

## *Strongyloides*

(helminth: nematode)

### Overview

Nematodes are triploblastic pseudocoelomate unsegmented worms that undergo protostomial embryonic cleavage and grow by cuticular moulting (ecdysis). Two groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Many phasmidian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including spirurids, rhabditinids and tylenchinids. The latter contains the infraorder Panagrolaimomorpha which includes the strongyloidoids which are capable of both parasitic and free-living reproductive cycles. They are small slender cylindrical worms with the long oesophagus and uterus intertwined, giving the appearance of a twisted thread, hence their common name of 'threadworms'. Adults have a small buccal capsule and the males are non-bursate (lack a copulatory bursa). Only parthenogenetic female worms are parasitic, living in the small intestinal mucosa of various mammals, birds, reptiles and amphibians. Transmission involves a geo-helminth phase, where rhabditiform larvae in the soil form infective filariform larvae which penetrate the skin of their hosts. Sometimes, however, larvae develop into male and female worms which undergo one or more free-living cycles in the soil before producing infective larvae. *Strongyloides* infections in humans and some domestic animals have been associated with enteric, dermal, pulmonary and disseminated diseases.

### 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: Tylenchina (fungal, plant and animal parasites)  
Infraorder: Panagrolaimomorpha (free-living or parasitic (insects, reptiles, amphibians, mammals))  
Superfamily: Strongyloidoidea (dauer stages, lip region without processes, striated cuticle)  
Family: Strongyloidae (threadworms, parasitic parthenogenetic females, free-living sexual generations)  
Genus: *Strongyloides* (parasitic in small intestines of mammals/birds)  
Species: various species cause larval currrens, diarrhoea and wasting in mammals, including humans

**Parasite biodiversity and host range:** Most Metazoa are multicellular triploblastic animals with differentiated tissues, many being bilaterally symmetrical with a body cavity. Most invertebrate animals are protostomes as their embryonic development involves spiral determinate cleavage. Those that moult their external cuticles during their life-cycles (process known as ecdysis) are grouped together in the unique clade Ecdysozoa, including the nematodes (roundworms), onychophorans (velvet worms), tardigrades (water bears) and arthropods (myriapods, chelicerates, crustaceans and hexapods, all with jointed limbs). Nematodes (roundworms) are unsegmented tubular worms with a fluid-filled body cavity (pseudocoelom) that acts as a hydrostatic skeleton. They have longitudinal muscles and typically exhibit a sideways thrashing motion. They have well developed digestive tracts with various partitions: the foregut comprising the mouth (often with lips and papillae), buccal capsule (sometimes with ridges, rods, plates, spears, stylets or teeth) and oesophagus (glandular, muscular or both); the midgut (nonmuscular absorptive section); and hindgut (rectum) emptying through a subterminal anus (cloaca in males). Most nematodes are dioecious and form separate sexes. Male worms have a single testis (sometimes 2), an elongate vas deferens often equipped with a seminal vesicle and ejaculatory duct (glandular and/or muscular), 1-2 copulatory spicules (sometimes with an accessory gubernaculum), and bursate species with elaborate posterior claspers. Female worms are usually didelphic with 2 ovaries (some monodelphic or polydelphic), 2 oviducts usually with spermatheca, 2 uteri opening into a common vagina and a vulva often equipped with a muscular ovejector. Female worms are oviparous or viviparous and produce numerous eggs or larvae, respectively. Larval stages undergo several moults (L1-L4) before maturing into adult worms. Some nematodes have direct life-cycles where eggs or larvae infect definitive hosts (per os or per cutaneous), but many have indirect cycles where larvae first develop in invertebrate intermediate hosts before infecting definitive hosts (by ingestion, injection or deposition). Many nematode species are free-living in terrestrial and aquatic habitats, while some species from diverse groups have become plant or animal parasites. Two nematode groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Most Enoplia are free-living marine organisms but some are found in freshwater, and on land as plant parasites. The Dorylaimia comprise numerous freshwater and terrestrial species, including major groups of plant and animal parasites. The Chromadoria is represented by many marine groups as well as a terrestrial

group of plant and animal parasites. The taxonomic ranks of many nematode assemblages vary considerably depending on which classification system has been followed. Molecular phylogenetic studies, however, have supported the separate classification of most groups, particularly at the level of superfamily. Collectively, species from at least 16 superfamilies are considered to pose serious threats to human and animal health as infectious diseases.

CLASSIFICATION* OF SUPERFAMILIES OF PARASITIC NEMATODES
Class: Enoplea (Aphasmidea, Adenophorea) (gland-bearers, cylindrical oesophagus, no phasmids, setae, two testes)
Subclass: Dorylaimia (five or more oesophageal glands, buccal stylet (odontostyle), free-living or parasitic)[clade I(2)]
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short anterior muscular and long posterior glandular portions)
Class: Chromadorea (spiral amphids, 3 oesophageal glands, usually annulated bodies, free-living and parasitic)
Order: Rhabditida (Secernentea, Phasmidea) (secretors, phasmids present, amphids anterior, bulbous oesophagus)
Suborder: Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)[clade V(9)]
Infraorder: Rhabditomorpha ('rod-shaped' buccal cavity)
Superfamily: Rhabditoidea (open tube stoma, excretory system with lateral canals)
Superfamily: Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Suborder: Spirurina (animal parasites, many use invertebrate intermediate hosts (IH))[clade III(8)]
<i>Incertae sedis</i> Superfamily: Dracunculoidea (elongate parasites of vertebrate tissues, freshwater crustacean IH)
Infraorder: Ascaridomorpha (large roundworms, three large lips, numerous caudal papillae)
Superfamily: Ascaridoidea (ascarids, eggs thick-shelled, larvae may undertake hepato-pulmonary migration)
Superfamily: Heterakoidea (preanal sucker anterior to cloaca in males, direct cycle, infection by egg ingestion)
Infraorder: Gnathostomatomorpha ('jaw-mouthed' due to unique bulbous armed heads)
Superfamily: Gnathostomatoidea (first IH copepod, often use paratenic hosts)
Infraorder: Oxyuridomorpha (pinworms, pointed tails, oesophagus with terminal bulb, males with single spicule)
Superfamily: Oxyuroidea (common in mammals, birds, reptiles, amphibians)
Infraorder: Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily: Acuarioidea (small parasites mostly of birds, with cephalic cordons, ptilina or serrated shields)
Superfamily: Camallanoidea (conspicuous phasmids, L1 with dorsal tooth, ovoviviparous, L1-L3 in copepod)
Superfamily: Filarioidea (tissue-dwelling filarial parasites, lack lips, infect tissues/vessels, arthropod IH)
Superfamily: Habronematoidea (unique head structures with small pseudolabia and median lips)
Superfamily: Physalopteroidea (stomach worms in mammals, insect IH)
Superfamily: Spiruroidea (pseudolabia, bipartite oesophagus, infect birds (crop/gizzard), arthropod IH)
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 Strongyloidoidea contains parasitic worms found in insects and other animals and is characterised by diovarial females and monorchic abursate males with small simple mouths (lip region without processes), striated cuticles and the formation of dormant (dauer) stages. It comprises 4 families, including the threadworm family Strongyloididae with 2 genera (*Strongyloides* and *Parastrongyloides*) [early authorities placed the family Strongyloididae in the superfamily Rhabditoidea, until molecular studies indicated their separate classification]. Members of the genus *Strongyloides* are small slender cylindrical worms with the long oesophagus and uterus intertwined, giving the appearance of a twisted thread, hence their common name of 'threadworms'. Only protandrogynous or parthenogenetic female worms are parasitic, living in the small intestinal mucosa of vertebrate hosts. Transmission involves a geo-helminth phase, where rhabditiform larvae (L1-2) in the soil form infective filariform larvae (L3) which penetrate the skin of their hosts. Sometimes, however, larvae develop into male and female worms which undergo one or more free-living cycles in the soil before producing infective larvae. Around 70 *Strongyloides* spp. have been described throughout the world; mostly in mammals but also in birds, reptiles and amphibians. Whilst *Strongyloides* spp. are commonly known as threadworms, in some countries they are enigmatically called pinworms (a common name generally applied to *Enterobius* spp.). This may cause great confusion when considering treatment options because the drugs used to treat these worms are different. *Strongyloides* infections occur predominantly in tropical and temperate regions with warmer climates favouring the survival of parasite developmental stages in soil. Different species vary in their host-specificity, the species *S. stercoralis* being found in humans and companion animals, and *S. fuelleborni* in primates and humans: thus both species should be considered zoonotic. There is evidence to suggest that geographic strains vary in their infectivity and virulence, thus complicating assessment of their zoonotic and pathogenic potential. It has been estimated that over 100 million people may be infected worldwide. Cross-transmission between humans and dogs has frequently been implicated in epidemiological studies in remote rural communities where sanitation is poor.

<i>Strongyloides</i> species	Definitive Hosts	Location [Clinical signs]	Distribution
Mammalian hosts			
<i>S. agoutii</i>	Rodentia: dasyproctid (red-rumped agouti)	small intestines	South America
<i>S. akbari</i>	Eulipotyphla: soricid (common Indian shrew, Asian house shrew)	small intestines	Indo-Asia
<i>S. callosciureus</i>	Rodentia: sciurid (Pallas's squirrel, plantain squirrel)	intestines	Asia
<i>S. canis</i>	Carnivora: canid (dog); Primates: hominid (human)	small intestines	Europe
<i>S. cebus</i>	Primates: atelid (southern miqui), cebid (Panamanian white-faced capuchin, common squirrel monkey), hominid (human)	small intestines	South America
<i>S. chapini</i>	Rodentia: caviid (capybara), echimyid (coypu)	small intestines	South America
<i>S. dasypodis</i>	Cingulata: dasypodid (nine-banded armadillo)	small intestines	Americas
<i>S. elephantis</i>	Proboscidea: elephantid (Indian elephant)	small intestines	Asia
<i>S. erschowi</i>	Carnivora: canid (raccoon dog)	small intestines	Asia
<i>S. felis</i> (syn. <i>S. cati</i> p.p.)	Carnivora: felid (cat); Primates: hominid (human)	small intestines	India, Australia
<i>S. ferreirai</i>	Rodentia: caviid (rock cavy)	small intestines	South America
<i>S. fuelleborni</i> (syn. <i>S. kellyi</i> , <i>S. simiae</i> , incl. subspp. <i>S. f. fuelleborni</i> , <i>S. f. kellyi</i> )	Primates: hominid (human, mountain gorilla, Grauer's gorilla, chimpanzee, orangutan), atelid (Geoffroy's spider monkey), cercopithecid (vervet monkey, blue monkey, Allen's swamp monkey, Japanese macaque, rhesus macaque, Toque macaque, olive baboon, yellow baboon, Chacma baboon, sacred langur)	small intestines [bloody diarrhoea]	Africa, Asia, Americas, Papua New Guinea
<i>S. intestinalis</i>	Primates: hominid (human)	small intestines	Asia
<i>S. longus</i>	Rodentia: murid (brown rat)	small intestines	Europe
<i>S. lutrae</i>	Carnivora: mustelid (North American river otter, Eurasian otter)	small intestines	Holarctic
<i>S. martis</i>	Carnivora: mustelid (Eurasian otter, European polecat, sable, stoat, least weasel, American mink), sciurid (Caucasian squirrel)	small intestines	Europe
<i>S. muris</i>	Eulipotyphla: soricid (Indian musk shrew)	small intestines	Asia
<i>S. mustelorum</i>	Carnivora: mustelid (European polecat, European mink, least weasel)	small intestines	Europe
<i>S. myopotami</i>	Rodentia: echimyid (coypu), procyonid (raccoon); Primates: hominid (human)	small intestines	Americas
<i>S. nasua</i>	Carnivora: procyonid (white-nosed coati)	small intestines	Americas
<i>S. ovocinctus</i>	Artiodactyla: antilocaprid (pronghorn)	small intestines	North America
<i>S. papillosus</i>	Artiodactyla: bovid (sheep, argali, mouflon, goat, cattle, water buffalo, American bison, impala, nyala, blackbuck, greater kudu, red forest duiker, Maxwell's duiker, kob, suni), cervid (roe deer, red deer), camelid (dromedary), suid (pig); Perissodactyla: equid (zebra); Lagomorpha: leporid (snowshoe hare, rabbit); Rodentia: sciurid (squirrel), murid (mouse), echimyid (coypu); Carnivora: mustelid (European polecat); Primates: hominid (human)	small intestines [diarrhoea, anorexia]	worldwide
<i>S. planiceps</i> (syn. <i>S. cati</i> p.p.)	Carnivora: felid (cat, flat-headed cat, leopard cat), mustelid (Japanese weasel), canid (dog, Japanese raccoon dog, red fox); Primates: hominid (human)	small intestines	worldwide
<i>S. procyonis</i>	Carnivora: procyonid (raccoon); Primates: hominid (human)	small intestines	North America
<i>S. putorii</i>	Carnivora: mustelid (European polecat)	small intestines	Europe
<i>S. ransomi</i>	Artiodactyla: suid (pig), cervid (red deer); Lagomorpha: leporid (rabbit); Primates: hominid (human)	small intestines [bloody diarrhoea]	worldwide
<i>S. ratti</i>	Rodentia: murid (mouse, Mongolian gerbil, ricefield rat, Polynesian rat, brown rat, black rat, dusky field rat), cricetid (muskrat)	small intestines	Eurasia, North America
<i>S. robustus</i>	Rodentia: sciurid (northern flying squirrel, southern flying squirrel), cricetid (golden hamster), sciurid (eastern gray squirrel, fox squirrel, Richardson's ground squirrel, thirteen-lined ground squirrel, eastern chipmunk, American red squirrel)	small intestines	North America

<i>S. rostombekowi</i>	Eulipotyphla: erinaceid (European hedgehog)	small intestines	Europe
<i>S. sciuri</i>	Rodentia: sciurid (eastern fox squirrel)	small intestines	North America
<i>S. shastensis</i>	Xenarthra: nothrotheriid (Shasta ground sloth)	small intestines	North America
<i>S. sigmodontis</i>	Rodentia: cricetid (hispid cotton rat)	small intestines	Americas
<i>S. spearei</i>	Diprotodontia: vombatid (wombat)	small intestines [enteritis]	Australia
<i>S. stercoralis</i> (threadworm)	Primates: hominid (human, chimpanzee, orangutan), atelid (Geoffroy's spider monkey), hylobatid (Hoolock gibbon, white-handed gibbon), callitrichid (pygmy marmoset), cercopithecoid (Patas monkey, rhesus macaque, yellow baboon, golden snub-nosed monkey); Carnivora: canid (dog, Arctic fox, golden jackal), felid (cat, Iberian lynx), mustelid (beech marten), procyonid (raccoon); Rodentia: murid (Mongolian gerbil, mouse); Artiodactyla: suid (pig)	small intestines [bloody diarrhoea]	worldwide
<i>S. suis</i>	Artiodactyla: suid (pig)	small intestines	Europe
<i>S. thylacis</i>	Peramelemorphia: peramelid (northern brown bandicoot)	small intestines	Australia
<i>S. tumefaciens</i>	Carnivora: felid (cat)	small intestines [mucosal tumours]	worldwide
<i>S. ultrajectinus</i>	Rodentia: cricetid (vole)	small intestines	Eurasia
<i>S. venezuelensis</i>	Rodentia: murid (Mongolian gerbil, mouse, Polynesian rat, brown rat, black rat)	small intestines	Americas, Asia
<i>S. vituli</i>	Artiodactyla: bovid (cattle)	intestines	Asia
<i>S. vulpis</i>	Carnivora: canid (Arctic fox, red fox), mustelid (wolverine)	small intestines	Holarctic
<i>S. westeri</i>	Perissodactyla: equid (horse, donkey, zebra); Artiodactyla: suid (pig); Rodentia: caviid (guinea pig), murid (mouse); Lagomorpha: leporid (rabbit)	small intestines [diarrhoea]	worldwide
Avian hosts			
<i>S. ardeae</i>	Pelecaniformes: ardeid (yellow-crowned night heron)	intestines	Americas
<i>S. avium</i>	Galliformes: odontophorid (northern bobwhite quail), phasianid (chicken, turkey); Gruiformes: rallid (water rail); Columbiformes: columbid (rock dove)	intestines	worldwide
<i>S. cubaensis</i>	Pelecaniformes: ardeid (green heron)	intestines	Americas
<i>S. herodiae</i>	Pelecaniformes: ardeid (great blue heron)	intestines	Americas
<i>S. minimum</i>	Anseriformes: anatid (white-cheeked pintail)	intestines	South America
<i>S. oswaldoi</i>	Galliformes: phasianid (chicken)	intestines	Europe
<i>S. pavonis</i>	Galliformes: phasianid (chicken, green peafowl)	intestines	Asia
<i>S. quisicali</i>	Passeriformes: icterid (greater Antillean grackle)	intestines	Central America
<i>S. turkmenica</i>	Gruiformes: rallid (common moorhen, Baillon's crane); Charadriiformes: recurvirostrid (black-winged stilt, stilt-legged plover), scolopacid (Eurasian woodcock)	intestines	Europe
Reptilian hosts			
<i>S. cruzi</i>	Sauria: gekkonid (tropical house gecko)	intestines	Africa
<i>S. darevskiyi</i>	Sauria: lacertid (felseneidechse)	intestines	Europe
<i>S. gulae</i>	Serpentes: colubrid (green water snake), pythonid (Burmese python)	intestines	North America, Asia
<i>S. mirzai</i>	Serpentes: colubrid (grass snake, oriental rat snake), viperid (Okinawa habu), typhlopod (European blind snake)	intestines	Eurasia
<i>S. natricis</i>	Serpentes: colubrid (grass snake, viperine water snake)	intestines	Eurasia
<i>S. ophidae</i>	Serpentes: colubrid (Rio tropical racer)	intestines	South America
<i>S. ophiussensis</i>	Sauria: lacertid (Ibiza wall lizard)	intestines	Europe
<i>S. serpentis</i>	Serpentes: colubrid (green water snake)	intestines	North America
Amphibian hosts			
<i>S. amphibiophilus</i>	Anura: bufonid (Cuban toad)	intestines	Cuba
<i>S. bufonis</i>	Anura: bufonid (natterjack, Asian common toad)	intestines	Eurasia
<i>S. carinii</i>	Anura: leptodactylid (Cerrado oven frog, striped frog, Joly's white-lipped frog)	intestines	South America
<i>S. mascomai</i>	Anura: ranid (Perez's frog)	intestines	Europe
<i>S. pereira</i>	Anura: hylodid (torrent frog)	intestines	South America
<i>S. physali</i>	Anura: bufonid (Gulf Coast toad)	intestines	Central America
<i>S. prokopici</i>	Anura: bufonid (subdesert toad)	intestines	Africa
<i>S. spiralis</i>	Anura: ranid (edible frog, pool frog)	intestines	Europe

The genus *Parastrongyloides* contains 12 species that are parasitic in the small intestines of marsupials, monotremes, moles and shrews, where they form parasitic males as well as females. These species are also able to undergo multiple free-living generations outside of their hosts (> 90 generations recorded for one species).

<i>Parastrongyloides</i> species	Definitive Hosts	Location	Distribution
<i>P. australis</i>	Peramelemorphia: peramelid (southern brown bandicoot, eastern barred bandicoot, long-nosed bandicoot); Dasyuromorphia: dasyurid (brown antechinus, dusky antechinus, white-footed dunnart)	small intestines	Australia
<i>P. caenolesti</i>	Paucituberculata: caenolestid (Tate's shrew opossum)	small intestines	South America
<i>P. callipygus</i>	Afrosoricida: potamogalid (giant otter shrew)	small intestines	Africa
<i>P. chrysochloris</i>	Afrosoricida: chrysochlorid (Congo golden mole); Rodentia: murid (rusty-bellied brush-furred rat)	small intestines	Africa
<i>P. nadgeensis</i>	Dasyuromorphia: dasyurid (agile antechinus, dusky antechinus, fat-tailed dunnart)	small intestines	Australia
<i>P. neotropicalis</i>	Eulipotyphla: soricid (Ecuadorian small-eared shrew)	small intestines	South America
<i>P. peramelis</i>	Peramelemorphia: peramelid (long-nosed bandicoot, northern brown bandicoot); Dasyuromorphia: dasyurid (agile antechinus, brown antechinus)	small intestines	Australia
<i>P. skrjabini</i>	Eulipotyphla: talpid (European mole)	small intestines	Europe
<i>P. tachyglossi</i>	Monotremata: tachyglossid (short-beaked echidna)	small intestines	Australia
<i>P. timbillicensis</i>	Dasyuromorphia: dasyurid (white-footed dunnart, fat-tailed dunnart)	small intestines	Australia
<i>P. trichosuri</i>	Diprotodontia: phalangerid (common brush-tailed possum, short-eared possum, mountain brushtail possum), petaurid (sugar glider)	small intestines	Australia
<i>P. walterae</i>	Dasyuromorphia: dasyurid (dusky antechinus)	small intestines	Australia
<i>P. winchesi</i>	Eulipotyphla: talpid (European mole, Spanish mole, Roman mole, Kobe mole, Sado mole, Japanese mole, blind mole), soricid (northern short-tailed shrew, bicolored shrew, greater white-toothed shrew, lesser white-toothed shrew, Mediterranean water shrew, common shrew, Tien Shan shrew, Shinto shrew, Laxmann's shrew, Eurasian pygmy shrew, long-clawed shrew)	small intestines	Europe, Asia

**Parasite morphology:** The parasite has an unusual developmental cycle involving the formation of eggs, free-living and parasitic larvae, free-living male and female adult worms, as well as parasitic (protandrogonous or parthenogenetic) female worms. Eggs appear as small oval thin-shelled bodies, measuring 40-60 µm in length by 25-40 µm in width, and may be partially (2-8 cell stage) or fully embryonated (larvated) when passed in faeces. Free-living larvae (L1 and L2) measure up to 380 µm in length and 20 µm in width and they have a short buccal cavity, rhabditiform pharynx and a muscular bulbed oesophagus (ideal for feeding on particulate material, incl. bacteria). Infective third-stage larvae (L3) measure from 524-710 µm in length and 20 µm in width and have a long tubular filariform oesophagus extending over a third of the body length (ideal for sucking fluids after penetrating host tissues). These larvae do not feed in the soil and have closed uneven mouths and pointed tails (sometimes bifid (notched) in some species). Parasitic worms are all females, measuring from 2-9 mm in length by 80-100 µm in width and characterised by the presence of an extremely long cylindrical (filariform) oesophagus (one third of body length), a posterior vulva and a blunt pointed tail. Free-living male and female worms have a tiny buccal capsule, a rhabditiform pharynx and are smaller in size, measuring up to 1 mm in length. Males have two simple spicules and a gubernaculum, and a pointed tail curved ventrally. Females are stout with 2 ovaries and uteri opening into a vulva located around the middle of the body. The uteri of parasitic females only contain a few eggs at a time, while those of free-living females contain far more eggs.

**Site of infection:** Parasitic female worms become embedded in the small intestinal mucosa, forming tunnels under the epithelium at the bases of villi and in the crypts of the small intestines. Eggs and first-stage larvae are passed with host faeces. Infective third-stage larvae penetrate the skin and undergo pulmonary migration before forming parthenogenetic females in the intestines.

**Pathogenesis:** Light threadworm infections remain asymptomatic, even though they may persist for years due to auto-infection or re-infection. Heavier infections, however, can cause several forms of disease; including dermal, pulmonary, enteric and disseminated disease. In humans, migrating *S. stercoralis* larvae can race through the skin (up to 10 mm per hour) causing larval

*currens*, characterised by urticaria, pruritus, eosinophilia, dermatitis, and inflammation. In animals, larvae may cause erythematous lesions where they penetrate the skin. In all cases, pulmonary migration may cause petechiae, mild transient pneumonia or bronchial pneumonitis, with coughing, wheezing, shortness of breath, and transient eosinophilic pulmonary infiltrates (Loeffler's syndrome). Lesions caused by adult worms generally consist of catarrhal inflammation, although severe infections may result in necrosis and sloughing of the mucosa, haemorrhage, epigastric pain (may mimic peptic ulcer or Crohn's disease), vomiting, abdominal distention, diarrhoea with voluminous stools (formerly known as Cochin-China diarrhoea) and a malabsorption syndrome with dehydration and electrolyte disturbance, peripheral eosinophilia, and possibly reactive arthritis. Fulminant hyper-infection syndrome may develop in patients with malnutrition, chronic infections and immunosuppression resulting in severe gastrointestinal and/or respiratory symptoms due to inflammation, haemorrhage and malfunction. Fatal disseminated infection may also develop when large numbers of filariform larvae penetrate the bowel and disseminate, causing colitis, polymicrobial sepsis, pneumonitis or neurological manifestations, such as meningitis and cerebral or cerebellar abscesses. Latent infections may also be reactivated by immunosuppressive chemotherapy leading to hyper-infection syndrome with high worm burdens and disseminated larval migration. In animals, many infections are asymptomatic but some cause diarrhoea and wasting, particularly in neonates infected by transmammary transmission and exacerbated by recurrent autoinfection. Most infections by *S. stercoralis* in puppies and kittens are mild and self-limiting due to the development of a strong protective immunity within weeks, but heavy infections may be associated with pododermatitis, pneumonitis, diarrhoea, catarrhal enteritis, impairment of digestion and absorption, and wasting. Infections in pigs by *S. ransomi* have been associated with erythematous skin reactions, urticaria, pulmonary petechiae, interstitial pneumonia, intestinal inflammation, catarrhal enteritis (with mucosal hyperaemia, petechiae and ecchymoses), villous atrophy, bloody diarrhoea, anaemia, subcutaneous oedema, malabsorption, hypoproteinaemia and emaciation. Infections by *S. westeri* cause enteritis and diarrhoea in foals but are generally asymptomatic in adult horses. Infections by *S. papillosus* may appear early in lambs due to transmammary infection but protective immunity is rapidly acquired and worm burdens decline before weaning. Heavy infections, however, have been associated with sudden death in lambs and calves as well as with a wasting disease in rabbits.

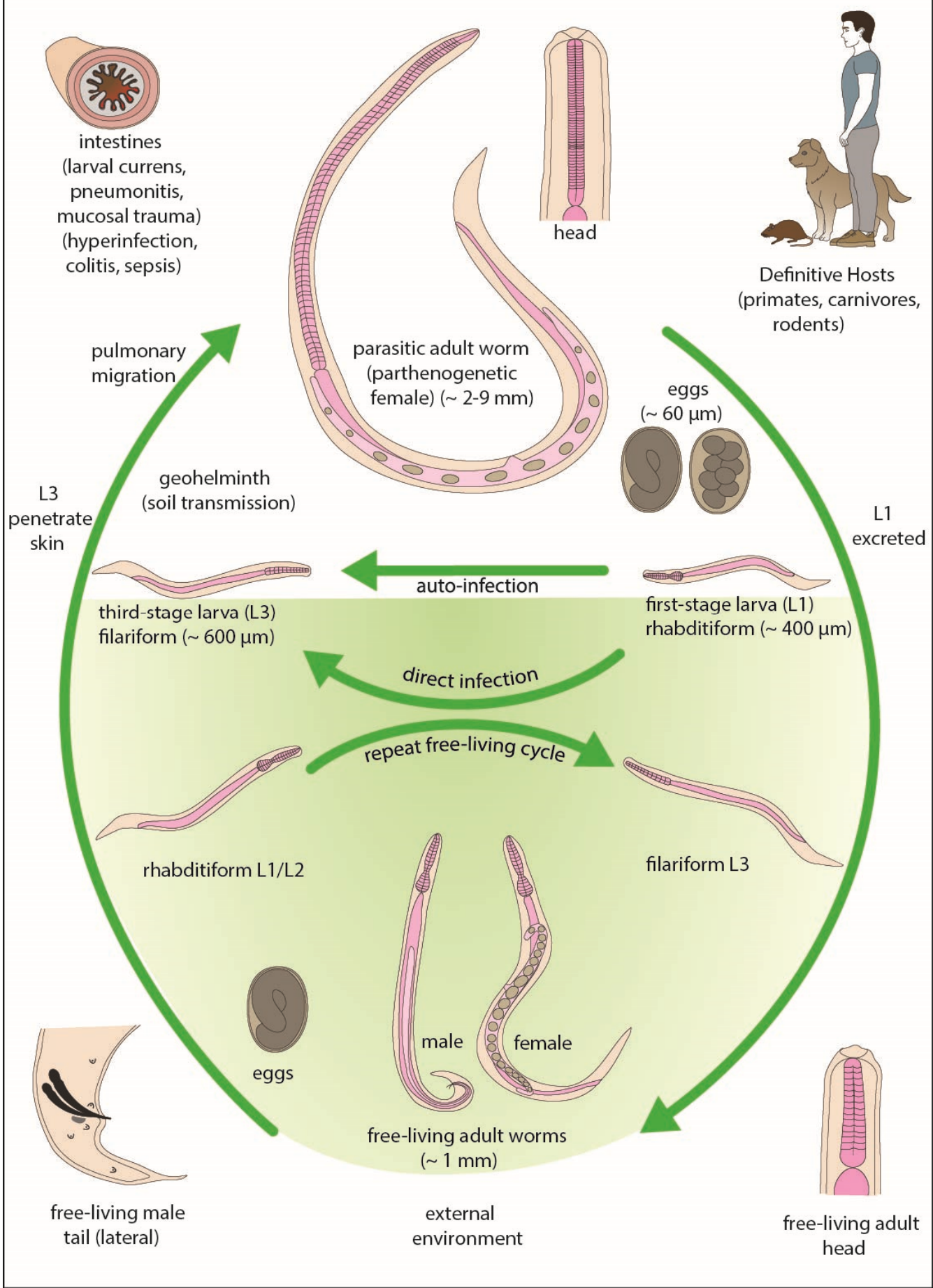
**Developmental cycle and mode of transmission:** Threadworms have direct life-cycles not involving vectors or intermediate hosts. However, they are unique in that they may form parasitic or free-living adult stages, either as alternating or perpetuating generations. Parasitic stages consist entirely of female worms located in the host intestines, although these worms are protandrogynous (in that male reproductive organs develop first and then disappear) with female reproductive organs then developing and producing larvated eggs (giving the impression of parthenogenetic reproduction). The prepatent period (time from infection to first egg release) often ranges from 25-30 days, but in some species, it may be as short as 6-10 days. The female worms produce several dozen eggs per day, most of which complete embryonation and hatch internally within the host releasing first-stage rhabditiform larvae (L1) which are passed with host faeces. These L1 feed on bacteria and organic debris, moult to second-stage rhabditiform larvae (L2) which feed and then moult to form third-stage filariform larvae (L3). Different L3 strains then undergo free-living (heterogonic) or parasitic (homogonic) development. Heterogonic L3 moult twice to form a generation of free-living males and females which feed on bacteria with their rhabditiform pharynxes. Free-living female worms producing partially-embryonated eggs which eventually hatch releasing rhabditiform L1 that grow and moult twice to form filariform L3. These larvae may give rise to another free-living generation or they may infect hosts as parasites. Infective L3 (homogonic strains and those produced by free-living adults) may survive in moist soil for several weeks (geo-helminth phase) before infecting hosts usually by penetrating the skin (or oral mucosa) although some may simply be ingested. Larvae that are swallowed pass to the intestines where they develop without further migration. Larvae penetrating the skin, however, enter the circulation and are carried to the lungs where they undergo pulmonary migration by penetrating alveoli and moving up the trachea to be swallowed. Other non-pulmonary routes of larval migration have been shown experimentally for several species, mostly involving nasofrontal regions in rodents. After infections have become established in the intestines, further incoming larvae may migrate to deeper tissues and undergo arrested development (hypobiosis) leading to the persistence of chronic infections. Migrating larvae and re-mobilized arrested larvae have been associated with trans-mammary infections by *S. stercoralis*, *S. ransomi*, *S. papillosus* and *S. westeri* in dogs, pigs, sheep and horses respectively, as well as prenatal infections by *S. ransomi* and *S. papillosus* in pigs and sheep. Only adult female (parthenogenetic) worms develop in the small intestines and they live for only a few months. Chronic and hyper-infections by *S. stercoralis* and *S. felis* may develop in their hosts because parasitic stages may continue indefinitely through the process of auto-infection [eggs hatching in the intestines may develop into infective L3 which directly penetrate the lower gut (internal auto-infection) or peri-anal region (external auto-infection), thus leading to a new cycle of infection].

**Differential diagnosis:** Infections are diagnosed by the detection of larvae in faecal samples (or in duodenal endoscopic biopsies), as most eggs hatch internally within the host releasing rhabditiform larvae. Filariform larvae may occasionally be detected, especially during hyper-infection, and they can be identified by their notched tails. Although eggs are rarely detected even in fresh faeces, they are similar in size, shape and appearance to hookworm eggs. Larvae and/or eggs may be present in very low numbers so multiple samples should be examined over a short time course. Larvae may be detected in wet mounts, stained faecal smears, faecal concentrates or cultures. Faecal culture can increase the sensitivity of microscopic diagnosis, by either concentrating larvae (Harada Mori or Baermann technique) or amplifying populations through a generation of free-living males and females. Larval cultures are also used to differentiate between threadworm (*Strongyloides*) and hookworm (*Ancylostoma* and *Necator*) infections, as threadworm larvae have a smaller buccal cavity and a larger genital primordium (such differentiation is crucial as treatment options differ). Non-nutrient agar plate cultures of faeces have also been used to detect motile larvae. The diagnosis of infections by the direct detection of parasites can often be complicated by the sporadic shedding of eggs/larvae, the senescence of parasitic worms (no longer

producing eggs), the presence of dormant larvae in tissues (hypobiosis) or extended larval migration (particularly following auto-infection and hyperchronic infections). Recourse is therefore often made to indirect methods of diagnosis. Eosinophilia is a characteristic finding of many helminth infections (including strongyloidiasis), but it is relatively nonspecific and also not persistent during hyperinfections. Radiology may reveal reflux of oral contrast into the biliary tree, possibly due to inflammation affecting the sphincter of Oddi. Several immunoserological tests (agglutination, fluorescent-antibody, enzyme immunoassays and Western blots) have been developed to detect host antibodies against threadworm antigens, but they have difficulty in distinguishing between past and active infections and may sometimes cross-react with other helminths (such as roundworms, filarial worms and even schistosomes). Several molecular biological tests have recently been developed using polymerase chain reactions (PCR) to amplify parasite DNA sequences, including the hypervariable region (HVR) IV of small subunit (18S) ribosomal DNA, ribosomal protein L10 (rpl-10), mitochondrial cytochrome c-oxidase subunit 1 gene (*cox1*) and  $\beta$ -tubulin gene.

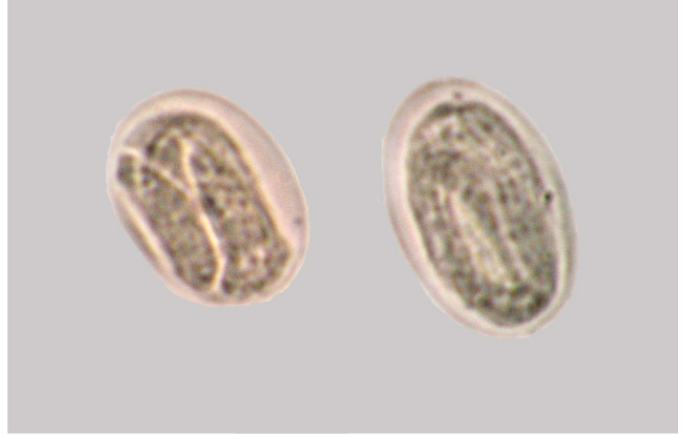
**Treatment and control:** Several anthelmintics are reasonably effective against threadworm infections, but none are entirely satisfactory. Treating hyperinfections is difficult as drugs are ineffective against migrating auto-infective larvae. Thiabendazole has been widely used but it has unpleasant side-effects, including nausea, vomiting, dizziness, malaise and smelly urine. Other benzimidazoles (albendazole, fenbendazole, flubendazole), imidazothiazoles (levamisole) and macrocyclic lactones (ivermectin, abamectin, doramectin) show good activity, and variable results have been obtained with mebendazole and piperazine. Treatment should be repeated after a week because of difficulty in confirming cure. Immuno-suppressive treatments should be avoided as they can result in rampant auto-infection, as can corticosteroid treatment of mistaken asthmatic respiratory signs. Preventive measures include the wearing of solid shoes in endemic areas, thoroughly washing salad vegetables, prohibiting the use of nightsoil to fertilise gardens, the sanitary disposal of faeces, the provision of latrines in poor areas, and public education campaigns. Infections in animals can be alleviated by improving husbandry, avoiding overcrowded and unhygienic conditions, regularly removing faeces from holding areas, disinfecting pens/stalls, isolating infected individuals and monitoring and treating lactating dams and suckling neonates.

# Strongyloides





*Strongyloides* adult worms



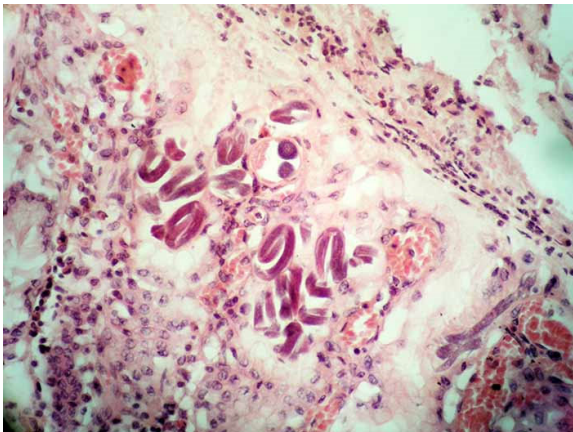
*Strongyloides* eggs



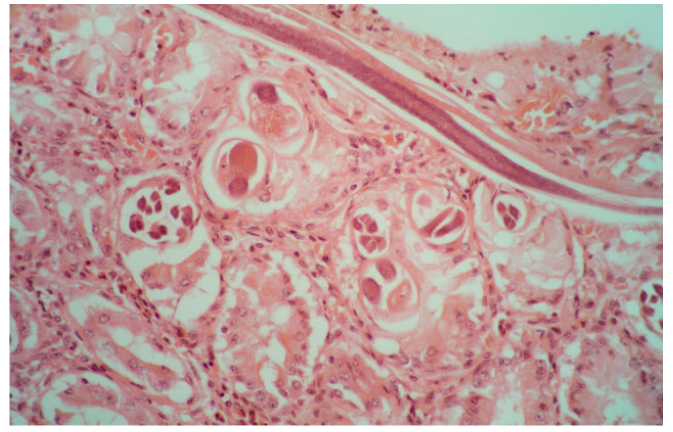
*Strongyloides* rhabditiform larva



*Strongyloides* filariform larva



*Strongyloides* in gut section



*Strongyloides* in gut section