

## *Passalurus*

(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 phasmodian parasites of vertebrates are grouped in the chromadorian order Rhabditida; including tylenchinids, rhabditinids and spirurids. The latter contains the infraorder Oxyuridomorpha which includes the oxyuroids (pinworms) characterised by their small tapering shape, pointed tails, oesophagus with a terminal bulb, and the males are non-bursate with a single spicule. They have simple direct life-cycles involving faecal-oral transmission of eggs containing infective larvae. The eggs, however, are oviposited around the anus (perineum) where they are subsequently dislodged and ingested by their hosts. Pinworms are common in the large intestines of many mammals, birds, reptiles, amphibians and some insects. Infections by *Passalurus ambiguus* in rabbits are generally asymptomatic, but their presence in rabbit colonies can be problematic.

### 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, Phasmodia) (secretors, with phasmids, bipartite oesophagus, single testis)  
Suborder: Spirurina (mostly parasitic in vertebrate hosts)  
Infraorder: Oxyuridomorpha (small pinworms, pointed tails, oesophagus with terminal bulb, males with single spicule)  
Superfamily: Oxyuroidea (common in mammals, birds, reptiles, amphibians)  
Family: Oxyuridae (direct cycle, females deposit sticky eggs around anus, infection by ingestion of egg)  
Genus: *Passalurus* (parasitic in large intestines of rabbits)  
Species: *P. ambiguus* (causes subclinical infections in rabbits)

**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, spines, 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 (some monodelphic or polydelphic) with 2 ovaries, 2 oviducts usually with spermatheca, 2 uteri opening into a common vagina and a vulva often equipped with a muscular ovejector. Female worms are oviparous or viviparous and produce numerous eggs or larvae, respectively. Larval stages undergo several moults (L1-L4) before maturing into adult worms. Some nematodes have direct life-cycles where eggs or larvae infect definitive hosts (per os or per cutaneous), but many have indirect cycles where larvae first develop in invertebrate intermediate hosts before infecting definitive hosts (by ingestion, injection or deposition). Many nematode species are free-living in terrestrial and aquatic habitats, while some species from diverse groups have become plant or animal parasites. Two nematode groups identified by the presence/absence of sensory phasmids have partly been ratified by molecular studies recognising three subclasses: Enoplia and Dorylaimia (both without phasmids) and Chromadoria (most with phasmids). Most Enoplia are free-living marine organisms but some are found in freshwater, and on land as plant parasites. The Dorylaimia comprise numerous freshwater and terrestrial species, including major groups of plant and animal parasites. The Chromadoria is represented by many marine groups as well as a terrestrial group of plant and animal parasites. The taxonomic ranks of many nematode assemblages vary considerably depending on which classification system has been followed. Molecular phylogenetic studies, however, have supported the separate

classification of most groups, particularly at the level of superfamily. Collectively, species from at least 16 superfamilies are considered to pose serious threats to human and animal health as infectious diseases.

CLASSIFICATION* OF SUPERFAMILIES OF PARASITIC NEMATODES
Class: Enoplea (Aphasmidea, Adenophorea) (gland-bearers, cylindrical oesophagus, no phasmids, setae, two testes)
Subclass: Dorylaimia (five or more oesophageal glands, buccal stylet (odontostyle), free-living or parasitic)[clade I(2)]
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short anterior muscular and long posterior glandular portions)
Class: Chromadorea (spiral amphids, 3 oesophageal glands, usually annulated bodies, free-living and parasitic)
Order: Rhabditida (Secernentea, Phasmidea) (secretors, phasmids present, amphids anterior, bulbous oesophagus)
Suborder: Rhabditina (free-living or parasitic in invertebrates/lower vertebrates)[clade V(9)]
Infraorder: Rhabditomorpha ('rod-shaped' buccal cavity)
Superfamily: Rhabditoidea (open tube stoma, excretory system with lateral canals)
Superfamily: Strongyloidea (bursate males, prominent buccal capsules, parasites of mammals, birds, reptiles)
Suborder: Spirurina (animal parasites, many use invertebrate intermediate hosts (IH))[clade III(8)]
<i>Incertae sedis</i> Superfamily: Dracunculoidea (elongate parasites of vertebrate tissues, freshwater crustacean IH)
Infraorder: Ascaridomorpha (large roundworms, three large lips, numerous caudal papillae)
Superfamily: Ascaridoidea (ascarids, eggs thick-shelled, larvae may undertake hepato-pulmonary migration)
Superfamily: Heterakoidea (preanal sucker anterior to cloaca in males, direct cycle, infection by egg ingestion)
Infraorder: Gnathostomatomorpha ('jaw-mouthed' due to unique bulbous armed heads)
Superfamily: Gnathostomatoidea (first IH copepod, often use paratenic hosts)
Infraorder: Oxyuridomorpha (pinworms, pointed tails, oesophagus with terminal bulb, males with single spicule)
Superfamily: Oxyuroidea (common in mammals, birds, reptiles, amphibians)
Infraorder: Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily: Acuarioidea (small parasites mostly of birds, with cephalic cordons, ptilina or serrated shields)
Superfamily: Camallanoidea (conspicuous phasmids, L1 with dorsal tooth, ovoviviparous, L1-L3 in copepod)
Superfamily: Filarioidea (tissue-dwelling filarial parasites, lack lips, infect tissues/vessels, arthropod IH)
Superfamily: Habronematoidea (unique head structures with small pseudolabia and median lips)
Superfamily: Physalopteroidea (stomach worms in mammals, insect IH)
Superfamily: Spiruroidea (pseudolabia, bipartite oesophagus, infect birds (crop/gizzard), arthropod IHs)
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 infraorder Oxyuridomorpha comprises the pinworms, unique microphagous nematodes with pointed tails, an oesophagus with a terminal bulb and the males having only a single spicule. Pinworms are conventionally classified in the order Oxyurida, the only major nematode group with adult representatives in either vertebrates or invertebrates. Two superfamilies are recognised: Oxyuroidea (parasites of the posterior gut of vertebrates (including mammals, birds and some reptiles) and Thelastomatoidea (parasites of invertebrates, especially herbivorous arthropods with a fermentation chamber (such as cockroaches, diplopods, orthopterans)). Members of the superfamily Oxyuroidea are distinguished by small nonbursate males with reduced numbers of caudal papillae and females with complex ovejectors producing thin-shelled eggs flattened on one side. The parasites have monoxenous transmission cycles whereby unembryonated eggs are passed into the environment with host faeces or gravid females migrate to the anus and deposit eggs in the perianal region. Three families are recognised: Oxyuridae (amphids non-pedunculate, genital cone without sclerotized supporting structure, male tail irregular, often bluntly truncate with or without dorsal point, sometimes with large digitiform papillae extending into caudal alae, parasitic in mammals and rarely birds); Pharyngodonidae (amphids pedunculate, genital cone supported by V-shaped sclerotized structure, parasitic in lower cold-blooded vertebrates, and a few in archaic mammals); and Heteroxyematidae (amphids non-pedunculate, genital cone without sclerotized supporting structure, male tail regular, conical or flattened dorsoventrally, parasitic in mammals and birds).

The family Oxyuridae contains 25 genera classified into 3 subfamilies: Oxyurinae (short oesophagus, male tail short with broad alae supported by long narrow papillae, single spicule, *Austroxyuris*, *Paraustroxyuris*, *Macropoxyuris* and *Potoroxyuris* in Australian marsupials, *Auchenacantha* in Dermoptera, *Citellina* in sciurids, *Hoplodontophorus* in hyracoids, *Oxyuris* in perissodactyls and *Skrjabinema* in artiodactyls); Syphaciinae (male gubernaculum with hook, area rugosa with parallel transverse grooves, well-developed caudal appendix, 5 tribes: Syphaciini (*Syphacia* (incl. subgenera *Syphacia*, *Seuratoxyuris*, *Cricetoxuris*, *Segienamsyphacia*, *Rumbaisyphacia*), *Syphatineria* (incl. subgenera *Syphatineria*, *Africanoxys*, *Quentenora*, *Orientoxys*), *Sypharista* (incl. subgenera *Sypharista*, *Petauxyuris*, *Quentinema*), *Syphabulea*); Hilgertini (*Hilgertia*, *Heteromyoxyuris*, *Rauschtineria*); Passulurini (*Passalurus*); Acanthoxyurini (*Acanthoxyurus*, *Idiuoxyuris*, *Petronema*, *Zenkoxyuris*); and Protozoophagini

(*Protozoophaga*, *Helminthoxys*, *Wellcomia*); parasitic in rodents and lagomorphs); and Enterobiinae (sexual dimorphism of lateral alae (single-crested in males, double-crested in females), uterine tube with dividing diaphragm, *Enterobius* (incl. subgenera *Enterobius*, *Colobenterobius*), *Trypanoxyuris* (incl. subgenera *Trypanoxyuris*, *Hapaloxoyuris*, *Paraoxyuronema*, *Rodentoxoyuris*), *Lemuricola* (incl. subgenera *Lemuricola*, *Protenterobius*, *Madoxyuris*), *Xeroxyuris* in primates and sciurids). Representative pinworm genera of medical and veterinary significance are tabulated below:

Genus	No. spp.	Definitive Hosts	Location	Adult worms	Eggs	Transmission
Family: Oxyuridae						
Subfamily: Syphaciinae						
<i>Passalurus</i> (pinworm)	3	lagomorphs, rodents	large intestines	3-11 mm long, circular cuticular striations, oesophagus with terminal bulb, eggs passed in faeces	93-105 x 43-45 µm, D-shaped, thin-shelled	ingestion of larvated eggs
<i>Syphacia</i>	88	rodents	large intestines	1-6 mm long, small cervical alae, oesophagus with terminal globular bulb, eggs oviposited around anus	72-153 x 25-55 µm, reniform, thin-shelled	ingestion of larvated eggs
Subfamily: Oxyurinae						
<i>Oxyuris</i> (pinworm)	21	mammals, birds, reptiles	caecum, large intestines	1-16 cm long, oesophagus with terminal globular bulb, pin-tailed, eggs oviposited around anus	85-95 x 40-45 µm, D-shaped, thin-shelled	ingestion of larvated eggs
Subfamily: Enterobiinae						
<i>Enterobius</i> pinworms	27	primates, rodents	large intestines	1-15 mm long, lateral alae, oesophagus with terminal bulb, slender pointed tails, eggs oviposited around anus	50-60 x 20-30 µm, D-shaped, thin-shelled	ingestion of larvated eggs
Family: Heteroxynematidae						
Subfamily: Heteroxynematinae						
<i>Aspicularis</i>	23	rodents	large intestines	2-5 mm long, prominent cervical alae, oesophagus with terminal oval bulb, eggs passed in faeces	70-98 x 29-50 µm, spindle-shaped, thin-shelled	ingestion of larvated eggs

The genus *Passalurus* contains only a few species of structurally-simple pinworms which are parasitic in the caecum and large intestines of leporid lagomorphs, and sometimes sciurid rodents. The parasites have direct monoxenous life-cycles involving the excretion of eggs into the external environment where they embryonate and are ingested when hosts feed (including auto-infection via coprophagy). Most infections in leporids are benign, even when high worm burdens develop, but their presence may compromise the microbiological integrity required of laboratory animal colonies.

<i>Passalurus</i> species	Definitive hosts	Location [Clinical signs]	Distribution
<i>P. abditus</i>	Rodentia: sciurid (rock squirrel)		North America
<i>P. ambiguus</i> (syn. <i>Oxyuris ambigua</i> ) (rabbit pinworm)	Lagomorpha: leporid (European rabbit, desert cottontail, antelope jackrabbit, black-tailed jackrabbit, European hare, Granada hare, Cape hare, mountain hare); Rodentia: sciurid (red squirrel); Carnivora: felid (cat); Primates: hominid (human)	caecum, colon	worldwide
<i>P. nonannulatus</i>	Lagomorpha: leporid (European rabbit, volcano rabbit, eastern cottontail, snowshoe hare)		North America

**Parasite morphology:** *Passalurus* spp. form 3 different types of developmental stages: eggs; larvae (4 successive stages designated L1-L4); and adult worms. The eggs are elongate measuring 93-105 x 43-45 µm and are asymmetrical being flattened on one side (forming a D-shape). They are thin-walled and have a pseudo-operculum at one pole. The eggs are laid unembryonated containing a single central gastrula stage but they quickly embryonate to form first-stage larvae (L1). Two larval moults occur within the egg resulting in the formation of infective L3 that measure up to 400 µm long. L4 are transient parasitic stages measuring 700-800 µm long and they have begun to develop genitalia. Adults are elongate cylindrical worms measuring from 3-11 mm in length and they are slightly thicker anteriorly. They are bound by a white semitransparent cuticle and have an anterior triangular mouth surrounded by 3 simple inconspicuous lips, 4 cephalic papillae arranged in a square and 2 lateral amphidia. They lack a distinct buccal capsule but have a unique club-shaped oesophagus with a well-developed posterior bulb with a tri-radiate valvular apparatus. Adult worms are sexually dimorphic, with females being larger than males (5-11 mm cf. 3-5 mm). Mature females have 2 ovaries and uteri

connected to a ventral ojector apparatus and an anterior vulva surrounded by protruding lips. They are further characterised by having a long narrow tail (pin-tail) with prominent annular thickenings (up to 40 circular striations). Mature males have finely-pointed tails ending in a long spike, 2 caudal alae supported by a pair of papillae, 4 pairs of papillae surrounding the cloaca, and a single short spicule, often protruding (gubernaculum absent).

**Site of infection:** Adult worms live in the lumen of the caecum and colon of lagomorphs, while earlier larval stages develop in the mucosa of the small intestine and the caecum. The only stages contaminating the external environment are worm eggs, in which the first 3 larval stages develop.

**Pathogenesis:** Infections are generally considered to be benign, remaining asymptomatic or subclinical even when large worm burdens (>1,000) may be present. Some early workers mooted that this nematode may be a nonpathogenic commensal, a few even suggesting a symbiotic relationship with respect to plant digestion. However, *Passalurus* spp. are endoparasites living at the expense of the host. The early larval stages develop in the intestinal mucosa causing local inflammation, and the adult worms move about in the lumen feeding on intestinal content. The pathological consequences of infection are minimal, and clinical signs are infrequently reported. The detection of mucus threads in faeces may indicate intestinal infections, but should be differentiated from mucoid enteritis. Infections have been associated with a scouring syndrome observed around weaning, sometimes with anorexia and loss of body condition, but rarely with mortality. The movement of worms along the colon and the production of inflammatory metabolites is thought to overexcite local nerves leading to a pruritus and an itchy-scratchy syndrome (particularly of the perineum). Large worm populations are thought to sometimes cause intestinal stasis, caecal impaction, abdominal colicky pain, bloat (gas production) and rectal prolapse. On rare occasions, infections have been linked with intestinal granulomas, appendicitis and lymphadenitis. Normally, infections do not present problems in rabbit production, except when their presence compromises the microbiological and immunological integrity of laboratory animals required to be free of spurious infection (e.g. germ-free or specific-pathogen-free colonies).

**Developmental cycle and mode of transmission:** The parasites have direct monoxenous life-cycles usually involving the faecal-oral transmission of worm eggs contaminating food sources, but possibly also including their transmission via grooming or caecotrophy (coprophagy of soft pellets). Gravid female worms lay unembryonated eggs in the intestines where they undergo rapid development and are embryonated when excreted with faeces, often being contained in the mucus coating of faeces. Early studies suggested that female worms may also migrate to the anus and deposit eggs on the perianal skin, but subsequent studies indicated that oviposition outside the host was unusual for *Passalurus* spp. as any emergent worms quickly desiccated and died. In the external environment, L1 within the worm eggs moulted twice over 7-8 days to form infective L3 still contained within the eggshell. The eggs become very resistant to desiccation as they undergo larval development and may survive for months in mild conditions. Final hosts become infected when they ingest eggs containing infective L3 in contaminated food and water. Auto-infection also occurs during the unique process of caecotrophy exhibited by lagomorphs (night-time coprophagy of soft pellets rich in endosymbiotic microbes) or possibly during grooming of perianal areas. Ingested eggs hatch in the gut releasing L3 which burrow into the mucous layer and glandular crypts of the small intestine, caecum and colon where they moult twice over several days. Young adults emerge into the lumen by 11 days after infection where they slowly mature, mate and begin egg production. The prepatent period (time from infection to first excretion of eggs) ranges from 56-64 days, and adult worms were found to live for up to 106 days.

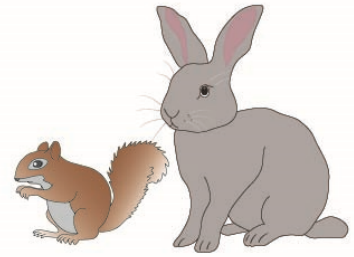
**Differential diagnosis:** Infections rarely cause any clinical signs, so diagnosis is based on the direct detection of parasites. Live adult worms can occasionally be detected by macroscopic (visual) examination of freshly excreted faeces, where they may be observed writhing slowly on the surface of faecal pellets. More conventionally, worm eggs are detected by the microscopic examination of faecal samples, usually following their concentration by faecal floatation, but sometimes following their recovery by sticky-tape impression smears taken around the anus. Infections may also be detected at post-mortem by examination of the large intestinal mucosa and contents. Molecular biological techniques have been used to characterize parasites and infer phylogenetic relationships following the polymerase chain reaction (PCR) amplification of nuclear genes (18S ribosomal RNA) and mitochondrial genes (cytochrome oxidase 1, cytochrome b).

**Treatment and control:** When chemotherapy is deemed necessary to treat atypical clinical infections or to rear worm-free laboratory animals, various anthelmintic drugs have proven useful, including benzimidazoles (fenbendazole, thiabendazole, mebendazole, oxbendazole) and diethylenediamines (piperazine). These drugs were effective against larval stages and adult worms but not against eggs, so multiple or sustained treatments were required (e.g. medications in feed or water). Several studies noted that the macrocyclic lactone, ivermectin, was not effective. Preventive control measures may be instituted in breeding and rearing facilities to break transmission cycles: mostly by reducing environmental contamination by worm eggs (regular removal of faeces and bedding, cleaning and disinfection of hutches, runs and hides) as well as limiting opportunities for their uptake (provision of clean food and water, avoid overcrowding, segregation of cohorts, quarantine and isolation procedures, and raising animals in cages).

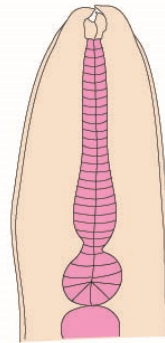
# Passalurus



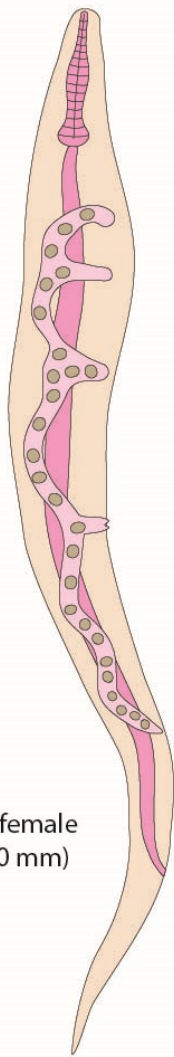
intestines  
(mild enteritis, scours,  
mostly subclinical)



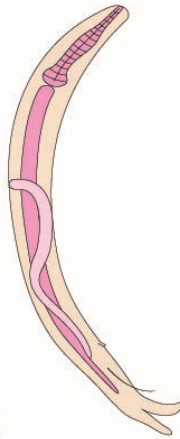
Definitive Hosts  
(lagomorphs,  
rodents)



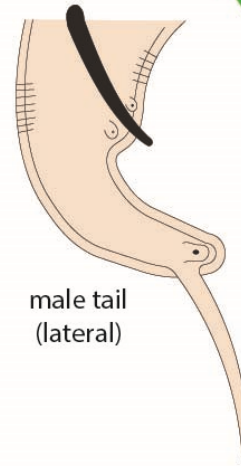
head



adult female  
(~ 10 mm)



adult male  
(~ 4 mm)



male tail  
(lateral)



eggs ingested  
with food/water,  
or via grooming  
or caecotrophy

L3 develop  
within eggs



eggs  
(~ 100  $\mu$ m)

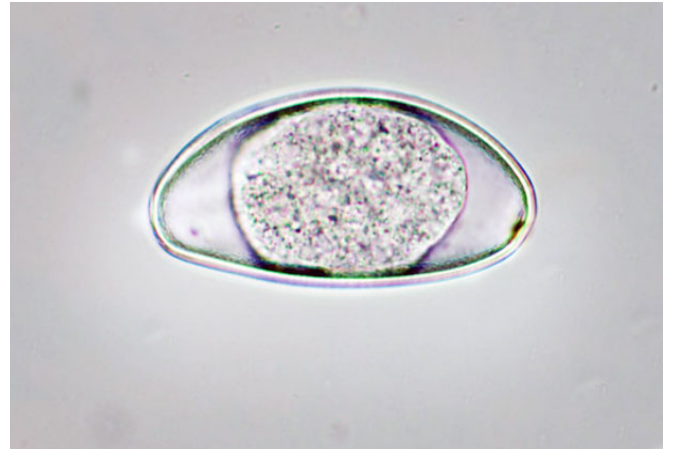
eggs often dislodged  
and contaminate  
environment

sticky  
eggs  
attached  
around  
anus

contaminative transmission



*Passalurus* adult worm



*Passalurus* worm egg