Ancylostoma
(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. 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 (some species causing cutaneous larval migrans). Larvae undergo pulmonary migration through the lungs (sometimes causing pneumonitis) before developing into blood-feeding adults in the small intestines. Some larvae may undergo arrested development (hypobiosis) and vertical transmission may occur (transplacental and transmammary). Infections by *Ancylostoma* cause Old World hookworm disease, characterised by iron-deficiency anaemia and growth retardation in humans, particularly in children and malnourished individuals.

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:	*Ancylostoma* (parasitic in small intestines of humans/dogs/cats)
Species:	*A. duodenale* [causes Old World hookworm disease in 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)]
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						
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
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
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 *Ancylostoma* contains over 30 species which have been described from a range of mammalian species throughout the world, mainly in tropical and subtropical regions because the larvae cannot develop below 22°C. They are most common in rural areas with high annual rainfall and shaded sandy or loam soils ideal for larval development (not clay or gravel). It is estimated that around 450 million people are infected with hookworms (*Ancylostoma* and *Necator*) worldwide, with 1.6 million suffering from anaemia and 55,000 deaths annually. *A. duodenale* is the Old World human hookworm and is entrenched on most continents. Similar hookworm species occur in domestic and wild carnivores, and they vary in their host specificity. *A. ceylanicum* normally occurs in carnivores but has been reported from humans in the Asia-Pacific region. *A. braziliense* has also been found in humans from several countries, but some infections may have been confused with *A. ceylanicum*. The larvae of many species can undergo partial development in humans, and the dog hookworm *A. caninum* can almost complete its development in humans. *A. tubaeforme* occurs worldwide in cats, but only rarely in dogs.

Ancylostoma species	Oral structures	Definitive Hosts	Clinical signs	Geographic distribution
A. ailuropodae	4 pairs ventral teeth	Carnivora: ursid (giant panda)	anaemia	China
A. bidens	3 pairs ventral teeth	Carnivora: procyonid (crab-eating raccoon, South American coati)		South America
A. braziliense (hookworm)	2 pairs ventral teeth	Carnivora: felid (cat, bobcat, cheetah, cougar, leopard, leopard cat, lion, African wildcat, serval, jaguarundi, ocelot), canid (dog, wolf, dingo, side-striped jackal, black-backed jackal, fennec fox, bat-eared fox, grey fox), hyaenid (spotted hyena, aardwolf), viverrid (common genet, masked palm civet, large Indian civet), procyonid (crab-eating raccoon); Primates: hominid (human)	diarrhoea, cutaneous larva migrans in humans	Africa, Brazil, India, Sri Lanka, Indonesia, Philippines
A. buckleyi	5 pairs teeth (3 ventral, 2 dorsal)	Carnivora: felid (puma, cougar), canid (short-eared fox, crab-eating fox, Pampas fox, dog)		South America, Australia
A. caninum [canine hookworm]	3 pairs ventral teeth	Carnivora: canid (dog, dingo, coyote, red wolf, red fox, grey fox, fennec fox, bat-eared fox, corsac fox, Atlas fox, Iberian fox, maned wolf, black-backed jackal, side-striped jackal, golden jackal, raccoon dog), hyaenid (spotted hyena, striped hyena), felid (cat, bobcat, lynx, cheetah, jungle cat, wildcat, African wildcat, lion, tiger, leopard, clouded leopard, leopard cat), viverrid (common genet, cape genet, large Indian civet), ursid (American black bear, Florida black bear, polar bear, sloth bear); Cingulata: chlamyphorid (six-banded armadillo); Artiodactyla: suid (pig); Rodentia: murid (mouse); Primates: hominid (human); Diptera: muscid (house fly)	pneumonitis, anaemia	worldwide in tropics and temperate zones
A. ceylanicum	2 pairs ventral teeth	Carnivora: felid (cat, leopard cat, fishing cat), canid (dog, dingo), viverrid (Malabar large-spotted civet, small Indian civet); Rodentia: murid (Natal multimammate mouse), cricetid (golden hamster); Primates: hominid (human)	anaemia, diarrhoea	Sri Lanka, India, Asia, Philippines
A. conepati	3 pairs ventral teeth	Carnivora: mephitid (Molina's hog-nosed skunk)		South America
A. ctenomys	4 pairs teeth (3 ventral, 1 dorsal)	Rodentia: ctenomyid (Steinbach's tuco-tuco, Bolivian tuco-tuco)		South America
A. duodenale [Old World human hookworm]	2 pairs ventral teeth	Carnivora: hyaenid (spotted hyena), felid (cat, lion), canid (dog, golden jackal, black-backed jackal, fennec fox), viverrid (Malabar large-spotted civet, genet); Artiodactyla (suid (pig); Primates: cercopithecid (rhesus macaque), hominid (human); Diptera: muscid (house fly)	pneumonitis, anaemia	Eurasia, Africa, Indo-China, patchy distribution in North and South America
A. galogoi		Primates: galagid (brown greater galago)		Africa
A. genettae	5 pairs teeth (3 ventral, 2 dorsal)	Carnivora: viverrid (common genet)		Africa
A. gilsoni		Rodentia: sciurid (Pallas's squirrel, Berdmore's ground squirrel), murid (Himalayan field rat)		Asia
A. guentini	3 pairs ventral teeth	Carnivora: canid (golden jackal)		Asia
A. hescheleri	1 pair ventral teeth	Tubulidentata: orycteropodid (aardvark)		Africa

A. iperodontatum	6 pairs teeth (3 ventral, 3 dorsal)	Carnivora: felid (cheetah, African wild cat, caracal)		Africa
A. japonica sp. inq.		Primates: hominid (human)		Asia
A. kusimaense	2 pairs ventral teeth	Carnivora: canid (raccoon dog, Japanese red fox), procyonid (raccoon)		Asia, North America
A. longespiculatum	3 pairs ventral teeth	Carnivora: felid (European wildcat)		Europe
A. lucknowense	n pairs teeth (3 ventral, many dorsal)	Carnivora: felid (leopard cat)		Asia
A. malayanum	2 pairs ventral teeth	Carnivora: ursid (Asian black bear); Primates: hominid (human)		Asia
A. martinagliai	5 pairs teeth (3 ventral, 2 dorsal)	Carnivora: canid (black-backed jackal); Cingulata: chlamyphorid (screaming hairy armadillo)		Africa
A. martinezi		Carnivora: viverrid (common genet)		Africa
A. mephitis	2 pairs ventral teeth	Carnivora: mustelid (striped polecat)		Africa
A. minimum	-	Carnivora: felid (rusty-spotted cat)		Asia
A. mucronatum	3 pairs ventral teeth	Cingulata: dasypodid (nine-banded armadillo)		South America
A. mycetis	2 pairs ventral teeth	Primates: atelid (howler monkey)		South America
A. paraduodenale	2 pairs ventral teeth	Carnivora: felid (cheetah, lion, serval, cat, caffer cat, wildcat)		Africa
A. pluridentatum (syn. *Uncinaria*) [feline hookworm]	5 pairs teeth (2 ventral, 3 small dorsal)	Carnivora: felid (bobcat, cougar, tiger, oncilla, maracayo, ocelot, jaguar, jaguarundi, Florida panther, margay cat)	anaemia	Americas
A. protelesis	3 pairs ventral teeth	Carnivora: hyaenid (aardwolf)		Africa
A. somaliense	3 pairs ventral teeth	Carnivora: canid (black-backed jackal)		Africa
A. taxideae	3 pairs ventral teeth	Carnivora: mustelid (American badger)		North America
A. tubaeforme [feline hookworm]	3 pairs ventral teeth	Carnivora: felid (cat, bobcat, cougar, Geoffroy's cat, Iberian lynx, cheetah, lion, wildcat, African wildcat, South African wildcat, caffer cat, caracal, jaguarundi, leopard, leopard cat, ocelot, marbled polecat), canid (dog, black-backed jackal, red fox, grey fox), ursid (black bear), viverrid (common genet); Primates: hominid (human)	anaemia	worldwide

Parasite morphology: Hookworm developmental stages include eggs, four larval stages and adult worms. Eggs appear as oval thin-shelled bodies, measuring 55-95 µm in length by 32-58 µm in width. Freshly-excreted eggs contain a developing embryo (morula) in the early stages of cleavage with 2-8 cells (blastomeres). The first two larval stages (L1 and L2) are free-living stages characterised by a long narrow buccal chamber and a muscular rhabditiform (flask-shaped) oesophagus. Third stage larvae (L3) measure up to 600 µm in length and are non-feeding infective stages characterised by a closed mouth, elongate oesophagus with posterior bulb (strongyliform) and pointed non-notched tail. Fourth-stage larvae (L4) migrate and live in host tissues. Adult hookworms have a creamy-white tough cuticle (synlophe absent), a prominent anterior hook (dorsally deviated) and a large subglobular buccal capsule with specialised structures to aid in feeding; most species having ventral lancets with 2-3 pairs of fused teeth. The buccal capsule also has a dorsal gutter connected to the oesophagus. Adult worms are sexually dimorphic, with females being larger than males (6-25 x 0.4-0.6 mm cf. 5-13 x 0.3-0.5 mm). Females have 2 ovaries connected by oviducts to a posterior vulva and their tails have a terminal spine. Males have a single testis, a conspicuous posterior copulatory bursa consisting of two broad lateral lobes and a smaller dorsal lobe, all supported by fleshy rays consisting of muscular elements following nerve channels to terminal papillae (the short dorsal ray having 4 or 6 branchlets), a gubernaculum and 2 needle-like spicules with simple tips that are not fused distally.

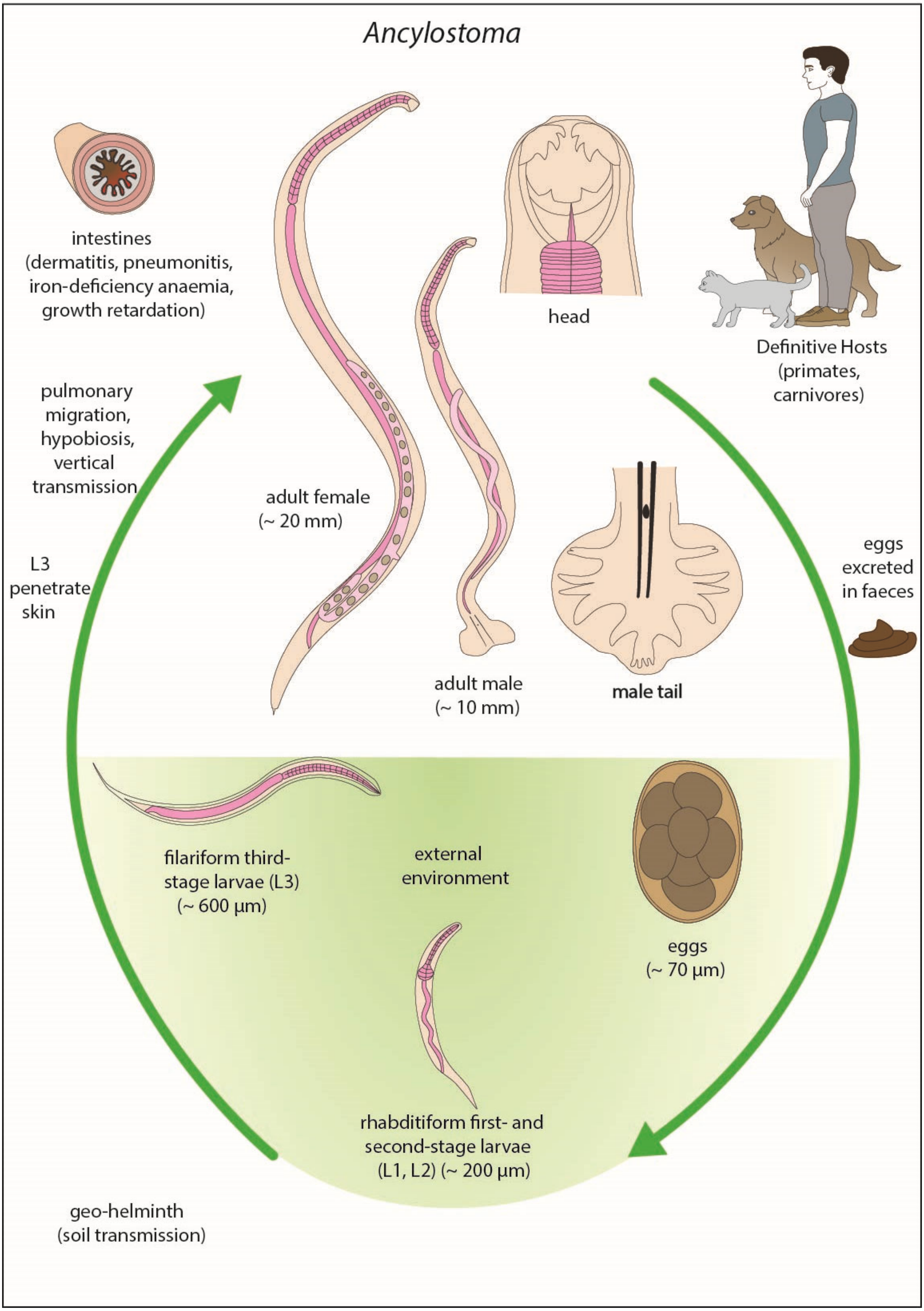
Site of infection: Adult hookworms use their bent mouths to attach to the small intestinal mucosa. Infective larvae invade dermal tissues, particularly in sites which have come into close contact with the ground (feet, hands and buttocks). Migrating larvae move through the lungs (pulmonary migration) and some may undergo arrested development deeper in the gut tissues or in muscles (hypobiotic larvae of *A. duodenale*).

Pathogenesis: Many people may be infected with hookworms but remain asymptomatic. In general, disease development depends on the parasite species involved, the intensity of infection, and the nutritional condition of the individual. Sequential parasite development causes three phases of disease; a cutaneous phase where invading larvae may cause dermatitis, a pulmonary phase where migrating larvae may cause pneumonitis, and an intestinal phase where adult worms may cause gastrointestinal pain and iron-deficiency anaemia. Infective larvae penetrate the skin and invade blood vessels in the dermis, moderate to heavy infections giving rise to an allergic dermatitis with papular, and sometimes vesicular, focal rash and pruritus (condition known as ground itch). Larvae from animal hookworms (especially *A. caninum* and *A. braziliense*) can also penetrate human skin but do not complete their development. Instead, they aimlessly tunnel through the skin for several days or weeks, with *A. braziliense* leaving red itchy wounds that may become secondarily infected. The resultant condition is known as cutaneous *larval migrans* (or ground itch or creeping eruption) and is characterised by local dermatitis, pruritus (itching) and inflammation (oedema, erythema). The next phase of disease occurs when larvae undergo pulmonary migration, having been carried to the lungs where they break out into airspaces (alveoli) causing focal haemorrhages and allergic pneumonia (severity dependent on numbers). Once worms reach the small intestines, they attach to the mucosa by ingesting a tissue plug into their mouths and commence feeding on blood. Moderate to heavy infections result in significant gastrointestinal haemorrhage, iron-deficiency anaemia, and protein malnutrition in heavily infe3cted children, women of reproductive age and malnourished individuals. The adult worms have voracious appetites and individual adult *Ancylostoma* worms may take up to 0.26 ml blood per day. Blood loss from the host may result in an initial normocytic, normochromic anaemia that may worsen to a profound iron-deficiency microcytic, hypochromic anaemia with hypoproteinaemia. *Ancylostoma* spp. appear to be wasteful feeders as not all blood ingested is digested, some is apparently used for respiration and passes through the worm but degrades in the intestines resulting in black tarry faeces (melena). Blood loss is further exacerbated by intestinal lacerations as worms move to new feeding sites from time to time, secreting proteolytic enzymes and anticoagulants, and leaving microscopic ulcers. Infections by as few as 100 worms may cause severe disease in children or malnourished individuals. Hookworm infections are a major cause of anaemia in developing countries, particularly in young children and pregnant women. It is generally considered to be a disease of the poor (low socioeconomic status), with high rates of infection in rural impoverished tropical areas with poor sanitation and barefoot populations. Patients with heavy infections have severe protein deficiency, dry skin and hair, oedema, and potbelly in children with delayed puberty, mental dullness, heart failure and death. Disease is intensified by malnourishment and immunological impairment. Hookworm infections elicit profound humoral and cellular immune responses in their hosts, involving polyclonal antibody production, marked eosinophilia and Th2 lymphocyte proliferation with characteristic cytokine profiles (interleukins 4, 5, 10, 13), but such responses fail to eliminate infections, possibly due to parasites secreting a myriad of proteins that facilitate immune evasion. It is somewhat paradoxical that hookworms elicit allergenic-like responses but survive by modifying those responses. It is thought that these anti-inflammatory properties may benefit patients suffering from various autoimmune or hypersensitivity conditions. While this might provide the basis for alternative medical treatments using helminths, there have been few independent case-controlled studies to provide any supportive medical evidence. In animals, *A. ceylanicum* causes transient dermatitis, anaemia and bloody diarrhoea in dogs which may develop into a nonregenerative iron deficiency anaemia. This species has become recognised as the most important human hookworm in some areas of the Asia-Pacific region. *A. caninum* causes similar clinical manifestations in dogs, the severity of intestinal disease compounded by multiple haemorrhagic lesions associated with worms changing feeding sites. Peracute infection involving transmammary transmission may cause severe haemorrhagic diarrhoea, anaemia, dehydration, weakness and death in puppies. This species has been associated with several cases of eosinophilic enteritis in humans. *A. tubaeforme* may cause significant blood loss in cats with accompanying anaemia, diarrhoea, inappetence and depression, but this species has not been found to be zoonotic.

Developmental cycle and mode of transmission: Hookworms have direct life-cycles involving a geo-helminth (soil-transmitted) stage where infective larvae in the soil actively penetrate the skin or oral mucosa of their hosts. Female worms produce numerous unembryonated eggs (10,000-30,000 eggs per day) which are excreted with host faeces. The eggs embryonate rapidly in warm moist conditions and hatch within 1-2 days releasing free-living rhabditiform larvae which feed on bacteria and organic debris. The larvae moult once after ~3 days and then transform 2-5 days later into non-feeding ensheathed filariform larvae (L3) which are the infective stages. They remain viable for several weeks in shaded sandy or loamy soils under warm moist conditions. The larvae also exhibit short vertical migration, moving to the surface in moist conditions and host-seeking by rhythmically waving back and forth, but retreating back into the soil in dry conditions. Infective L3 may penetrate the skin to infect their definitive hosts (transdermal or percutaneous transmission), but they can also penetrate the oral mucosa following ingestion (*per os* transmission). Vertical transmission has also been reported for some species when larvae are passed in mother's milk (transmammary transmission) and when they cross the placenta to infect the foetus (transplacental transmission). Some evidence suggests that *A. duodenale* larvae may survive in paratenic (transport) hosts and lead to human infections through the ingestion of undercooked meat, including rabbit, lamb, beef and pork. *A. caninum* and *A. tubaeforme* larvae may infect other small animal species (rodents, birds) where they undergo arrested development until these transport hosts are eaten by canine or feline predators. In the definitive (final) host, ingested larvae may undertake pulmonary migration, but most undergo a histotrophic stage by penetrating mucosal glands before returning to the lumen and maturing into adults. Larvae which penetrate the skin actively secrete collagenase to break down basement membranes and dermal ground substances. The larvae enter the circulation and migrate over 2-7 days to the lungs where they break into respiratory alveoli and move up the trachea to be swallowed. Once they reach the small intestines, they moult, attach to mucosa and become sexually differentiated, moult again and grow into adult worms. The prepatent period (time from infection to first egg excretion) ranges from 2-7 weeks for most species, but intestinal infections by several species may be delayed for months (up to 38 weeks) when migrating larvae undergo developmental arrest (hypobiosis) within somatic tissues. Hypobiotic larvae lay dormant in host tissues (gut or muscles) and only recommence their development coincident with the seasonal return of environmental conditions more favourable to transmission. Larvae may become reactivated by host hormonal cues during the latter stages of pregnancy and migrate to the mammary glands where they are transferred to suckling offspring. Infections may persist for years, with adults of some species living for up 5 years.

Differential diagnosis: The diagnosis of hookworm disease on the basis of clinical symptomatology (notably chronic anaemia and debility) is highly suggestive, but requires confirmation by the detection of parasite eggs in faecal samples by microscopy, preferably after concentration although they can be found in direct smears or wet mounts. Because the eggs of many hookworms (*Ancylostoma* and *Necator*) and threadworms (*Strongyloides*) are virtually identical, faeces should be kept for larval cultures (usually Harada-Mori filter paper technique in closed tubes for a few days) to differentiate genera (hookworm larvae have a larger buccal cavity and smaller genital primordium), since treatment options are quite different for each group. Several studies have also been conducted in attempts to detect drug resistance in hookworms using egg hatch, larval development or larval motility assays. Radiographic findings include intestinal hypermotility, proximal jejunal dilatation and coarsening of the mucosal folds. Several immunoserological tests (enzyme immunoassays and Western blots) have been developed to detect host antibodies against hookworm antigens, but they generally do not discriminate between patent or previous infections and often exhibit some cross-reactivity with other helminths. More recently, several polymerase chain reaction (PCR) tests have been developed to detect specific parasite DNA sequences of nuclear (internal transcribed spacers (ITS-1, ITS-2), ribosomal RNA) and mitochondrial genes (cytochrome oxidase 1 gene, cAMP-dependent protein kinase catalytic subunit), but they have not yet found widespread use outside of research laboratories.

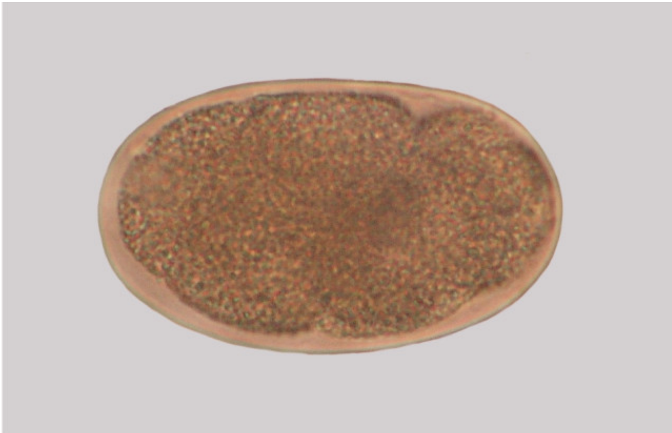
Treatment and control: Various anthelmintic drugs have been used to cure infections, and are best used in conjunction with dietary supplementation, especially iron replacement. While many nematocides are active against adult worms, migrating and arrested larvae might not be affected so it is necessary to treat individuals several times or on a regular basis. The most effective drugs are mebendazole, albendazole and pyrantel pamoate. Levamisole is less effective and treatment has adverse side-effects. Older drugs, such as bephenium and tetrachlorethylene, are still used in many areas throughout the world because they are cheap. Salicylanilides have also proven effective against animal *Ancylostoma* infections and emodepside is active against mature and immature stages. In hosts with severe hookworm disease, treatment should be combined with supportive care involving fluid and electrolyte therapy, iron supplementation, high protein diet and even blood transfusion if deemed necessary. While chemotherapy works, mass treatment programmes are only partly effective as most cured individuals return to heavily contaminated areas and rapidly become re-infected. Infection appears to stimulate little protective immunity. Control programmes must include prophylaxis to prevent infections as well as environmental management to reduce soil contamination. People should be encouraged to wear solid shoes in endemic regions and to thoroughly wash salad vegetables. Building and education campaigns should be introduced to provide latrines/toilets and improve sanitary conditions, as promiscuous defaecation, associated with poverty and ignorance, keeps soil contamination high. Nightsoil (faecal waste) should not be used to fertilise gardens or vegetable crops. Dog faeces should not be left on lawns or parks (especially well-watered ones) where people congregate. Sound hygienic practices should be instituted in animal holding facilities (regular removal of faeces) and concrete surfaces can be sprayed with bleach (hypochlorite) solutions after hosing and scrubbing clean of organic debris. Companion animals should be regularly treated pre- and post-weaning to prevent vertical and horizontal transmission and preventing them from hunting will curb transmission from paratenic (prey) animals. Several countries have successfully controlled infections in human populations, predominantly by using periodic mass treatment programs and encouraging people to wear shoes and use latrines through public education campaigns. Considerable effort has also been made in developing vaccines against hookworm infections, particularly using secreted larval proteins to prevent infections or by inhibiting adult gut enzymes (aspartic proteases, cysteine proteases, haemoglobinases) to reduce worm burdens. Variable results have been obtained, although several formulations are currently undergoing clinical trials.


Ancylostoma
intestines
(dermatitis, pneumonitis,
iron-deficiency anaemia,
growth retardation)
head
Definitive Hosts
(primates,
carnivores)
pulmonary
migration,
hypobiosis,
vertical
transmission
adult female
(~ 20 mm)
L3
penetrate
skin
eggs
excreted
in faeces
adult male
(~ 10 mm)
male tail
filariform third-
stage larvae (L3)
(~ 600 µm)
external
environment
eggs
(~ 70 µm)
rhabditiform first- and
second-stage larvae
(L1, L2) (~ 200 µm)
geo-helminth
(soil transmission)

Ancylostoma adult worms

Ancylostoma adult worm, head

Ancylostoma adult worm, male bursa



Ancylostoma worm egg

Ancylostoma rhabditiform larvae

Ancylostoma filariform larva