Globocephalus
(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 ancylostomatids (hookworms) which are characterised by their bent mouths, the anterior ends being bent dorsally. They have a well-developed buccal capsule with cutting plates or teeth, and are voracious blood-feeders in the small intestines of mammals, esp. humans and companion animals. They have direct life-cycles, involving a geo-helminth phase. Eggs voided with faeces hatch releasing free-living rhabditiform larvae which subsequently develop into infective filariform L3 that are ingested or actively penetrate the skin of their hosts. Larvae undergo pulmonary migration through the lungs (sometimes causing pneumonitis) before developing into blood-feeding adults in the small intestines. *Globocephalus urosubulatus* causes mild hookworm disease (anaemia and diarrhoea) in pigs on most continents, except Australia.

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:	Ancylostomatidae (hookworms, buccal capsule bent dorsally, armed with teeth/cutting plates)
Genus:	*Globocephalus* (parasitic in small intestines of pigs)
Species:	*G. urosubulatus* causes anaemia 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**
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
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
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
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

Hookworms are characterised by their dorsally bent heads with prominent buccal capsules containing paired ventral lancets as well as teeth, cutting plates or lateral jaw-like structures. They are parasitic in the small intestines of mammals and reptiles and infections are acquired by the ingestion or skin penetration of infective L3 followed by tracheal migration. Two families are recognised: Ancylostomatidae (dorsally deviated head, buccal capsule usually armed with teeth or cutting plates, 20 genera in intestines of mammals); and Diaphanocephalidae (anteriorly directed head, buccal capsule forming 2 lateral jaw-like structures, 2 genera in intestines of reptiles). The family Ancylostomatidae contains 2 subfamilies: Ancylostomatinae (buccal capsule subglobular, with dorsal gutter, bursa with short dorsal ray, gubernaculum present, posterior vulva, female tail with terminal spine, most in carnivores); and Bunostominae (buccal capsule subglobular, with tooth-like dorsal cone, bursa with long dorsal ray, gubernaculum absent, anterior vulva, female tail without terminal spine, most in herbivores). Ancylostomatid genera of particular medical and/or veterinary significance are tabulated below.

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Worm eggs	Transmission
Ancylostominae						
Globocephalus	18	artiodactyls, rodents, primates	caecum, small intestines	3-9 mm long, large buccal capsule without cutting plates or teeth, larval pulmonary migration	60-75 x 35-41 µm, ovoid, thin-shelled	oral, transdermal
Ancylostoma	32	carnivores, primates	small intestines	5-25 mm long, bent heads, buccal capsule with ventral lancets and fused teeth, larval pulmonary migration, hypobiosis	55-95 x 32-58 µm, ellipsoidal, thin-shelled	oral, transdermal, transplacental, transmammary
Uncinaria	22	carnivores	small intestines	3-15 mm long, well-developed buccal capsule with pair of ventral cutting plates, no pulmonary migration	65-98 x 35-58 µm, ovoid, thin-shelled	oral (direct or via PH), rarely transdermal
Bunostominae						
Bunostomum	9	artiodactyls, proboscidea	small intestines	10-30 mm long, buccal capsule with ventral cutting plate and 1-2 pairs subventral teeth, larval pulmonary migration, hypobiosis	79-117 x 40-70 µm, ovoid, thin-shelled	oral, transdermal, transplacental, transmammary
Gaigeria	1	artiodactyls	small intestines	10-45 mm long, buccal capsule with pair ventral cutting plates, elongate lancets and teeth, larval pulmonary migration	108-115 x58-61 µm, ellipsoidal, thin-shelled	transdermal
Necator	7	primates, artiodactyls	small intestines	7-11 mm long, buccal capsule with cutting plates, larval pulmonary migration	55-77 x 35-42 µm, ovoid, thin-shelled	oral, transdermal

The subfamily Ancylostominae contains 8 genera classified in 4 tribes: Ancylostomatinea containing worms with oral openings armed with teeth, and globular buccal capsules not divided into articulating plates (*Ancylostoma* (syn. *Agchylostoma*, *Anchylostomum*, *Ankylostoma*, *Ankylostomum*, *Ceylancylostoma*, *Diploodon, Dochmius*) and *Galoncus*) parasitic in carnivores, primates, edentates, rodents, and suids; Uncinarinea containing worms with oral openings with well-developed cutting plates, and buccal capsule not divided into articulating plates (*Uncinaria* (syn. *Dochmoides*, *Dochmius*, incl. subgenera *Uncinaria*, *Megadeirides*) and *Bioccastrongylus*) parasitic in insectivores, primates, and carnivores; Arthrocephalinea containing worms with buccal capsules divided into articulating plates (*Arthrocephalus*, *Arthrostoma*, and *Placoconus*) parasitic in carnivores; and Globocephalinea containing worms with oral openings lacking teeth and cutting plates (*Globocephalus* (syn. *Characostomum*, *Crassisoma*, *Cystocephalus*, *Raillietostrongylus*)) parasitic in suids, primates, mustelids, rodents, ruminants, and South American marsupials. The genus *Globocephalus* contains 18 species of hookworms, 9 species infecting pigs. The species *G. urosubulatus* is found throughout many tropical and sub-tropical regions and infections have tentatively been associated with anaemia in domestic animals.

***Globocephalus* species**	**Hosts**	**Location [Clinical signs]**	**Distribution**
G. amucronatus (syn. *Characostomum*)	Artiodactyla: suid (pig)		Java
G. asmilium (syn. *Characostomum*)	Primates: cercopithecid (southern pig-tailed macaque)		Africa, Asia
G. callosciuri	Rodentia: sciurid (grey-bellied squirrel)		Malaysia
G. connorfilii	Artiodactyla: suid (pig, wild boar); Rodentia: murid (black rat)		
G. gigantospiculatus	Carnivora: mustelid (hog badger)	caecum	Vietnam
G. howelli (syn. *Characostomum*)	Rodentia: nesomyid (Gambian pouched rat)	small intestines	Africa
G. longemucronatus (possible syn. of *G. urosubulatus*)	Artiodactyla: suid (pig, wild boar, Japanese boar); Primates: cercopithecid (Campbell's mona monkey)	small intestines	Africa, Eurasia
G. lutrae	Carnivora: mustelid (Eurasian otter)		Asia
G. macaci (probably *Ternidens deminutus*)	Primates: cercopithecid (southern pig-tailed macaque)		Africa

G. madagascariensis	Artiodactyla: suid (bushpig)		Africa
G. marsupialis	Didelphimorphia: didelphid (southern opossum, grey four-eyed opossum)		South America
G. maplestoni	Artiodactyla: suid (warthog)		Africa
G. mexicanus	Rodentia: geomyid (smoky pocket gopher)		North America
G. samoensis	Artiodactyla: suid (wild boar, Japanese boar)		Asia
G. sichuanensis	Artiodactyla: suid (pig)		Asia
G. simiae	Primates: cercopithecid (macaque)	intestines	
G. urosubulatus (pig hookworm)	Artiodactyla: suid (pig, wild boar, Sardinian wild boar)	small intestines [occasionally anaemia]	Americas, Europe, Africa, Asia
G. versteri	Artiodactyla: suid (bushpig)		Africa

Parasite morphology: *Globocephalus* spp. form 3 different types of morphological stages during their development: eggs; larvae (4 successive stages designated L1-L4); and adult worms. The eggs are thin-shelled and ovoid measuring 60-75 x 35-41 µm and contain an embryo at the 4-8 cell (blastomere) stage of development. L1 are free-living stages measuring 300-360 µm with a cylindrical buccal cavity, a rhabditiform (double-bulbed) oesophagus and a long tail. L2 are similar in morphology but are larger measuring up to 620 µm. L3 are ensheathed stages measuring 630-730 µm with a striated cuticle, a strongyliform (flask-shaped) oesophagus, intestines with a palisade zig-zag appearance comprising > 20 triangular cells, and a long filamentous tail sheath. L4 are transient parasitic stages that are beginning to show adult characteristics, particularly with respect to feeding structures. Adults are small stout white worms measuring 3-9 mm long and have heads bent dorsally like most hookworms. They have large subglobular buccal capsules without lips, leaf crowns, teeth or cutting plates. The buccal capsule contains a pair of large bicuspid subventral lancets near its base, and has an elongate dorsal gutter (containing the duct of the dorsal oesophageal gland) usually extending to the top margin. Adult worms are sexually dimorphic, with female worms being larger than males (4-9 cf. 3-7 mm). Mature females have 2 large ovaries and uteri that connect to a common vulva located posterior to the midbody, and tails containing a small terminal spine. Mature males have a caudal copulatory bursa with 2 lateral lobes supported by 6 pointed rays (consisting of muscular elements following nerve channels to terminal papillae) and a dorsal lobe (supported by a short dorsal ray with 4-6 branches). They also have a gubernaculum and 2 slender spicules measuring around 400 µm in length.

Site of infection: Adult worms infect the small intestinal mucosa of their vertebrate hosts, while developing larval stages undertake a pulmonary migration through the lungs before returning to the gut to mature as adults. Worm eggs excreted into the external environment release free-living (pre-parasitic) larval stages that become infective to their hosts.

Pathogenesis: Infections in pigs are often asymptomatic or subclinical, but heavy infections, particularly in young animals, may cause disease with anaemia and enteritis. Adult hookworms suck blood from the intestinal mucosa and frequently change their sites of attachment leaving behind haemorrhagic lesions that may contribute to anaemia. In addition, mucosal trauma and inflammation disrupt digestive function and fluid flow leading to maldigestion, hypoproteinaemia, oedema, diarrhoea (often black in colour due to the presence of blood), colic, reduced weight gain or weight loss, and sometimes emaciation. On occasion, earlier developing larvae migrating through the lungs may cause pneumonitis predisposing to pneumonia.

Developmental cycle and mode of transmission: *Globocephalus* spp. have direct monoxenous life-cycles involving the uptake of infective larvae (L3) from the external environment by oral ingestion or transdermal penetration. Gravid female worms in the intestines of the hosts lay eggs which are excreted with faeces. The eggs embryonate and hatch in 1-3 days releasing free-living L1 which feed and then moult to free-living L2 which also feed. These larvae moult to form L3 which retain the L2 cuticle as a protective sheath and are thus unable to feed. L3 may be formed in 8-12 days and while they may survive for several weeks in favourable warm moist conditions, they are not very resistant to cold, desiccation or direct sunlight. Hosts become infected when they ingest infective L3 on contaminated foods or when L3 in the soil penetrate the skin. In either case, exsheathed L3 undertake a pulmonary migration whereby they move through host tissues and reach the lungs via the circulation. The larvae then invade the alveolar air-spaces and ascend the respiratory mucociliary escalator to the trachea where they are swallowed and move to the intestines. The larvae attach to the gut mucosa where they develop through 2 moults to form adult worms which mature and mate. The prepatent period (time from infection to first egg excretion) ranges from 4-7 weeks. In endemic subtropical regions, egg production often shows seasonal variation, being highest during summer rainfall months.

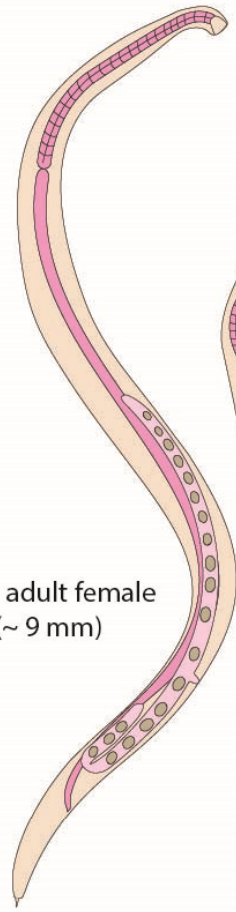
Differential diagnosis: Infections cannot be diagnosed on the basis of symptomatology as most clinical signs are vague and nonspecific (anaemia, illthrift) although the occurrence of black diarrhoea in young piglets may raise suspicions. Coprological techniques are conventionally used to diagnose infections by the detection of hookworm eggs in faecal samples, usually in concentrates following faecal floatation. Regrettably, the eggs are typically strongylid in appearance (elliptical, thin-walled, partially

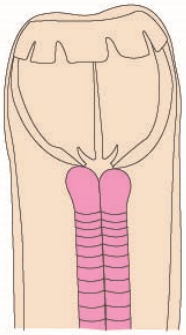
embryonated) and appear similar to those of other hookworms as well as some trichostrongyles, strongyles and metastrongyles. Definitive diagnosis is therefore usually achieved at post-mortem by the detection of adult worms attached to the small intestinal mucosa.

Treatment and control: Clinical infections have been treated with a range of broad-spectrum anthelmintics, including benzimidazoles (albendazole, fenbendazole, flubendazole, mebendazole, oxfendazole), imidazothiazoles (levamisole), macrocyclic lactones (abamectin, doramectin, ivermectin, moxidectin) and even organophosphonates (dichlorvos). The drugs were effective against adult worms, while the macrocyclic lactones were also effective against migrating larvae. Infections are usually not problematic in intensive piggeries due to the higher levels of sanitation and hygiene practiced compared to the conditions experienced by free-range, pastured, feral or wild swine. The regular removal of faeces and cleaning of pens and sties reduces environmental contamination by worm eggs. In addition, many infections occur by the percutaneous transmission of infective larvae when pigs come into direct contact with contaminated soils, so animals housed on solid floors and without access to soil are not at high risk.

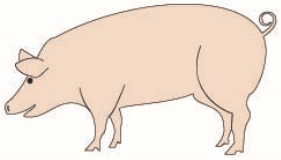
Globocephalus

intestines
(enteritis, diarrhoea,
anaemia)





head

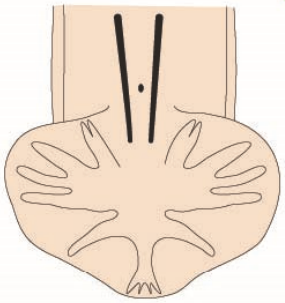


Definitive Hosts
(suids, primates)

pulmonary
migration

adult female
(~ 9 mm)

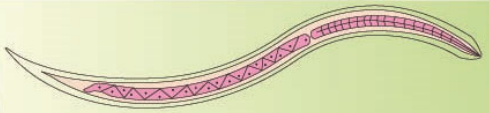
adult male
(~ 5 mm)



male tail

L3 ingested
or
penetrate
skin

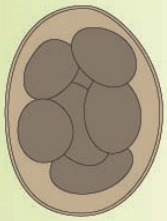
eggs
excreted
in faeces



filariform third-
stage larvae (L3)
(~ 700 µm)

external
environment

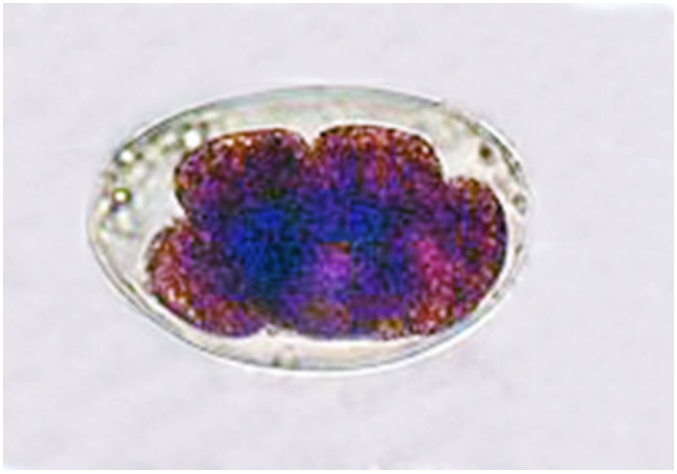
rhabditiform first- and
second-stage larvae
(L1, L2) (~ 450 µm)



eggs
(~ 70 µm)

geo-helminth
(soil transmission)

Globocephalus adult worms



Globocephalus worm egg

*Globocephalus t*hird-stage larva