Stephanurus
(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 stephanurids which are stout worms with a prominent buccal capsule often armed with teeth, small leaf crowns and external epaulettes. They have direct life-cycles, usually involving eggs passed in faeces developing to L3 which are ingested by new hosts and develop to adults. *Stephanurus*, however, may also infect hosts percutaneously, when L3 penetrate the skin, moult to L4, wander in the liver parenchyma during maturation before completing development in cysts in peri-renal regions. Worm eggs are voided via the ureter with host urine. Earthworms may also act as paratenic (transport) hosts for L3. *S. dentatus* (pig kidneyworm) causes hepatic cirrhosis in pigs 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:	Syngamidae (buccal capsule with basal teeth, in respiratory, urinary or digestive tract of mammals/birds)
Subfamily:	Stephanurinae (rudimentary leaf crown, kidney-worm in pigs)
Genus:	*Stephanurus* (parasitic in kidneys of pigs)
Species:	*S. dentatus* causes cirrhosis in pigs

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**
Strongylina (strongyles)				
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
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
Trichostrongylina (trichostrongyles)				
Trichostrongylidae (trichostrongyles)	reduced buccal capsule, ridged synlophe, oesophagus lacking bulb, thin-shelled eggs	artiodactyls, birds	ingestion of L3	50
Molineidae (stomach/intestinal worms)	reduced buccal capsule, cephalic vesicle, female tail with spine or cusps, oviparous/viviparous	mammals, birds, reptiles	ingestion of L3	61
Heligmonellidae (hookworm-like)	body coiled, cephalic vesicle, ridged synlophe, bursa asymmetrical	mammals, birds	transdermal penetration of L3	56
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

Strongyle worms are characterised by their prominent buccal capsules with lips, leaf crowns or labial collars at the mouth opening, sometimes with teeth or cutting plates. They are parasitic in a variety of organ systems in a range of animals, including the large intestines of mammals (ruminants, suids, elephants, perissodactyls, rodents, marsupials and primates), tortoises and ratite birds, the forestomach of marsupials, the trachea of birds and mammals, and the renal system of suids. Four families are recognised: Strongylidae (buccal capsule globular or cylindrical, oral opening circular, dorsal ray with 6 terminal branchlets, 32 genera in large intestines of mammals, reptiles and birds); Chabertiidae (buccal capsule globular or cylindrical, oral opening circular or oval, with leaf crown or labial collar, with up to 3 teeth at base of buccal capsule, dorsal ray with 4 terminal branchlets, 22 genera in gastrointestinal tract of mammals); Syngamidae (buccal capsule subglobular, oral opening hexagonal, numerous teeth at base of buccal capsule, dorsal ray with 4 terminal branchlets, 7 genera in respiratory, urinary and digestive tracts of mammals and birds); and Deletrocephalidae (oral opening hexagonal, dorsal ray with 6 terminal branches, 2 genera in large intestines of birds). The family Syngamidae contains 3 subfamilies: Syngaminae (leaf crown absent, teeth at base of buccal capsule, anterior vulva, 5 genera in trachea of birds and some mammals); Stephanurinae (rudimentary leaf crown, teeth at base of buccal capsule, rudimentary bursa, posterior vulva, 1 genus in urinary system of suids); and Archeostrongylinae (leaf crown absent, teeth absent at base of buccal capsule, 1 genus in intestines of porcupines).

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm eggs
Stephaurinae					
Stephanurus (kidney-worm)	1	suids	urinary tract	2-5 cm long, stout reddish bodies, white reproductive organs, prominent buccal capsule often armed with teeth, small leaf crowns and external epaulettes, eggs passed in faeces and urine, L3 ingested or percutaneous, earthworm PH	90-136 x 53-70 µm, ellipsoidal, thin-shelled
Syngaminae					
Syngamus (gape worm)	10	birds	respiratory tract	2-30 mm long, hexagonal cup-shaped buccal capsule armed with teeth, no leaf crowns, small male permanently attached to female vulva imparting Y-shape, L3 develop in eggs before hatching, invertebrate PH	70-100 x 42-62 µm, ellipsoidal, operculate

The subfamily Stephanurinae is monotypic and contains a single genus (*Stephanurus*) with a single species (*S. dentatus*) which forms cysts attached to the ureters of suids (commonly known as pig kidneyworms). Worm eggs are passed in urine to the external environment where they embryonate. Hosts become infected by eating infective L3 or when L3 penetrate the skin resulting in extra-intestinal migration. Infections are common in free-ranging and wild pigs in tropical and sub-tropical areas, and may affect domestic pigs with access to unfloored or outdoor areas (occasionally infecting cattle).

***Stephanurus* species**	**Definitive Hosts [plus Paratenic Hosts (PH)]**	**Location [Clinical signs]**	**Distribution**
S. dentatus (pig kidneyworm) (syn. *S. morai, S. nattereri, Sclerostoma dentatum, pinguicola, renium, Strongylus dentatus, pinguicola*)	Artiodactyla: suid (pig, wild boar, Japanese boar), bovid (cattle); rarely Rodentia: caviid (guinea pig) [plus PH: Clitellata: octochaetid (*Eutypheus waltoni*), megascolecid (*Pheretima diffringens*)]	kidney, perirenal fat [abscesses]	worldwide (except western Europe), esp. tropics

Parasite morphology: The pig kidneyworm forms 3 different types of developmental stages: eggs; larvae (4 successive stages designated L1-L4); and adult worms. Eggs are thin-shelled ovoid stages measuring 90-136 x 53-70 µm with one end broadly rounded and the other narrowly rounded. The contain a multicellular morula (32-64 blastomere stage) which is centrally located but usually surrounded by a clear space. L1 are free-living stages measuring from 360-560 µm with a rhabditiform (bulbed) oesophagus and an elongate tapering tail. L2 are similar but measure from 540-710 µm and have a slender tail. L3 are ensheathed in that the second moult was incomplete and they retained the L2 cuticle as a protective sheath. These larvae measure from 510-610 µm and have a mouth bordered by inconspicuous lips, a spindle-shaped buccal cavity, a strongyliform oesophagus, intestines with 32 cells, and a short conical tail. L4 are parasitic stages that migrate through host tissues. They are initially small (320-790 µm) but grow markedly throughout their development (up to 1-3 mm long). The have a well-developed and heavily-sclerotized buccal capsule, and an elongate tubular oesophagus. Adult worms have stout bodies 20-50 mm long that are pink-red in colour but frequently appear mottled as the light-coloured internal reproductive organs are visible through the translucent cuticle. Adults have a hexagonal oral opening leading to a prominent subglobular (cup-shaped) buccal capsule armed with 6 cusped teeth at the base, and surrounded by small rudimentary leaf crowns (absent in *Syngamus*) and 6 external cuticular thickenings (epaulettes). Mature worms are sexually dimorphic, with females being larger than males (30-50 cf. 20-30 mm). Males have a short rudimentary bursa reduced to short thick blunt rami (the dorsal ray having 4 terminal branches) and 2 dark elongate spicules almost equal in length. Females are didelphic with 2 ovaries and connecting ducts terminating in a common posterior vulva (anterior in *Syngamus*).

Site of infection: Adult worms are usually found encysted within the peri-renal fat or in the pelvis of the kidneys of their suid hosts. Eggs are voided in host urine and give rise to free-living larval stages (L1, L2 and ensheathed L3) that contaminate the external environment. Parasitic L4 migrate through the liver before young adults infect the kidneys.

Pathogenesis: Infections by adult worms are generally not associated with disease, even though worms become encysted around the kidneys. The cysts range in diameter from 5-40 mm and usually contain a pair of worms surrounded by inflammatory cells (sometimes greenish pus) and a dense fibrous capsule. In rare cases, the ureters may become thickened and partially occluded or stenosed, with subsequent hydronephrosis. Blood may also be passed occasionally in the urine (haematuria) together with worm eggs. Most of the pathogenic effects, however, are caused by earlier larval stages damaging tissues when feeding and migrating.

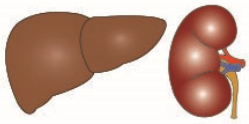
Percutaneous infections may result in transient inflammation of the skin with oedema and enlarged superficial lymph nodes, but migrating L4 and young adults (often called L5) with their well-developed mouthparts cause significant damage to host tissues, particularly during their obligatory and lengthy development in the liver. Infections cause inflammation (hepatitis) with eosinophilia, abscess formation, extensive fibrosis (evident as patchy cirrhosis), thrombosis of hepatic vessels, and fluid accumulation (ascites), all contributing to liver dysfunction. Clinical signs include anorexia, loss of body condition, illthrift with depressed growth, weight loss, and in severe cases, muscle wasting, emaciation, liver failure and death. Migrating stages may also undertake aberrant migrations to ectopic sites and cause tissue damage and abscess formation in various organs, including pulmonary lesions, portal phlebitis, splenitis, pancreatitis, lymphadenitis, myositis and myelitis leading to paralysis.

Developmental cycle and mode of transmission: *Stephanurus* varies in its route of transmission, with direct cycles involving infective L3 being ingested (faecal-oral transmission) or penetrating the skin (percutaneous or transdermal transmission), or an indirect cycle involving the ingestion of L3 in invertebrate paratenic (transport) hosts. Gravid female worms are very fecund and lay thousands of eggs per day which are excreted in host urine (up to 1.5 million eggs per urination have been recorded). Voided eggs hatch in the external environment in about 30 hours releasing free-living rhabditiform L1 which feed on soil bacteria and then moult to L2 which also feed. These larvae undergo an incomplete moult producing a strongyliform L3 still ensheathed in the L2 cuticle. These stages do not feed but are highly active and migrate through damp soil and onto vegetation. In warm moist conditions, L3 may form in 2-7 days and they may survive for 2-5 months. They are highly susceptible to cold and desiccation, so infections are most prevalent in warm wet countries, often in association with poorly-drained damp soils. Hosts become infected when they ingest infective L3 on pastures or when L3 come into contact with their skin and penetrate dermal tissues. It was also discovered that L3 ingested by earthworms could survive unchanged within them for up to a year, and were still infective for pigs that consumed infected earthworms. Irrespective of route, L3 exsheathed and moulted to L4 within 3 days of infection. However, in the case of oral infections, this moult occurred in the stomach wall and L4 migrated to the liver via the portal veins. In the case of transdermal infections, the moult takes place in the skin or muscles and L4 migrated to the liver via the lungs and systemic circulation. Within the liver, the larvae moult to L5 and the young worms wander in the parenchyma for 3 or more months before piercing the capsule and moving through the peritoneal cavity to the peri-renal region (although some may undertake aberrant migrations to ectopic sites). Adult worms become encapsulated by host reactions in the peri-renal fat or in the kidney, with the cysts communicating with the ureter directly or via fine connecting canals. Inside the cysts, worm pairs mature and mate, with eggs being liberated into the ureter and excreted with host urine. The prepatent period (time from infection to first egg excretion) ranges considerably from 6-19 months (usually 9 months) and the adult worms may live for up to 2-3 years. Pigs of all ages are susceptible to infection, but most patent infections are observed in animals > 2 years of age (usually breeders) due to the long prepatent period. Prenatal infections have also been reported involving the transplacental transmission of migrating larvae.

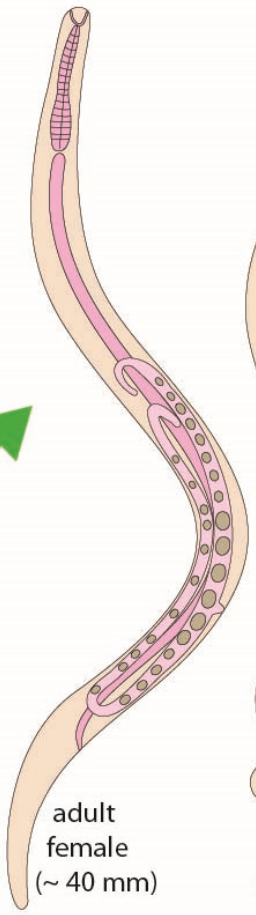
Differential diagnosis: Infections cannot be diagnosed on the basis of symptomatology due to their vague nonspecific nature (essentially illthrift with liver signs). Diagnosis is usually made at necropsy by the detection of milk spot liver lesions or an extensively-scarred and enlarged liver, or by the detection of cysts or abscesses containing worms. Ante-mortem diagnosis may be made by the microscopic detection of worm eggs in urine sediments, especially those prepared from the first urine passed in the morning. Experimental studies using immunodiffusion and immunoelectrophoretic techniques detected specific antibody responses against both juvenile and adult worms, but they were transient and short-lived compared to the long course of infection. Molecular phylogenetic studies have recently been used to characterize adult worms following the polymerase chain reaction (PCR) amplification and sequencing of nuclear genes (small subunit ribosomal DNA).

Treatment and control: Infections have responded well to treatment with several anthelmintic drugs, including macrocyclic lactones (ivermectin) and benzimidazoles (fenbendazole) which were effective against migrating and adult stages, and the imidazothiazole (levamisole) which was effective against adult worms. It is recommended that producers treat breeders before and after farrowing to limit the transmission of infections between generations. Given the long prepatent period, several authorities have recommended that only a single generation be bred from gilts and young boars prior to their slaughter before infections become patent (i.e. before egg production begins). Intensive indoor piggeries usually do not have problems with kidneyworms because the concrete pens are cleaned regularly and pigs have no access to soil or pastures contaminated with larvae. However, infections can become problematic in traditional extensive holdings where pigs are kept outdoors or have access to earthen areas or pastures, particularly those with moist loose soils and earthworms. Nonetheless, some measure of control can be afforded by improving hygiene to reduce environmental contamination by urine, placing feeding and watering equipment on concrete in sunny well-drained locations, rotating livestock between locations, separating cohorts (especially adults from weaners), avoiding mud wallow formation by fencing or draining, and preventing foraging for earthworms.

Stephanurus

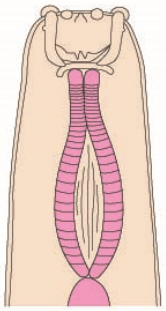


liver, kidneys
(hepatic cirrhosis,
perirenal abscesses)

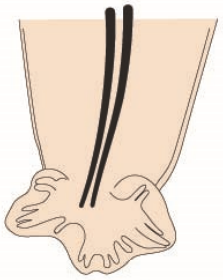


adult
female
(~ 40 mm)

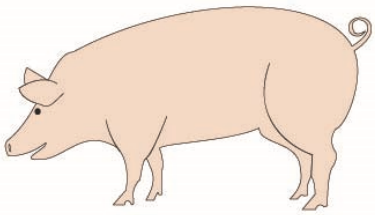
adult
male
(~ 25 mm)



head



male tail

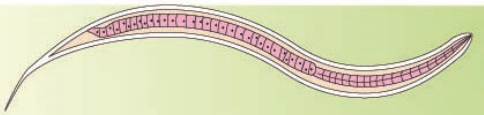


Definitive Hosts
(suids)

somatic migration

L3
penetrate
skin or
ingested
in PH

eggs
passed
in urine



filariform third-
stage larvae (L3)
(~ 600 µm)

external
environment

eggs
(~ 110 µm)

rhabditiform first- and
second-stage larvae (L1, L2)
(~ 500 µm)

Paratenic Hosts
(earthworms)
(gut, viscera?)

Stephanurus adult worms

Stephanurus worm egg