cause ocular setariasis (commonly known as eye worm) in horses and donkeys, with clinical signs including excessive lacrimation, photophobia, blepharospasm, corneal opacities and blindness.

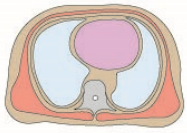
Developmental cycle and mode of transmission: Like other filarial worms, *Setaria* spp. have indirect life-cycles involving transmission between vertebrate definitive hosts (mammals) and invertebrate intermediate hosts (haematophagous insects). Adult female worms release microfilariae which move from the host abdominal cavity into the bloodstream where they are taken up by blood-feeding dipteran insects. Some *Setaria* spp. exhibit nocturnal subperiodicity (with maximum microfilaraemia observed at night) while other species do not demonstrate any periodicity. The former apparently utilize blood-sucking culicid mosquitoes as intermediate hosts, while the latter often use pool-feeding muscid or tabanid flies. Ingested microfilariae exsheath in the insect gut and migrate through the haemocoel to the thoracic muscles (sometimes the fat body). Here they transform to sausage-shaped first-stage larvae (L1) in 5 days, moult to second-stage larvae (L2) in 5-12 days and then to third-stage larvae (L3) in 10-15 days. L3 migrate to the haemocoel where they develop into infective stages over several days before moving to the insect mouthparts. When the insect next feeds, infective L3 are expelled from the labium and are deposited on the skin of the mammalian host where they penetrate the puncture wound (contaminative transmission rather than inoculative salivary transmission). Infective larvae migrate to the peritoneal cavity where they moult and complete development to adult worms over several months. After mating, female worms birth live microfilariae which accumulate in the host circulation. The prepatent period (time between infection and first release of

microfilariae) ranges from 5-8 months depending on the host and worm species. Adult worms may live for several years and continue to produce microfilariae. Transplacental transmission has also been reported in several pregnant animals.

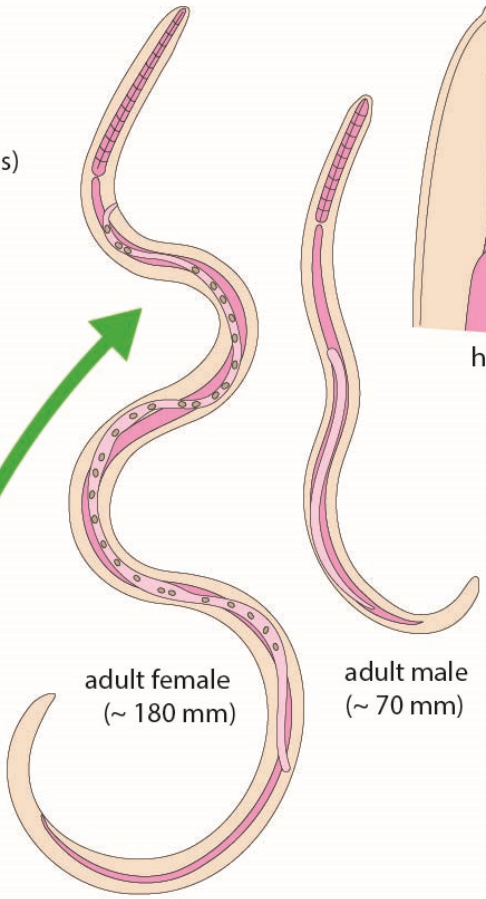
Differential diagnosis: Infections are conventionally diagnosed by the microscopic detection of microfilariae in blood samples, either wet mounts, thick or thin blood smears or concentrates following membrane filtration (5 μm pore size) or centrifugation of lysates (after formalin or saponin haemolytic treatment). Microfilariae may be visualized in wet mounts or concentrates using methylene blue or cresyl blue supravital stains or permanent mounts may be stained with Giemsa, Delafield's haematoxylin, or Field's rapid stain. Many infections are detected as incidental gross or histopathological findings during surgery or following necropsy, particularly migrating larvae in nervous tissues. Ocular eyeworm infections may sometimes be diagnosed by the detection of parasites in the anterior chamber and aqueous humor of the eye.

Treatment and control: Several anthelmintic drugs have been found to be reasonably effective against *Setaria* microfilariae, including the macrocyclic lactones (ivermectin, moxidectin) and the diethylenediamine (diethylcarbamazine), but they were not effective against adult worms. Some hosts required supportive therapy with anti-inflammatory agents to minimise adverse reactions to material suddenly released from many dying parasites. There have been reports of the successful surgical removal of worms from the anterior chamber of equids, but various complications have also been reported, such as corneal oedema, phthisis bulbi (shrunken nonfunctional eye), and scarring and prolapse of the iris. Various preventive measures have been used to break transmission cycles, mainly in cattle, through the use of insecticides to control vector populations, environmental management to eliminate vector breeding sites, and protecting hosts against vector bites through the use of insect repellents (topical applications or impregnated tags) and indoor housing (with screens).

Setaria

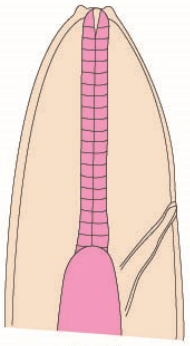


body cavity
(fibrosis, peritonitis)

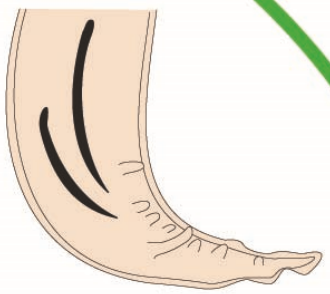


adult female
(~ 180 mm)

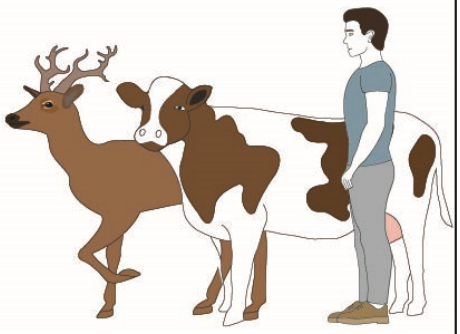
adult male
(~ 70 mm)



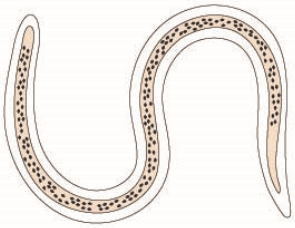
head



male tail (lateral)

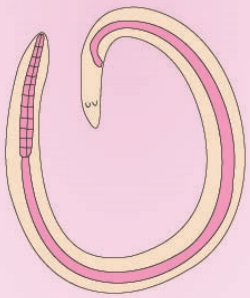


Definitive Hosts
(primates, ungulates,
rodents)



microfilariae (mf) (~ 200 µm)
(released into blood)

mf
ingested

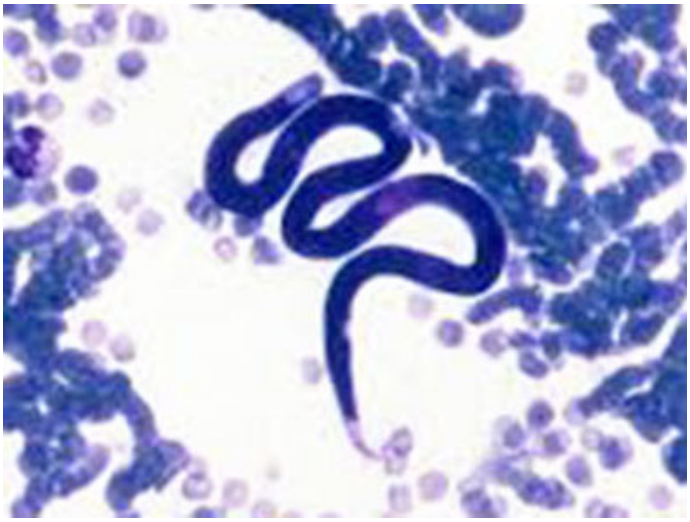


third-stage larvae
(L3) (~ 2 mm)

L3
deposited
on skin

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

vector-borne transmission

	
Setaria adult worms	*Setaria* microfilaria