Nematodirus
(helminth: nematode)

Overview

Nematodes are triploblastic pseudocoelomate unsegmented worms that undergo protostomial embryonic cleavage and grow by cuticular moulting (ecdysis). Two groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Many phasmidian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including spirurinids, tylenchinids and rhabditinids. The latter contains the infraorder Rhabditomorpha which includes strongyloid nematodes characterised by an expansion of the tail of the male known as the copulatory bursa (clasper with one dorsal and two lateral lobes with muscular rays). Many families are recognised: including the trichostrongyles which are small hair-like worms with a small buccal capsule. Adults are usually found in the stomach/abomasum or small intestines of mammals or birds. They have direct life-cycles where eggs passed in faeces develop to L3 (L2 cuticle retained as a sheath). Hosts ingest L3 which exsheath, migrate into the mucosa and moult into L4 (some may undergo arrested development, termed hypobiosis) before returning to the lumen to moult into adults. *Nematodirus* spp. (thin-necked or thread-necked intestinal worms) contribute to diarrhoea and illthrift reducing production in sheep and cattle worldwide.

Classification:

Domain:	Eukaryota (membrane-bound nucleus)
Supergroup:	Amorphea (unikonts with single flagellum, or nonflagellated amoebae)
Kingdom:	Metazoa (multicellular eukaryotes, heterotrophs, notably animals)
Group:	Protostomia (triploblastic, spiral cleavage)
Subgroup:	Ecdysozoa (cuticle moulted = ecdysis)
Phylum:	Nematoda (unsegmented, pseudocoelomate roundworms, tubular digestive tract, dioecious)
Class:	Chromadorea (spiral amphids, three oesophageal glands, usually annulated bodies, free-living and parasitic)
Order:	Rhabditida (Secernentea, Phasmidea) (secretors, with phasmids, bipartite oesophagus, single testis)
Suborder:	Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)
Infraorder:	Rhabditomorpha (‘rod-shaped’ buccal cavity)
Superfamily:	Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Family:	Molineidae (reduced buccal capsule, cephalic vesicle, female tail with spine/cusps, direct cycles)
Subfamily:	Nematodirinae (corona radiata, neodont formation, oviparous, herbivores)
Genus:	*Nematodirus* (parasitic in small intestines of ruminants)
Species:	various species cause scours and illthrift in lambs and calves

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

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

CLASSIFICATION* OF SUPERFAMILIES OF PARASITIC NEMATODES
Class: Enoplea (Aphasmidea, Adenophorea) (gland-bearers, cylindrical oesophagus, no phasmids, setae, two testes)
Subclass: Dorylaimia (five or more oesophageal glands, buccal stylet (odontostyle), free-living or parasitic)[clade I(2)]
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short anterior muscular and long posterior glandular portions)
Class: Chromadorea (spiral amphids, 3 oesophageal glands, usually annulated bodies, free-living and parasitic)
Order: Rhabditida (Secernentea, Phasmidea) (secretors, phasmids present, amphids anterior, bulbous oesophagus)
Suborder: Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)[clade V(9)]
Infraorder: Rhabditomorpha (‘rod-shaped’ buccal cavity)
Superfamily: Rhabditoidea (open tube stoma, excretory system with lateral canals)
Superfamily: Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Suborder: Spirurina (animal parasites, many use invertebrate intermediate hosts (IH))[clade III(8)]
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 His
Superfamily: Thelazioidea (eye-worms of birds and mammals, transmitted by insects)
Suborder: Tylenchina (fungal, plant and animal parasites)[clade IV(10,11,12)]
Infraorder: Panagrolaimomorpha (free-living or parasitic (insects, reptiles, amphibians, mammals))
Superfamily: Strongyloidoidea (dauer stages, lip region without processes, striated cuticle)

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

The superfamily Strongyloidea comprises a range of worms often with prominent buccal capsules and specialised oral structures well-suited to their feeding habits on host tissues and/or fluids. Adults of most species are parasitic in the gastrointestinal tracts of mammals and some birds, while larval stages feed on bacteria in the external environment, although some larvae may infect invertebrates as intermediate or paratenic hosts. The adult worms are sexually dimorphic, the smaller males characterised by an expansion of the tail (bursa) which is used as a copulatory clasping organ. Many classification schemes group these ‘bursate’ nematodes into one or more superfamilies in the order Strongylida (with suborders containing the strongyles, trichostrongyles, hookworms and lungworms), although the families essentially remain the same. Many families are recognised on the basis of parasite morphology, biology, life-cycle, host specificity and tissue tropism; including the following which contain many notorious parasites of vertebrates.

Representative Strongyloidea (cf. Strongylida) [with bursate males]				
Family	**Characters**	**Definitive Hosts**	**Transmission***	**No. genera**
Trichostrongylina (trichostrongyles)				
Molineidae (stomach/intestinal worms)	reduced buccal capsule, cephalic vesicle, female tail with spine or cusps, oviparous/viviparous	mammals, birds, reptiles	ingestion of L3	61
Trichostrongylidae (trichostrongyles)	reduced buccal capsule, ridged synlophe, oesophagus lacking bulb, thin-shelled eggs	artiodactyls, birds	ingestion of L3	50
Heligmonellidae (hookworm-like)	body coiled, cephalic vesicle, ridged synlophe, bursa asymmetrical	mammals, birds	transdermal penetration of L3	56
Strongylina (strongyles)				
Strongylidae (strongyles)	large buccal capsule often armed with teeth, leaf crown around mouth	mammals, reptiles, birds	ingestion of L3	32
Chabertiidae (nodule worms)	large buccal capsules, leaf crown of labial collar, L3 sheathed	artiodactyls, primates	ingestion of L3	22
Syngamidae (gapeworm)	cup-shaped buccal capsule, armed with teeth, male attached to female	birds, mammals	ingestion of L3 or invertebrate PH	7
Stephanurinae (kidneyworm)	buccal capsule armed with teeth, leaf crowns and external epaulettes	suids	transdermal penetration or ingestion of L3 or PH	1
Ancylostomatina (hookworms)				
Ancylostomatidae (hookworms)	large buccal capsule bent dorsally, armed with teeth/cutting plates	primates, carnivores, artiodactyls	transdermal penetration of L3 (sometimes *per os*)	20
Metastrongylina (lungworms)				
Metastrongylidae (lungworms)	small buccal capsule, 2 trilobed lips, bursa with reduced dorsal lobe	suids	ingestion of IH carrying L3	1
Protostrongylidae (lungworms)	small buccal capsule, bursa with large lobes, gubernaculum	artiodactyls	ingestion of IH carrying L3	17
Angiostrongylidae (lungworms)	no or reduced buccal cavity, short club-shaped oesophagus	carnivores, rodents	ingestion of IH or PH carrying L3	28
Dictylocaulidae (lungworms)	small buccal capsule, bursa with large lobes, short stout spicules	ungulates, reptiles	ingestion of L3	5
Filaroididae (lungworms)	small buccal capsule, reduced male bursa, infective L1	carnivores	ingestion of L1	4

*IH = intermediate host, PH = paratenic (transport) host, L1 = first-stage larva, L3 = third-stage larva

Some authorities recognize a superfamily Molineoidea comprising 4 families: Molineidae in mammals, birds and reptiles; Amphibiophilidae mainly in amphibians; Mackerrastrongylidae in monotremes and marsupials; and Strongylacanthidae in bats. These worms have a buccal capsule reduced to an annulus, most have a cephalic vesicle and a bilaterally symmetrical synlophe, the males have an asymmetrical bursa and females have a tail with a caudal spine or numerous tubercles. The family Molineidae contains 6 subfamilies: Nematodirinae (corona radiata, neodont formation, bursa with short dorsal ray split to base, didelphic, oviparous, 6 genera in herbivorous mammals); Ollulaninae (synlophe absent, cephalic vesicle absent, bursa with short dorsal ray, monodelphic, viviparous, female tail with 3-5 tubercles, 1 genus in felids and occasionally suids); Molineinae (bursa with short dorsal ray not split to base, synlophe with perpendicular ridges, 26 genera in amphibians, reptiles and mammals); Dromaeostrongylinae (bursa with elongate dorsal ray, 1 genus in birds); Merstensinematinae (bursa with short dorsal ray not split to base, synlophe absent, 2 genera in reptiles and amphibians); and Anoplostrongylinae (cephalic vesicle with armature, synlophe with dorsoventral ridges, bursa with short dorsal ray not split to base, 25 genera in edentates and bats). Specific molineid genera of veterinary and medical importance are compared in the following table.

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm eggs/larvae
Subfamily Nematodirinae					
Nematodirus (thin-necked intestinal worm)	53	artiodactyls, lagomorphs	small intestines	10-30 mm long, cephalic inflation, thin neck, mid-body spiral coil, female with spiked tail, male with long thin spicules	150-260 x 67-118 µm, eggs ellipsoidal, thin-shelled
Subfamily Ollulanidae					
Ollulanus	1	carnivores	stomach	0.7-1.0 mm long, small buccal capsule, females with trifid tail, viviparous (eggs hatch *in utero*), larvae shed in vomitus (or auto-infection)	larvae 400-500 µm, tail with terminal cusps

The subfamily Nematodiriinae contains 6 genera (*Nematodirus, Lamanema, Murielis, Nematodirella, Nematodiroides,* and *Rauschia*) parasitic in small intestines of ruminants (esp. Holarctic cervids and bovids), camelids and lagomorphs. The genus *Nematodirus* is characterised by medium-sized worms with a distinct cephalic vesicle, synlophe with perpendicular ridges, and males possessing an asymmetrical bursa (type 2-3 tending to 2-1-2) with the dorsal ray divided into 2 projections, and 2 long spicules joining in a membrane at their tips (cf. short and unjoined in *Cooperia*). They are commonly known as thin necked intestinal worms (sometimes long-necked bankrupt worms, or thread-necked worms) and over 50 species have been described in ruminants particularly in temperate or cold regions, often from elevated mountainous areas. The parasites produce large eggs which are resistant to desiccation and freezing and hosts often become infected in warm months during spring, with mass hatching occurring under suitable conditions of moisture and temperature.

***Nematodirus* species**	**Definitive Hosts**	**Location [clinical signs]**	**Distribution**
N. abnormalis	Artiodactyla: bovid (cattle, sheep, bighorn sheep, mouflon, chamois, goat, alpine ibex, Iberian ibex, common duiker, bushbuck, Cuvier's gazelle, goitered gazelle), antilocaprid (pronghorn), cervid (mule deer), camelid (dromedary); Lagomorpha: leporid (rabbit); Primates: hominid (human)	small intestines [diarrhoea]	worldwide
N. andersoni	Artiodactyla: bovid (bighorn sheep, Dall sheep)		North America
N. andreevi	Artiodactyla: bovid (sheep, goitered gazelle)		Eurasia
N. antilocaprae	Artiodactyla: bovid (mountain goat), cervid (red deer)		North America
N. archari	Artiodactyla: bovid (sheep, bighorn sheep, argali, Dall sheep, mouflon, goat, goitered gazelle)		Eurasia, North America
N. arizonensis	Lagomorpha: leporid (rabbit)	small intestines	North America
N. aspinosus (*Rauschia*)	Lagomorpha: leporid (rabbit, mountain hare)		-
N. aznivi	Artiodactyla: bovid (sheep)		
N. battus (thread-necked worm)	Artiodactyla: bovid (cattle, sheep, chamois, goat), cervid (Reeve's muntjac),	small intestines [diarrhoea]	Europe, North America
N. becklundi	Artiodactyla: bovid (mountain goat)		North America
N. bioccai	Artiodactyla: bovid (sheep)		Iran
N. brevispiculus	Artiodactyla: bovid (sheep)		Kazakhstan
N. centripunctata	Artiodactyla: cervid (roe deer)		
N. chabaudi	Artiodactyla: bovid (Pyrenean chamois)		Europe
N. davtiani (incl. subspp. *davtiani, alpinus*, syn. *N. rufaevastitatis*)	Artiodactyla: bovid (bighorn sheep, Dall sheep, mountain goat, chamois, alpine ibex, Iberian ibex)		Europe, North America
N. dogieli	Artiodactyla: bovid (sheep, argali, saiga antelope)		Eurasia
N. dromedarii	Artiodactyla: bovid (dromedary)		
N. erschovi	Artiodactyla: cervid (roe deer)		Europe
N. europaeus	Artiodactyla: bovid (European bison, mouflon), cervid (roe deer)		Europe

N. filicollis (syn. *N. furcatus*, *Ascaris, Fusaria, Oesophagostomum, Strongylus*) (thread-necked worm)	Artiodactyla: bovid (cattle, sheep, bighorn sheep, argali, mouflon, chamois, Pyrenean chamois, goat, mountain goat, alpine ibex, Iberian ibex, Cuvier's gazelle, dama gazelle, dorcas gazelle, antilocaprid (pronghorn), cervid (roe deer, fallow deer, red deer, mule deer, Columbian black-tailed deer, white-tailed deer, reindeer), camelid (llama, alpaca): Rodentia: ctenodactylid (common gundi)	small intestines [diarrhoea]	worldwide (except Africa), esp. temperate zones
N. furcatus	Artiodactyla: bovid (sheep)		
N. gazellae	Artiodactyla: bovid (sheep, goitered gazelle, saiga antelope)		Eurasia
N. helvetianus (thread-necked worm)	Artiodactyla: bovid (cattle, muskox, American bison, European bison, sheep, bighorn sheep, mouflon, chamois, goat, mountain goat, alpine ibex, Cuvier's gazelle, greater kudu), cervid (moose, roe deer, fallow deer, red deer, mule deer, Hondo sika deer, Yezo sika deer, boreal woodland caribou), camelid (dromedary, llama); Carnivora: canid (coyote)	small intestines [diarrhoea]	worldwide
N. hsuei	Artiodactyla: bovid (sheep)		Asia
N. hugonnetae	Artiodactyla: bovid (chamois)		Europe
N. ibicis	Artiodactyla: bovid (chamois, goat, alpine ibex)		Eurasia
N. iranicus	Artiodactyla: bovid (sheep)		Iran
N. lamae	Artiodactyla: camelid (alpaca, vicuna), bovid (sheep)		South America
N. lanceolatus	Artiodactyla: bovid (goat)		
N. leporis (*Rauschia*)	Lagomorpha: leporid (rabbit, hare)		North America
N. maculosus	Artiodactyla: bovid (mountain goat, bighorn sheep)		North America
N. mauritanicus	Artiodactyla: cervid (moose, roe deer), camelid (dromedary), bovid (sheep, dorcas gazelle, goitered gazelle)		Eurasia
N. molini	Artiodactyla: tayassuid (collared peccary)		South America
N. nachitchivanicus	Artiodactyla: bovid (sheep, goat)		
N. nemorhaedi	Artiodactyla: bovid (long-tailed goral)	small intestines	Asia
N. neomexicanus (*Rauschia*)	Lagomorpha: leporid (rabbit)	small intestines	North America
N. neotoma (syn. *N. tortuosus*)	Rodentia: cricetid (bushy-tailed woodrat)		North America
N. odocoilei	Artiodactyla: cervid (moose, fallow deer, red deer, mule deer, southern mule deer, white-tailed deer, reindeer, boreal woodland caribou), bovid (sheep, bighorn sheep, mountain goat)		North America
N. oiratianus (incl. subspp. *oiratianus, interruptus*, syn. *N. lanceolatus*)	Artiodactyla: antilocaprid (pronghorn), bovid (cattle, sheep, bighorn sheep, Dall sheep, argali, chamois, goat, mountain goat, Iberian ibex, goitered gazelle), camelid (Bactrian camel, dromedary), cervid (roe deer, red deer)		worldwide
N. petrovi (*Rauschia*)	Lagomorpha: leporid (tolai hare)		Eurasia
N. roscidus	Artiodactyla: bovid (European bison, sheep), cervid (red deer, fallow deer)		Europe
N. rupicaprae	Artiodactyla: cervid (roe deer), bovid (mouflon, chamois)		Europe
N. schulzi	Artiodactyla: bovid (sheep)		
N. skrjabini	Artiodactyla: bovid (muskox), cervid (reindeer)		North America
N. spathiger (syn. *Strongylus*) (thread-necked worm)	Artiodactyla: antilocaprid (pronghorn), cervid (moose, roe deer, fallow deer, red deer, mule deer), bovid (cattle, sheep, bighorn sheep, Dall sheep, argali, mouflon, chamois, goat, alpine ibex, Iberian ibex, blackbuck, bushbuck, grey rhebok, Cuvier's gazelle, dama gazelle, dorcas gazelle, goitered gazelle, Cape grysbok, common duiker), camelid (dromedary, llama); Perissodactyla: equid (horse); Lagomorpha: leporid (rabbit); Rodentia: ctenodactylid (common gundi); Galliformes: phasianid (turkey); Struthioniformes: struthionid (ostrich)	small intestines [diarrhoea]	worldwide
N. sugatini	Artiodactyla: bovid (goitered gazelle)		Eurasia
N. tarandi	Artiodactyla: bovid (sheep, muskox), cervid (moose, reindeer, Greenland reindeer)		Eurasia

N. tortuosus	Rodentia: cricetid (pack rat)		North America
N. triangularis (*Rauschia*)	Lagomorpha: leporid (snowshoe hare)		North America
N. urichi	Artiodactyla: cervid (red brocket); Carnivora: procyonid (crab-eating raccoon)		South America
N. weinbergi	Primates: hominid (chimpanzee)		Africa
N. wittenbergi	Artiodactyla: bovid (goat)	intestines	Israel
N. zembrae	Lagomorpha: leporid (rabbit)		

Parasite morphology: *Nematodirus* spp. form 3 different morphological stages in their developmental cycles: eggs, larvae; and adult worms. Eggs laid by gravid female worms are unusual in that they are almost twice the size of other trichostrongyle eggs, measuring 150-260 x 67-118 µm. They are rhomboid in shape with curved sides and rounded poles, surrounded by thin clear-brown shells, and contain a central morula (comprising 2-8 blastomeres) only partially filling the fluid-filled interior. Larval development in the genus *Nematodirus* is also unique because formation of the first 3 larval stages (L1-L3) takes place within the eggs before they hatch. Embryonation generates L1 which moult to L2 which then moult to L3. Larval stages measured from 750-1,250 µm in length, including their long attenuated tails (up to 160 µm long). Upon hatching, L3 are released still encased within the L2 cuticle which appears as a closely-fitting sheath with a long tail sheath extension (207-309 µm) of which the terminal 50-60% is filamentous (the L1 cuticle is often left behind in the eggshell). Infective L3 have broad rounded heads, intestines comprising 8 cells, and their tails vary in morphology according to species, being pointed (*N. helvetianus*), lobed (e.g. *N. filicollis*), notched (e.g. *N. battus*) or stumpy (e.g. *N. spathiger*). Adults are slender red-brown worms measuring from 10-30 mm in length. They have a distinctive swelling or inflation of the head (cephalic vesicle) and thin thread-like anterior ends often coiled, twisted or tangled together. The oral opening is encircled by small perioral denticles (sometimes called the corona radiata) and the dorsal aspect of the anterior oesophagus bears a cuticularized tooth (neodont formation). Worms are bound by a cuticular synlophe with prominent transverse striations in the cephalic region followed by longitudinal body ridges, restricted to the anterior half in females. Adults are sexually dimorphic, with female worms being larger than males (15-30 mm cf. 10-16 mm). Mature males possess a well-developed copulatory bursa with 2 large lateral lobes, each with 5 supporting rays (comprising muscular elements following nerve channels to terminal papillae) arranged in a 2-3 configuration (sometimes tending to 2-1-2) whereby the 2 ventral rays are separate from the rest), and a smaller symmetrical dorsal lobe (with the supporting ray split into 2 parallel processes for *N. battus* or 4 processes for other species). Males lack a gubernaculum and telamon, but possess 2 long thin filiform spicules (0.9-1.3 mm) whose distal tips are fused and joined in a membrane (in contrast to the short and unjoined spicules of *Cooperia*). The spicule tips also differ in their ornamentation according to species; being heart-shaped (*N. battus*), lanceolate (*N. filicollis*), pointed (*N. helvetianus*) or rounded and spatulate (*N. spathiger*). Mature females are didelphic with 2 functional ovaries (whereas those of the genus *Ollulanus* are monodelphic). They are oviparous and developing eggs are found in the 2 uteri which open into a common vulva located in the posterior third of the body. The tip of the female tail is pointed in the case of *N. battus*, but is truncate with a prominent terminal spine for all other species.

Site of infection: Parasitic larval stages and adult worms infect the mucosa of the small intestines of their hosts, particularly the ileum. Worm eggs are excreted into the external environment with host faeces and produce preparasitic larval stages before hatching.

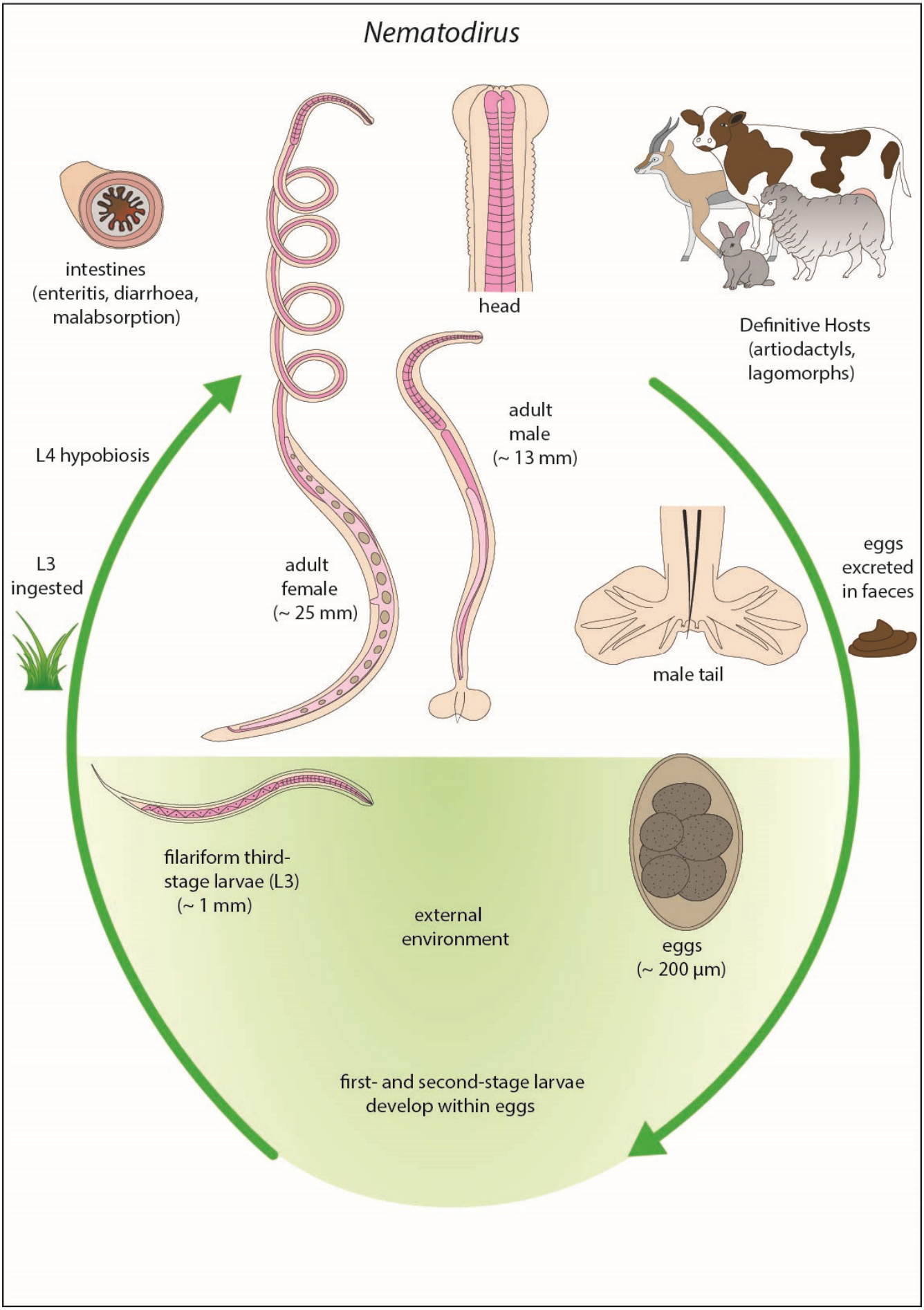
Pathogenesis: Infections by *Nematodirus* spp. are often asymptomatic in adult animals because the hosts acquire strong protective immunity following exposure. It has been suggested that most infections rarely cause disease by themselves, but contribute to the parasitic gastroenteritis observed in concomitant infections with other pathogens (especially other nematodes and some coccidia). Young animals, however, are susceptible to clinical disease due to their immunological immaturity and naivety. The severity of disease depends on the parasite species (*N. battus* being the most pathogenic), the intensity of infection (> 1,000 worms causing clinical disease), and host susceptibility (preweaners most at risk). The disease nematodirosis is characterised by the sudden onset of diarrhoea with marked dehydration, sometimes culminating in mortality. Infective L3 penetrate into the crypts of the small intestines where they develop to L4 and then young adults (L5) which emerge onto the mucosal surface, often coiling superficially around villi. All parasitic stages feed on host blood and tissues causing traumatic damage, erosive lesions, epithelial necrosis, hyperaemia and inflammation (catarrhal enteritis) which significantly alters villous architecture (distortion, compression and atrophy reducing mucosal surface area). The resultant malabsorption may result in profuse watery yellow-green diarrhoea, dehydration, anorexia, lethargy and unthriftiness with growth retardation, poor weight gain or weight loss. Clinical signs are mostly associated with larval development and the emergence of subadults into the lumen some 10-12 days after infection (note that this is during the prepatent period before adults become sexually mature and produce eggs). Disease may occur in calves and lambs as young as 6 weeks of age, but becomes more problematic at 9-15 weeks of age when preweaners begin to graze more regularly. Some larvae may undergo inhibited or arrested development (hypobiosis) in the mucosa over winter months, only resuming development in spring. Young animals placed on heavily contaminated spring pastures may therefore acquire intense infections over a short period of time resulting in acute disease.

Developmental cycle and mode of transmission: Like other trichostrongyles, *Nematodirus* spp. have direct monoxenous life-cycles involving faecal-oral transmission, but in this case infective L3 develop in excreted eggs before they hatch. Gravid female worms produce around 50 eggs per day which are passed into the external environment with host faeces. The large eggs embryonate and form L1, L2 and then L3 stages before hatching. This development may occur over 2-4 weeks in optimal conditions of moisture and temperature, but is often delayed for several months, with some reports extending up to 2 years. The eggs are highly resistant to both desiccation and freezing, so they may survive mild summers and cool winters. Indeed, most infections occur in temperate or cold regions, often in elevated mountainous areas. Eggs hatch in large numbers after rain, or following warming to > 10°C after prolonged cold periods. This may lead to an annual seasonal pattern of infection, predominantly in late spring, although hatching may be extended over a longer period under milder conditions making more than one annual generation possible for some species. Grazing animals become infected when they ingest infective L3 on herbage, either as free-living pasture stages or still contained within eggs. Ingested larvae exsheath in the gut and penetrate into crypts in the small intestines where they moult to L4 and then to subadults (sometimes designated L5). Young worms emerge back into the gut lumen where they become sexually mature. The prepatent period (time from infection to first egg excretion) ranges from 14-28 days.

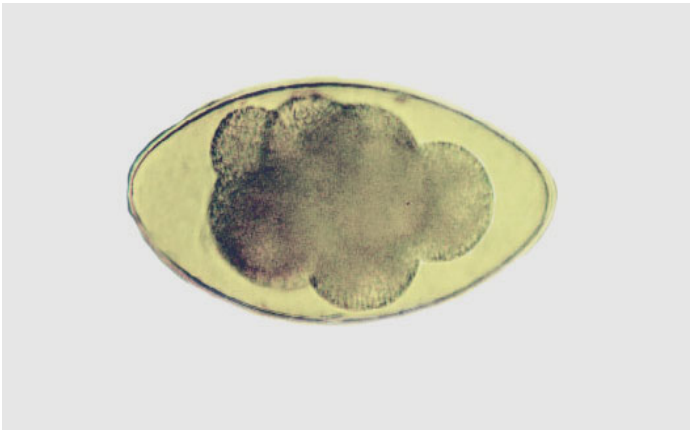
Differential diagnosis: Infections may be indicated on the basis of clinical symptomatology (sudden diarrhoea) and predisposing history (notably, host age and grazing season), but other aetiological agents may be involved Coprological techniques are often used to detect the large distinctive worm eggs in faecal samples, usually following their concentration by sedimentation in water and/or floatation in saturated sugar or heavy-metal salt solutions. While some tests may be quantitated using volumetric chambers (McMaster or Whitlock slides) to provide eggs counts per gram of faeces (epg), they show poor correlations with worm burdens and the severity of clinical disease, particularly since most clinical signs occur during the prepatent period when immature stages damage the gut before egg production commences. Egg counts also not account for male worms, or for females not producing eggs due to their immaturity, senescence or immune-induced suppression of egg production. Faecal samples may also be cultured to yield L3 which can be identified microscopically by their morphological characteristics (broad rounded heads, intestines comprising 8 cells, and unique tails, all encased within filamentous sheaths with long tapering tails). Gut samples may also be collected from dead or sacrificed animals and examined for adult worms. However, the numbers of worms are often difficult to enumerate in gut washes as the thin-necked adults may be found in tangled masses. It is also difficult to recover developing larvae from intestinal crypts without resorting to strong acid digestion techniques. Several research laboratories have recently used molecular biological techniques to characterize different species following the polymerase chain reaction (PCR) amplification and sequencing of several nuclear genes (large and small subunit ribosomal RNA and their internal transcribed spacers I and II).

Treatment and control: Several broad-spectrum anthelmintic drugs have been used to effectively treat clinical infections in young livestock, including the benzimidazoles (thiabendazole, mebendazole, fenbendazole, oxfendazole, albendazole), probenzimidazoles (thiophanate, febantel, netobimin), macrocyclic lactones (avermectins, milbemycins), imidazothiazoles (levamisole) and tetrahydropyrimidines (morantel, pyrantel). The macrocyclic lactones were the most effective, even providing some short-term prophylaxis, although oral and parenteral formulations differed in their efficacy (the latter being less effective). The imidazothiazoles and tetrahydropyrimidines also exhibited little activity against hypobiotic larvae. Fortunately, there have been few reports on the emergence of drug resistance in these worms, but treatment protocols should be followed scrupulously to avoid under-dosing or unwarranted repetitive dosing which can select for drug resistance. The best time for treatment can often be predicted on the basis of climatic information (especially soil temperature) conducive to the development and hatching of eggs on pastures, particularly when warm weather follows a prolonged cold period in late winter or early spring. Young animals should be treated as a group and moved to clean pastures (spelled or previously ungrazed pastures) with adequate nutrition. Because animals develop strong protective immunity with age, drug treatments should be used strategically to reduce worm burdens and minimise pasture contamination, but still allow subclinical (low-dose) exposure to stimulate immune responses. Various farm management practices can also be used to help reduce pasture contamination, including rotational and/or mixed grazing (different cohorts or different species at different times), keeping stocking rates low, quarantining new introduced livestock, and periodically spelling or cropping pastures.

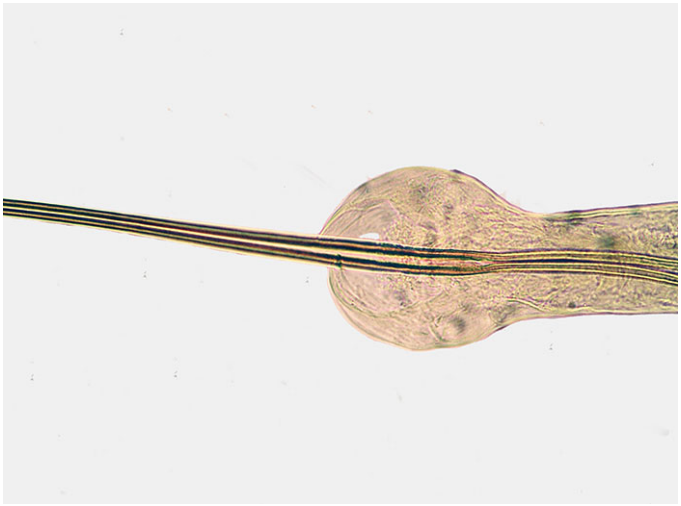
Nematodirus



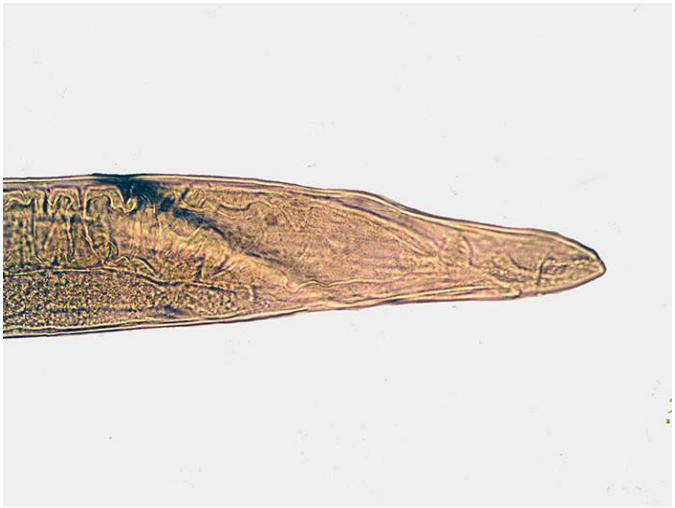
Nematodirus adult worm



Nematodirus worm egg



Nematodirus adult worm, male bursa



Nematodirus adult worm, head