

Trichinella

(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). Most aphasmid nematodes are free-living, although some are parasitic on plants or animals. They possess a non-muscular stichosome oesophagus (slender thin-walled tube) and their life-cycles involve infective L1 (rather than L3) which have a buccal stylet (very common for plant parasites). The males lack a bursa and have only one spicule when present. Three major families of animal parasites are grouped together in the dorylaimian order Trichinellida: trichurids in the caecum/colon of mammals, capillarids in the gut/lungs of mammals/birds, and trichinellids in the intestines and muscles of mammals. Trichinellids have unusual indirect life-cycles where viviparous females release L1 which encyst in striated muscle cells of the same host until they are ingested by carnivorous/omnivorous hosts where adults develop rapidly (2-6 days) in the small intestines. Infections ascend through the food chain via predation or carrion-feeding in domestic and sylvatic cycles. Several *Trichinella* spp. have been associated with enteric and muscular diseases in human populations around the world, and trichinoscopy is routinely used as a means of detecting L1 during meat inspection in many countries.

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: 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)
Order: Trichinellida (Trichocephalida, Trichurida) (single spicule, stichosome oesophagus, L1 with buccal stylet)
Superfamily: Trichinelloidea (oesophagus with short muscular anterior portion and long glandular posterior portion)
Family: Trichinellidae (males with pseudobursa, no spicules, viviparous, juveniles in skeletal muscle cells)
Genus: *Trichinella* (parasitic in small intestines/muscles of mammals, direct (carnivorism))
Species: *T. spiralis* (causes trichinellosis in mammals)

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 (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 superfamily Trichinelloidea is characterised by worms with a distinctive oesophagus consisting of a short anterior muscular section and a long posterior glandular section (stichosome) encircled by 1-3 rows of unicellular glands (stichocytes). Adult worms usually have long narrow anterior necks (containing only the stichosome) and stouter posterior bodies (containing the reproductive organs). Female worms produce thick-shelled eggs with bipolar mucoïd plugs giving them a lemon- or barrel-shape. Most genera pass unembryonated eggs, but those of some groups (Trichinellidae, Trichosomoididae) embryonate *in utero*. The first-stage larvae (L1) have an oral stylet, similar to their presumed soil-dwelling dorylaimid ancestors. Unlike other parasitic nematodes, the L1 of trichinelloids (rather than L3) is used to infect their final hosts, sometimes after a brief period in an invertebrate intermediate host (such as earthworms) to become infective. Adults worms are endoparasites in most classes of vertebrates, generally occurring within the intestinal mucosa but some infecting epithelia of the urinary, respiratory or integumentary systems. An increasing number of genera have been recognised but their higher classification is confounded as some authorities distinguish 6 families while others have demoted several to subfamily status. The former ranking has been retained in this resource to better help the reader differentiate genera on the basis of recognised apomorphic characters, although future studies may reveal different phylogenetic relationships. The 6 trichinelloid families include: Trichinellidae, Trichuridae, Anatrchosomatidae and Trichosomoididae primarily in mammals; Capillariidae in birds, mammals and fish; and Cystoospiidae in fish and reptiles.

The family Trichinellidae is monotypic with the single genus *Trichinella* (syn *Trichina*) containing some 9 species infecting almost all vertebrate classes (mammals, birds, reptiles, fish). Contemporary molecular characterization studies have also recognised a growing number of genotypes (encoded T1-T12), most of which conform to named species, but some (T6, T8, T9) possibly representing cryptic species. *Trichinella* spp. have unusual developmental cycles which can be completed within the same host. Adult worms rapidly develop embedded in the intestinal mucosa, and the ovoviviparous females release first-stage larvae (L1) into lymph and blood capillaries; these larvae are then disseminated to skeletal muscle cells which they enter and remain as L1 (they are arrested in terms of development, but still move). The larvae of some *Trichinella* spp. in mammals (such as *T. spiralis*) transform the host muscle cells into nurse cells which become encapsulated in collagen, while those of other species in birds,

reptiles and some mammals (such as *T. pseudospiralis*) do not cause modification of the muscle cell nor become encapsulated. The larvae are transmitted to carnivores when they feed on infected prey or carrion, infections being maintained in domestic and/or sylvatic cycles involving livestock and/or wildlife. The species *T. spiralis* infects pigs and rats as its primary hosts, but infections have also been found in more than 100 mammalian species, including humans. *T. spiralis* has a cosmopolitan distribution, but is absent from Australasia, the United Kingdom and Denmark. Infections are most prevalent in developing countries, particularly those where undercooked pork products are consumed. It is estimated that some 11 million people may be infected worldwide, with 10,000 clinical cases of the disease (known as trichinellosis or trichinosis) occurring annually.

<i>Trichinella</i> species [and genotype]	Definitive Hosts [adults in small intestines] [larvae in muscles]	Clinical signs	Distribution
Capsule forming (or 'encapsulated')			
<i>T. spiralis</i> [T1] (trichina or muscle worm) [domestic/sylvatic] (syn. <i>T. affinis</i> , <i>T. canis</i> , <i>T. circumflexa</i> , <i>T. pseudalius</i> , <i>Pseudalius trichina</i>)	Carnivora: canid (dog, wolf, coyote, golden jackal, red fox, Arctic fox, gray fox, blue fox, raccoon dog, Japanese raccoon dog), hyaenid (spotted hyena), felid (cat, bobcat, lion, cougar, Eurasian lynx, Canada lynx, European wildcat), viverrid (civet cat, common genet), procyonid (raccoon), mustelid (wolverine, Eurasian otter, American marten, American mink, European pine marten, fisher, stoat, sable, European badger, Asian badger, steppe polecat, European polecat, long-tailed weasel, least weasel), herpestid (Javan mongoose), memphitid (striped skunk), myocastorid (coyup), ursid (Asian black bear, Japanese black bear, American black bear, brown bear, polar bear); Cingulata: chlamyphorid (big hairy armadillo); Artiodactyla: suid (pig, boar, desert warthog), bovid (cattle, sheep, goat), cervid (roe deer, reindeer), phocid (bearded seal, ringed seal), odobenid (walrus), monodontid (beluga whale); Perissodactyla: equid (horse); Rodentia: murid (brown rat, black rat, mouse, striped field mouse, yellow-necked mouse, wood mouse, lesser bandicoot rat, Mongolian gerbil, golden hamster), caviid (guinea pig, montane guinea pig), cricetid (common vole, bank vole, muskrat, white-footed mouse, deer mouse, Oldfield mouse, hispid cotton rat), sciurid (American red squirrel, Columbian ground squirrel); Didelphimorphia: didelphid (common opossum, Virginia opossum); Eulipotyphla: talpid (European mole), soricid (white-toothed shrew, vagrant shrew), erinaceid (European hedgehog, northern white-breasted hedgehog); Primates: hominid (human); Urodela: ambystomid (axolotl); Cypriniformes: cyprinid (common bleak, common carp); Perciformes: percid (ruffe, European perch); Accipitriformes: accipitrid (common buzzard); Falconiformes: falconid (American kestrel); Galliformes: phasianid (chicken); Struthioniformes: struthionid (ostrich); Testudines: emydid (European pond turtle); Anura: ranid (edible frog) [plus carriage in Coleoptera: clerid (checkered beetle); Diptera: tabanid (horsefly), sarcophagid (fleshflies); Hymenoptera: vespid (umbrella wasp); Siphonaptera: pulicid (oriental rat flea)]	diarrhoea, myositis, eosinophilia	Eurasia, North America
<i>T. nativa</i> [T2] [sylvatic]	Carnivora: canid (dog, wolf, red fox, Arctic fox, corsac fox, blue fox, golden jackal, raccoon dog), felid (cat, leopard cat, lynx, Eurasian lynx, Siberian tiger, Far Eastern forest cat), mustelid (wolverine, stoat, American marten, European pine marten, European badger, European polecat), ursid (polar bear, brown bear), phocid (grey seal), obodenid (walrus), procyonid (raccoon); Rodentia: murid (mouse, brown rat), caviid (guinea pig), cricetid (deer mouse); Artiodactyla: cervid (reindeer), suid (pig, boar); Perissodactyla: equid (horse); Primates: hominid (human)	diarrhoea, myositis, eosinophilia	Holarctic
<i>T. britovi</i> [T3] (syn. <i>Bessonoviella britovi</i>) [sylvatic, rarely domestic]	Carnivora: canid (dog, wolf, golden jackal, raccoon dog, Japanese raccoon dog, red fox), felid (cat, European wildcat, Eurasian lynx), mustelid (beech marten, European pine marten, stoat, least weasel, European polecat, badger), viverrid (European genet, African palm civet, true civet), ursid (brown bear, Marsican brown bear, Asian black bear, Japanese black bear); Artiodactyla: bovid (goat, sheep), cervid (fallow deer), suid (pig, boar); Perissodactyla: equid (horse); Rodentia: murid (mouse, field mouse, brown rat, black	diarrhoea, myositis, eosinophilia	Palaearctic (Eurasia, Africa)

	rat), caviid (guinea pig), echimyid (coypu), cricetid (bank vole, European snow vole), glirid (garden dormouse), sciurid (red squirrel), histricid (crested porcupine); Eulipotyphla: soricid (common shrew, Eurasian pygmy shrew, greater white-toothed shrew, lesser white-toothed shrew), erinaceid (European hedgehog), talpid (European mole); Primates: hominid (human)		
<i>T. murrelli</i> [T5] [sylvatic]	Carnivora: canid (dog, coyote, red fox, American red fox), felid (bobcat, cat), mustelid (American mink), procyonid (raccoon), ursid (American black bear); Artiodactyla: suid (pig, boar, bushpig, warthog); Perissodactyla: equid (horse); Rodentia: murid (mouse), cricetid (deer mouse); Primates: hominid (human)	diarrhoea, myositis, eosinophilia	Nearctic
<i>Trichinella</i> T6 (related to <i>T. nativa</i>) [sylvatic]	Carnivora: canid (gray wolf, red fox, gray fox), felid (cougar, bobcat), mustelid (wolverine, fisher), ursid (grizzly bear, brown bear, American black bear); Rodentia: murid (mouse); Artiodactyla: suid (pig, boar); Primates: hominid (human)		North America
<i>T. nelsoni</i> [T7] [sylvatic]	Carnivora: hyaenid (striped hyena, spotted hyena), canid (dog, wolf, red fox, bat-eared fox, side-striped jackal, black-backed jackal,), felid (cat, lion, leopard, cheetah, serval cat), ursid (Marsican brown bear), herpestid (common slender mongoose); Rodentia: murid (mouse, brown rat, black rat, hamster, Natal multimammate mouse), caviid (guinea pig); Lagomorpha: leporid (rabbit); Artiodactyla: suid (pig, boar, bushpig, desert warthog); Perissodactyla: equid (horse); Primates: cercopithecid (grivet, dogface baboon), hominid (human)	diarrhoea, myositis, eosinophilia	equatorial Africa
<i>Trichinella</i> T8 (related to <i>T. britovi</i>) [sylvatic]	Carnivora: hyaenid (spotted hyena), felid (lion, leopard); Rodentia: murid (mouse)		South Africa
<i>Trichinella</i> T9 (related to <i>T. murrelli</i>) [sylvatic]	Carnivora: ursid (Asian black bear, brown bear), canid (raccoon dog, red fox), procyonid (raccoon); Rodentia: murid (mouse)		Japan
<i>T. patagoniensis</i> [T12] [sylvatic]	Carnivora: felid (cougar); Artiodactyla: suid (pig); Rodentia: murid (mouse, rat)		South America
Non-capsule forming (or 'non-encapsulated')			
<i>T. pseudospiralis</i> [T4] [sylvatic, domestic]	Carnivora: felid (cat, oncilla), canid (raccoon dog, red fox, corsac fox), procyonid (raccoon), felid (lynx); Artiodactyla: bovid (sheep), cervid (fallow deer, moose), suid (pig, boar); Rodentia: murid (mouse, brown rat, lesser bandicoot rat), caviid (guinea pig), cricetid (deer mouse), echimyid (coypu); Dasyuromorphia: dasyurid (tiger quoll, eastern quoll, Tasmanian devil); Diprotodontia: phalangerid (common brushtail possum); Primates: hominid (human); Cathartiformes: cathartid (black vulture); Accipitriformes: accipitrid (Cooper's hawk, tawny eagle, common buzzard, western marsh harrier); Galliformes: phasianid (chicken); Falconiformes: falconid (brown falcon, American kestrel); Strigiformes: strigid (little owl, great horned owl, tawny owl), tytonid (Australian masked owl); Anseriformes: anatid (mallard, greylag goose); Passeriformes: corvid (rook, crow), turdid (common blackbird); Charadriiformes: stercoracid (pomarine jaeger); Struthioniformes: struthionid (ostrich); Cypriniformes: cyprinid (common bleak, common carp); Perciformes: percid (ruffe, European perch) [plus carriage in Coleoptera: clerid (checkered beetle); Diptera: tabanid (horse fly); Hymenoptera: vespid (umbrella wasp)]		Nearctic, Oceania
<i>T. papuae</i> [T10] (syn. <i>Bessonoviella papuae</i>) [sylvatic]	Crocodylia: crocodylid (saltwater crocodile), alligatorid (caiman); Serpentes: pythonid (Indian python); Testudines: pelomedusid (African helmeted turtle); Rodentia: murid (mouse); Carnivora: canid (red fox); Artiodactyla: suid (pig); Primates: hominid (human)		Papua New Guinea
<i>T. zimbabwensis</i> [T11] [sylvatic]	Crocodylia: crocodylid (Nile crocodile); Sauria: varanid (Nile monitor lizard); Carnivora: hyaenid (spotted hyena), canid (red fox), felid (lion, leopard), viverrid (small spotted genet); Rodentia: murid (mouse, rat, hamster); Artiodactyla: suid (pig, boar); Primates: cercopithecid (baboon, vervet monkey)		Africa

Parasite morphology: *Trichinella* spp. form several different morphological stages in their developmental cycles: adult worms (male and female) and larvae (4 sequential stages, designated L1-L4). Female worms are ovoviviparous and birth live young in the form of first-stage larvae (L1). Newborn larvae are elongate and tubular, measuring from 80-160 μm in length by 7-9 μm in diameter, and have a thicker anterior end bearing a sword-like stylet at the oral cavity. They invade striated muscle cells where they grow to 800-1,000 μm in length but coil up inside ellipsoidal cysts measuring from 250-500 μm in length. The larvae of most *Trichinella* spp. in mammals (e.g., *T. spiralis*) are found in enlarged host cells (called nurse cells) encapsulated by a thick collagen capsule, whereas those of other species in birds, reptiles and some mammals (e.g., *T. pseudospiralis*) remain non-encapsulated (although a very thin collagen capsule may be detected by electron microscopy). The coiled larvae show precocious development of genital primordia, meaning males and females can be differentiated. When ingested by suitable hosts, the larvae undergo 4 moults to form adult worms which mature rapidly (1-6 days) but have short lifespans (up to 4 weeks). Adult worms are slender and tubular, measuring from 1-4 mm in length, being enclosed by a whitish cuticle that may be translucent or opaque (matte) in appearance. They have a small head with a simple mouth, an elongate non-muscular oesophagus (stichosome) encircled by a chain of single glandular cells (stichocytes), a thin-walled intestine, and a muscular rectum opening into a terminal anus. Mature worms are sexually dimorphic, with female worms being larger than males (2-4 mm by 60-90 μm in diameter compared to 1-2 mm by 40-60 μm). Males do not have spicules but have curved tails with 2 large conical projections (variously named pseudobursae, caudal alae, or copulatory appendages), a single posterior testis connected to the seminal vesicle and terminating at the anal aperture to form a cloaca. Females have blunted rounded tails and contain a single ovary, seminal receptacle, uterus and vagina opening into an anterior vulva. In gravid females, the uterus carries developing eggs and hatching larvae. The eggs are subspherical, measuring 30-40 μm in diameter and are surrounded by a delicate vitelline membrane (no true eggshell). They embryonate *in utero* and first-stage larvae escape from the surrounding membrane and are released through the vulva.

Site of infection: Adult worms infect the small intestines of their hosts where they embed themselves in the mucosa between villi. Gravid females release L1 which move through the lymphatics and circulation to invade striated (skeletal) muscles, particularly those of the diaphragm, jaw (masseter), tongue, eyes, arms, and legs.

Pathogenesis: The clinical consequences of infection are dose-related, in that light infections are often asymptomatic, whereas heavier infections may result in disease (known as trichinellosis or trichinosis) caused by damage to host tissues by adult and larval parasites as well as host hypersensitivity responses to worm excretory-secretory (ES) products. Clinical presentation varies over time with 3 phases recognised: an early enteric phase; an intermittent vascular phase; and an extended muscular phase. In most clinical infections, symptoms peak over 2-4 weeks and then gradually subside 6-8 weeks after infection. Heavy infections, however, may cause severe symptoms which persist for months or progressively worsen leading to death. The enteric phase is caused when ingested larvae invade the intestinal mucosa (within hours) where they become embedded and rapidly mature into adults (within days) producing more larvae. All stages cause tissue trauma and microscopic lesions in the intestines during the first week of infection, but only heavy infections produce symptoms, including catarrhal enteritis, loose stools or diarrhoea, abdominal pain, anorexia, nausea and/or vomiting. Pathological changes include villous atrophy, goblet cell and crypt hyperplasia, and cellular immune responses consistent with type I hypersensitivity (thought to be associated with subsequent worm expulsion). Most symptoms subside after 5-10 days, but diarrhoea, with or without abdominal pain, may last for several weeks. The vascular (parenteral) phase occurs when newborn larvae enter intestinal lymphatics or mesenteric venules and are carried to other tissues. Larval migration may last up to 3 weeks and wandering larvae damage blood vessels with local necrosis producing fever, chills, headache, weakness, profuse perspiration, tachycardia, facial oedema (e.g., periorbital), and retinal, conjunctival or subungual splinter haemorrhages, with eosinophilia, leucocytosis and hyperglobulinaemia. This acute stage develops into the muscular phase when migrating larvae invade skeletal muscle cells in the second or third week, particularly active muscles (such as those of the diaphragm, jaws, tongue, larynx, and/or eyes). The larvae cause structural and functional deficits when they penetrate muscle cells, coil up and encyst, and induce nurse cell formation with subsequent collagen encapsulation around 20 days later (even the non-encapsulated species can have a very thin collagen capsule). The muscle cells infected with encapsulated species are called nurse cells because they transform from contractile cells into turgid metabolically-active cells with few cytoskeletal elements surrounded by small blood vessels providing nutrients and removing wastes. Heavy infections reduce muscle contractibility and cause myositis (often in extraocular muscles progressing to masseters, neck muscles, limb and lumbar muscles), myalgia, weakness, fatigue, muscle degeneration and fibrosis, sometimes myocytosis (muscle breakdown), dyspnoea, cough, hoarseness, dysphagia, constipation, hepatomegaly, occasionally macular or petechial rash, pruritus, aching joints with eosinophilia, hypoalbuminaemia, proteinuria and haematuria (but rarely renal dysfunction). Many symptoms are generalised or resemble those occurring due to rheumatism, pneumonia, encephalitis, meningitis, pleurisy, myocarditis, peritonitis, nephritis, and conjunctivitis. Symptoms may progressively disappear 6-8 weeks after infection, although some may persist for months, including hypocalcaemia, hypomagnesaemia, fatigue and myalgia (esp. legs). Other symptoms may progress to cause serious cardiovascular, respiratory, neurological, psychiatric or allergic disorders, and mortalities have been attributed to heart failure (myocarditis), respiratory congestion (pneumonia), peritonitis (bacteraemia and sepsis due to tissue invasion by enteric flora) or cerebral involvement (encephalitis, eosinophilic meningitis). Survivors often enter a convalescent phase during which most of the intramuscular cysts (e.g., nurse-cell-parasite complexes) become calcified over time (6-18 months), although live larvae have been detected in some people decades after infection. Survivors

also appear to acquire some protective immunity to re-infection and disease. Different *Trichinella* spp. vary in their pathogenicity to humans: *T. spiralis* being the most pathogenic (apparently due to its high reproductive capacity and immuno-reactivity); *T. nelsoni*, *T. britovi* and *T. murrelli* being moderately pathogenic (low to medium reproductive capacities and immuno-reactivities); and *T. nativa*, *T. pseudospiralis* and *T. papuae* being more benign (lower reproductive capacities and slower development).

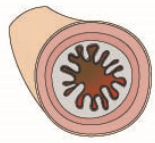
Developmental cycle and mode of transmission: *Trichinella* spp. have unusual life-cycles whereby infectious stages are not voided by the definitive host but become encysted in the muscles of the same host as first-stage larvae (the infectious stages of most other nematodes are third-stage larvae which develop in the external environment or in separate intermediate hosts). When muscle cysts are ingested by carnivores, they are digested in the small intestines releasing the L1 which penetrate the mucosa within several hours. The larvae embed themselves in the mucosa between villous folds and undergo 4 rapid moults developing into mature (dioecious) adult worms within days (1-3 days). After mating, male worms die and pass out of the host while female worms burrow deeper into the mucosa and submucosa, sometimes into lymph ducts and lymph nodes. Gravid females are ovoviviparous, and produce and release motile L1 by day 6. Females may produce up to 1,500 larvae over 5-10 days before dying around day 30. The L1 enter local lymphatics and blood capillaries and are spread throughout the body via the circulation. Larvae invade striated muscle cells, especially very active muscles (like the diaphragm, jaws, tongue, larynx, eyes). The larvae grow in size, coil up by day 17 and remain within cells. Some species (e.g., *T. spiralis*) cause the infected muscle cell to transform into a nurse cell (myofilaments disappear, smooth endoplasmic reticulum increases, nuclei enlarge to form a complex around the larva). The larvae derive nutrients from the sarcoplasm as well as from a growing network of capillaries surrounding the parasite-nurse cell complex. By day 21, the coiled larvae begin to become encased in a collagen capsule laid down by surrounding fibroblasts, this process of encapsulation takes up to 3 months. The capsule is thick and double-walled in encapsulated species (e.g., *T. spiralis*, but remains thin and membranous for non-encapsulated species (e.g., *T. pseudospiralis*). The larvae are infective after 8 weeks but may remain viable in developmental arrest for years, although most cysts eventually calcify within 6-18 months. Transmission occurs when infected raw flesh is eaten by carnivorous or omnivorous animals via predation, cannibalism, scavenging or carrion-feeding in sylvatic or domestic cycles. Zoonotic transmission to humans occurs when people eat raw or undercooked meat of infected animals, particularly pigs and wild boar, but also including other game animals, such as walrus and bear. All *Trichinella* species have sylvatic cycles in wildlife, either by ingestion of infected prey or fresh, frozen or decomposing carcasses. The larval cysts of different *Trichinella* spp. show variable resistance to being frozen in host tissues: those of species found in cold Arctic regions (*T. nativa* and *T. britovi*) may survive extended periods (weeks), while those of species found in more temperate regions (*T. spiralis*, *T. nelsoni*, *T. murrelli*, *T. pseudospiralis* and *T. papuae*) do not survive long (hours or days). Human activities often contribute to sylvatic cycles or lead to the development of domestic cycles: e.g. hunting wildlife for food, baiting traps with meat, leaving carcasses for scavengers, or feeding scraps to domestic or companion animals, including meat animals (pigs, crocodiles), fur animals, pets or working animals (especially sled dogs). In particular, urban cycles become established amongst pigs, rats and humans when high risk farming practices facilitate transmission through feeding offal and pork scraps back to pigs, disposing of waste in open garbage dumps and housing animals in facilities that are not vermin-proof. Infections in humans have been recorded around the world, with Europe and North America reporting some 150,000-300,000 infections per year, but only ~ 150 of these are clinical cases. Infections are rarer in tropical regions usually due to the lower consumption of pork, or meat in general, due to greater vegetable/fruit consumption, fish diets, or religious bans on eating pork.

Differential diagnosis: Although several clinical symptoms may be indicative of trichinellosis (e.g. myalgia, periorbital oedema, fever), they are relatively nonspecific and might be attributable to other disease conditions. Blood tests may reveal eosinophilia, leucocytosis and elevated levels of muscle enzymes (creatine kinase and lactate dehydrogenase) during infection, but these are similarly nonspecific. Infections are unequivocally diagnosed by the microscopic detection of parasite larvae in muscle biopsy samples (usually deltoid or gastrocnemius muscle) or necropsy samples (usually diaphragm), either in squash (glass compression) preparations (trichinoscopy) or following enzyme-acid (pepsin-HCl) digestion. Several immunoserological tests have been developed to detect host serum antibodies against infections, including intradermal, flocculation and agglutination tests and enzyme immunoassays), but they do not detect early infections as circulating antibodies only appeared 3-4 weeks after infection. Various molecular characterization studies have been used to demonstrate differences between *Trichinella* spp., including Western blots of parasite antigens and allozyme electrophoresis (ACO, ACP, ADA, ALAT, ALDO, EST, G6PD, GLDH, GOT, GPD, LDH, ME, 6PGD, PGM, SOD, TPI). More recently, molecular biological techniques have been used to detect parasite DNA in clinical samples (as restriction fragment length polymorphisms (RFLP), single strand conformational polymorphisms (SSCP), random amplified polymorphic DNA (RAPD) or partial gene sequences) following polymerase chain reaction (PCR) amplification of repetitive DNA (pPRA, pBP2, pT1.6), nuclear genes (small subunit ribosomal RNA, expansion segment V of ribosomal DNA repeat, internal transcribed spacer regions 1 and 2) and mitochondrial genes (cytochrome c oxidase subunit 1, large subunit ribosomal RNA).

Treatment and control: Several anthelmintic drugs have been found to be effective against adult worms in the gut if applied early enough in infection, but they were less effective against encysted larval stages in the muscles. The benzimidazole-methylcarbamates (mebendazole, albendazole and flubendazole) are the drugs of choice, but not in pregnant women or young children due to adverse

side effects, including bone marrow suppression. The tetrahydropyrimidine pyrantel has been used in children and pregnant women. The anthelmintic drugs are often given together with analgesics to relieve symptoms, antipyretics to reduce fever, and steroid therapy to reduce inflammation, particularly in cases involving the heart or central nervous system. Bed rest is advised to avoid exertion antagonizing muscular symptoms. Several strategies have been developed to prevent infections by breaking transmission cycles where possible. Strict regulations have been implemented governing the production of livestock for meat, especially pigs, with mandatory testing at slaughter (trichinotomy) and certification of *Trichinella*-free producers. Many countries have reported great success in controlling zoonotic infections in humans by banning the feeding of offal and scraps to pigs, prohibiting the consumption of wild boar, and advocating the thorough cooking of pork products. Larvae in muscle cysts are killed when pork is cooked to a core temperature of 71°C for at least one minute or 59°C for at least 10 minutes. It is recommended that thermometers be used to monitor roasting or microwave cooking of meat. Drying and curing meats have also been shown to be relatively effective, but they do not always kill larvae found in game meats. Freezing may be used to kill encapsulated larvae in pork when frozen at -15°C for at least 3 weeks or at -20°C for at least 3 days, but cooking is recommended for game meats which may be infected with non-encapsulated parasite species that have a high tolerance to freezing. Gamma-irradiation has also been used to sterilize meats in sealed packaged foods. It is critical that carcasses be disposed of properly (preferably by burning or burying), that unprocessed meat scraps are not dumped in garbage tips or fed to farmed or wild carnivores, and that farms undertake rodent control. Compliance with government regulations or recommendations is high in regions where intensive husbandry practices are used (indoor piggeries), but lower in regions where animals are kept in pig-sties or are free-ranging. Epidemiological investigations have shown that non-compliance has resulted in several outbreaks traced back to pigs and even horses fed pork scraps, and fur animals, sled dogs and crocodiles fed carcasses of the same animal species or other game animal species. Public education campaigns should be implemented in communities consuming pork products and the posting of warning signs in endemic wilderness areas should continue to warn hunters of the risks involved in eating wild game.

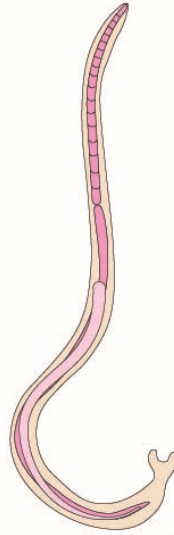
Trichinella



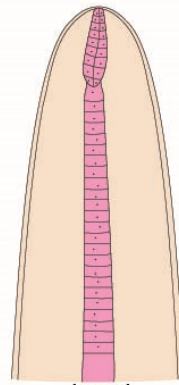
intestines
(enteric phase
with diarrhoea,
vascular phase
with oedema)



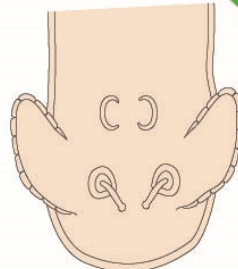
adult female
(~ 4 mm)



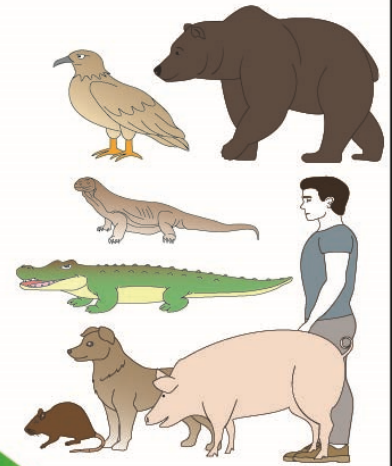
adult male
(~ 2 mm)



head



male
tail

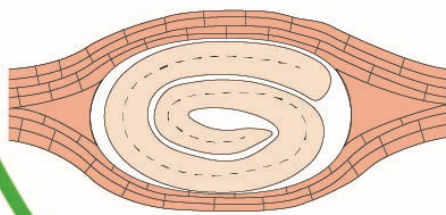


Definitive Hosts
(mammals, birds,
reptiles)

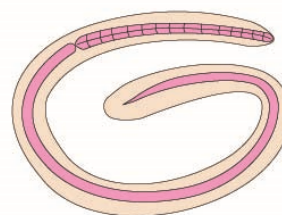
L1 in flesh ingested
(via predation, cannibalism,
scavenging, carrion-feeding)
(domestic and sylvatic cycles)

direct
transmission

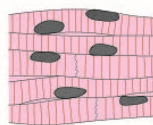
viviparous females release
first-stage larvae (L1) which
move through lymphatics
to striated muscles



encapsulated L1
in mammals
(~ 800 μ m)



non-encapsulated L1
in birds/reptiles
(~ 800 μ m)



striated muscles
(muscular phase with
myositis/myocytosis)

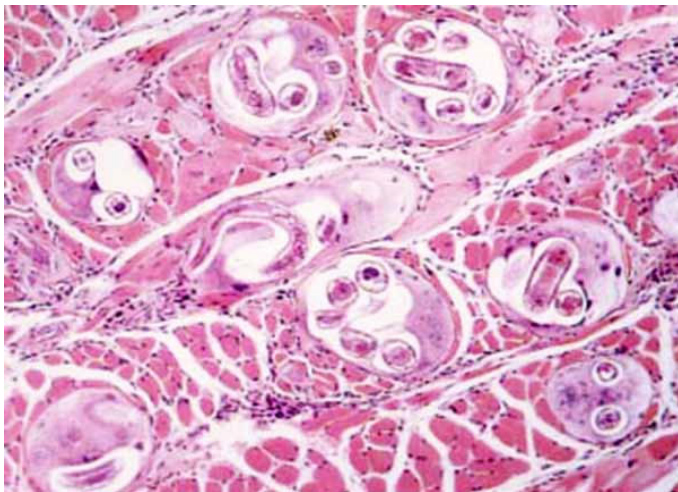


Trichinella adult worm



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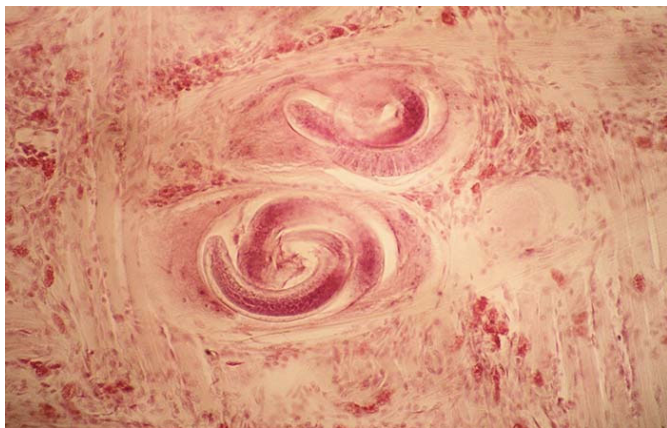
Trichinella in gut section



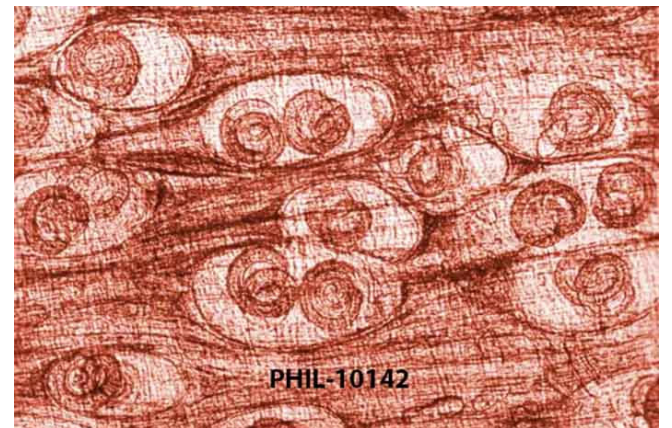
Trichinella larvae in muscles



Trichinella larvae in muscles



Trichinella larvae in muscles



PHIL-10142

Trichinella larvae in muscles