Loa
(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 tylenchinids, rhabditinids and spirurinids. The latter contains the infraorder Spiruromorpha: an enigmatic clade linked by molecular characters, but all having indirect life-cycles involving one or more intermediate hosts, the first invariably being an arthropod. Most possess two trilobed lips (sometimes greatly reduced), a bipartite oesophagus (anterior muscular, posterior glandular) and non-bursate males with coiled tails and two dissimilar spicules. Several superfamilies are recognised: including filarioids (without lips) living in subcutaneous, intermuscular, vascular or lymphatic systems of mammals. Two main families include the oviparous filariids (lay eggs) and the ovoviviparous onchocercids (eggs hatch internally releasing pre-larvae called microfilariae). Infections by the onchocercid genus *Loa* are transmitted by tabanid flies and cause subcutaneous Calabar swellings in humans in Africa.

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:	Spirurina (mostly parasitic in vertebrate hosts)
Infraorder:	Spiruromorpha (enigmatic clade linked by molecular characters, indirect cycles with IHs)
Superfamily:	Filarioidea (tissue-dwelling filarial parasites, lack lips)
Family:	Onchocercidae (adults loose in tissues or in nodules, viviparous (live birth of microfilariae))
Genus:	*Loa* (parasitic in subcutaneous tissues of humans, fly IH)
Species:	*Loa loa* (causes Calabar swellings 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 (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)]
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 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.

Molecular phylogenetic studies have grouped a variety of superfamilies into the infraorder Spiruromorpha whose members are parasites of vertebrates with indirect life-cycles involving larval development within invertebrate intermediate hosts. Most members were previously classified within the order Spirurida: either within the suborder Camallanina (worms with conspicuous phasmids, uninucleate oesophageal glands, larvae without cephalic hooks, usually with copepodid intermediate hosts); or the suborder Spirurina (worms with inconspicuous phasmids, multinucleate oesophageal glands, larvae with cephalic hooks or spines, usually with non-copepodid intermediate hosts). Ten spirurinid superfamilies are recognised: Gnathostomatoidea and Physalopteroidea (buccal cavity weakly cuticularized, 2 large lateral pseudolabia); Habronematoidea and Acuarioidea (buccal cavity well cuticularized, 2 large lateral pseudolabia); Filarioidea, Rictularioidea, Aproctoidea and Diplotriaenoidea (buccal cavity well cuticularized, without pseudolabia); Thelazioidea (long cylindrical buccal cavity well cuticularized, body without caudal alae); and Spiruroidea (short buccal cavity well cuticularized, body with caudal alae).

The superfamily Filarioidea contains long thread-like nematodes which are predominantly tissue-dwelling parasites infecting the body cavities, subcutis, intermuscular tissues, blood vessels or lymphatic systems of terrestrial hosts. These worms are known colloquially as 'filariae', 'filarids' or 'filarioids' [Note: take care with terminology as the cognate family Filariidae (esp. genus *Filaria*) are known colloquially as 'filariids', and the unrelated metastrongyle (lungworm) family Filaroididae (genus *Filaroides*) are known colloquially as 'filaroids']. Adult filariae have a cylindroid pharynx with an anterior muscular portion and a posterior glandular portion. Males often have spirally-coiled tails, well-developed alae and dissimilar spicules. Females of most species are ovoviviparous (eggs hatch within body of parent) releasing pre-larval stages known as microfilariae (sometimes sheathed). Filariae have indirect life-cycles whereby microfilariae are taken up by blood-sucking or tissue-feeding invertebrates (arthropods, esp. mosquitoes) which act as intermediate hosts for the development of infective L3 larvae. Ten families are recognised: Filariidae and Onchocercidae infecting mammals, birds, reptiles and amphibians; Setariidae infecting mammals; Aproctidae infecting birds; and Creagrocercidae, Drilonematidae, Homungellidae, Mesidionematidae, Scolecophilidae and Ungellidae infecting terrestrial annelids. Examples of filarioid genera covered in this resource are compared in the following table.

Genus	Definitive hosts	Adults (location)	Microfilariae (location)	Periodicity	Vectors	*Wolbachia* symbiotes
Family Onchocercidae						
Loa (3 spp.)	primates, ungulates, rodents	2-7 cm (subcutis, eye)	250-300 µm sheathed (blood)	diurnal	flies	absent
Onchocerca (35 spp.)	primates, carnivores, ungulates, rodents	1.5-80 cm (subcutis, ligaments)	105-440 µm unsheathed (skin)	-	flies, midges	present
Mansonella (29 spp.)	primates, carnivores, ungulates, rodents	3-8 cm (subcutis, serosa)	170-300 µm unsheathed (blood/skin)	-	midges, flies, mosquitoes	present
Dirofilaria (34 spp.)	primates, carnivores, ungulates, rodents, lagomorphs, marsupials	4-31 cm (blood vessels)	180-385 µm unsheathed (blood)	-	mosquitoes, flies	present
Dipetalonema, Acanthocheilonema (57 spp.)	primates, carnivores, ungulates, rodents, cingulates, marsupials	1-7 cm (subcutis, serosa)	85-300 µm unsheathed (blood)	-	flies, fleas, lice, ticks	absent
Wuchereria (2 spp.)	primates	2.5-10 cm (lymphatics)	210-320 µm sheathed (blood)	nocturnal, subperiodic	mosquitoes	present
Brugia (10 spp.)	primates, carnivores, rodents	1-9 cm (lymphatics)	170-380 µm sheathed (blood)	nocturnal, subperiodic	mosquitoes	present
Family Filariidae						
Parafilaria (4 spp.)	ungulates	2-7 cm (subcutis)	40-58 x 23-33 µm larvated eggs (skin)	diurnal	flies	absent
Stephanofilaria (7 spp.)	ungulates	0.2-1.4 cm (subcutis)	45-195 µm sheathed (skin)	-	flies	absent
Family Setariidae						
Setaria (42 spp.)	primates, ungulates, rodents, lagomorphs	4-19 cm (body cavities)	140-310 µm sheathed (blood)	-	mosquitoes	absent

Members of the family Onchocercidae form adult worms that live loose in body cavities or in tissue nodules. Female worms release microfilariae which disperse into the blood or dermal connective tissues (unlike filariids which live in the skin close to where they deposit eggs or larvae). Some 88 onchocercid genera are divided into 7 subfamilies: Onchocercinae and Dirofilariinae (syn. Loainae) mostly in mammals but some in birds and reptiles, Waltonellinae and Icosiellinae in amphibians, Oswaldofilariinae in reptiles, Splendidofilariinae and Lemdaninae in birds, reptiles and mammals (former subfamily Setariinae in large mammals recently elevated to family status as Setariidae). Members of the subfamily Dirofilariinae are characterised as forming males with highly developed caudal alae (while members of the subfamily Onchocercinae form males with markedly dissimilar spicules and long tails lacking caudal alae). Some 16 genera are recognised in the subfamily Dirofilariinae: namely, *Bostrichodera*, *Dirofilaria*, *Dirofilariaeformia*, *Edesonfilaria*, *Eulimdana*, *Foleyellides*, *Heimnema*, *Loa* (syn. *Paraloa*), *Loaina, Macacanema*, *Madochotera*, *Ochoterenella*, *Skrjabinodera* and *Tawila* in mammals, *Pelecitus* (syn. *Spirofilaria*, *Eulimdana*) in birds, and *Foleyella* (syn. *Foleyellides*) in saurians. Three groups of human filariasis are distinguished on the basis of their tissue tropism: cutaneous dermal filariasis (loiasis in Africa, onchocerciasis in Africa, Asia, Central and South America, *streptocerca* mansonelliasis in Africa); lymphatic filariasis (wuchereriasis in Africa and Asia, brugiasis in South Asia); and serous filariasis (*perstans* mansonelliasis in Africa, Central and South America, *ozzardi* mansonelliasis in Central and South America).

The genus *Loa* forms thread-like worms in subcutaneous and deep connective tissues predominantly in primates. Adult worms have cuticular coverings with irregular bosses (protrusions) and delicate transverse striations, simple heads lacking lips but with 8 cephalic papillae, and blunt tails. Mature female worms are ovoviviparous releasing sheathed microfilariae into the blood where they are taken up by day-biting tabanid flies (*Chrysops* spp. known variously as mango flies, horse flies, or deer flies). The species *L. loa* is endemic in humans and monkeys in equatorial rainforests of West and central Africa and it is estimated that up to 20 million people may be infected.

***Loa* species**	**Definitive Hosts (DH)**	**Location**	**Clinical signs**	**Vectors/Intermediate Hosts (IH)**	**Distribution**
L. loa (African eye worm) (includes human and monkey strains)	Human strain Primates: hominid (human, gorilla), cercopithecid (grey-cheeked mangabey, mandrill, olive baboon, patas monkey); Perissodactyla: equid (horse); Rodentia: murid (jird, Mongolian gerbil, mouse) Monkey strain Primates: cercopithecid (greater spot-nosed monkey, drill, mona monkey)	subcutaneous tissues, subconjunctiva, mf in blood (sheathed, human strain diurnally periodic, monkey strain nocturnally periodic)	skin (Calabar) swellings, allergic reactions	Diptera: tabanid human strain (*Chrysops dimidiata, silacea, atlanticus, distinctipennis, longicornis, zahrai*), monkey strain (*Chrysops centurionis, langi*)	tropical West and Central Africa
L. papionis (or *L. loa papionis*)	Primates: cercopithecid (yellow baboon)	larger worms in tissues, mf in blood (sheathed, nocturnally periodic)	simian loiasis	Diptera: tabanid (*Chrysops centurionis, langi*)	Africa
L. inquirenda	Primates: hominid (human)	subconjunctiva, neck			India

Parasite morphology: Filarial nematodes belonging to the genus *Loa* form 3 distinct morphological stages in their developmental cycles: adult worms, microfilariae and larvae (moulting through 4 stages). Gravid females produce embryonated eggs which hatch internally releasing live microfilariae (considered to be pre-larvae as they are not as developed as typical first-stage nematode larvae). Microfilariae are elongate and slender, measuring 250-300 x 6-8 µm. They are ensheathed in an eggshell-like membrane and have a tapering tail hooked or coiled within the sheath. The body contains a densely packed nuclear column which extends to the tip of the tail. Microfilariae exsheath and develop into first-stage larvae (L1) which undergo a series of 4 moults to eventually form sub-adult worms. Developing larvae vary in size, measuring from 1.1-5.3 mm in length depending on their stage of maturation in the moult cycle. Infective third-stage larvae (L3) grow to 1.3-2.6 mm long and the tip of the tail has a digitiform process with 2 ventrolateral papillae and 2 subterminal papillae. Fourth-stage larvae (L4) begin to show sexual differentiation in their genital primordia and the larvae vary in size according to gender, with developing female worms being larger than males (5.3 mm cf. 4.4 mm). Adult worms are sexually dimorphic, with females being larger than males (40-70 x 0.4-0.5 mm cf. 20-35 x 0.3-0.4 mm). They have long slender thread-like bodies with prominent bosses (protrusions) of cuticular material scattered in irregular patterns as well as delicate transverse striations, a short undivided oesophagus, simple heads with 8 cephalic papillae and blunt tails. Males have 2 uneven dissimilar spicules (around 120 and 90 µm long), 3 caudal lappets and often asymmetrical arrangements of 3 pairs of pre-anal and 5 pairs of post-anal papillae. Female worms are ovoviviparous and give birth to live microfilariae through an anteriorly-located vulva (posterior to nerve ring).

Site of infection: Adult male and female *Loa* worms live and migrate in subcutaneous connective tissues in their mammalian definitive hosts, particularly on the back, chest, axilla, groin, and scalp. Migrating worms may sometimes traverse the subconjunctiva of eye, and on rare occasions, they may infiltrate into deeper connective tissues, lymph nodes and the anterior chamber of the eye, causing serious complications. Microfilariae are found in predominantly in the bloodstream, although they have sometimes been isolated from cerebrospinal fluid, urine, sputum, and saliva. Larval stages develop in the thoracic muscles and fat body of their invertebrate intermediate hosts, and then migrate to the mouthparts.

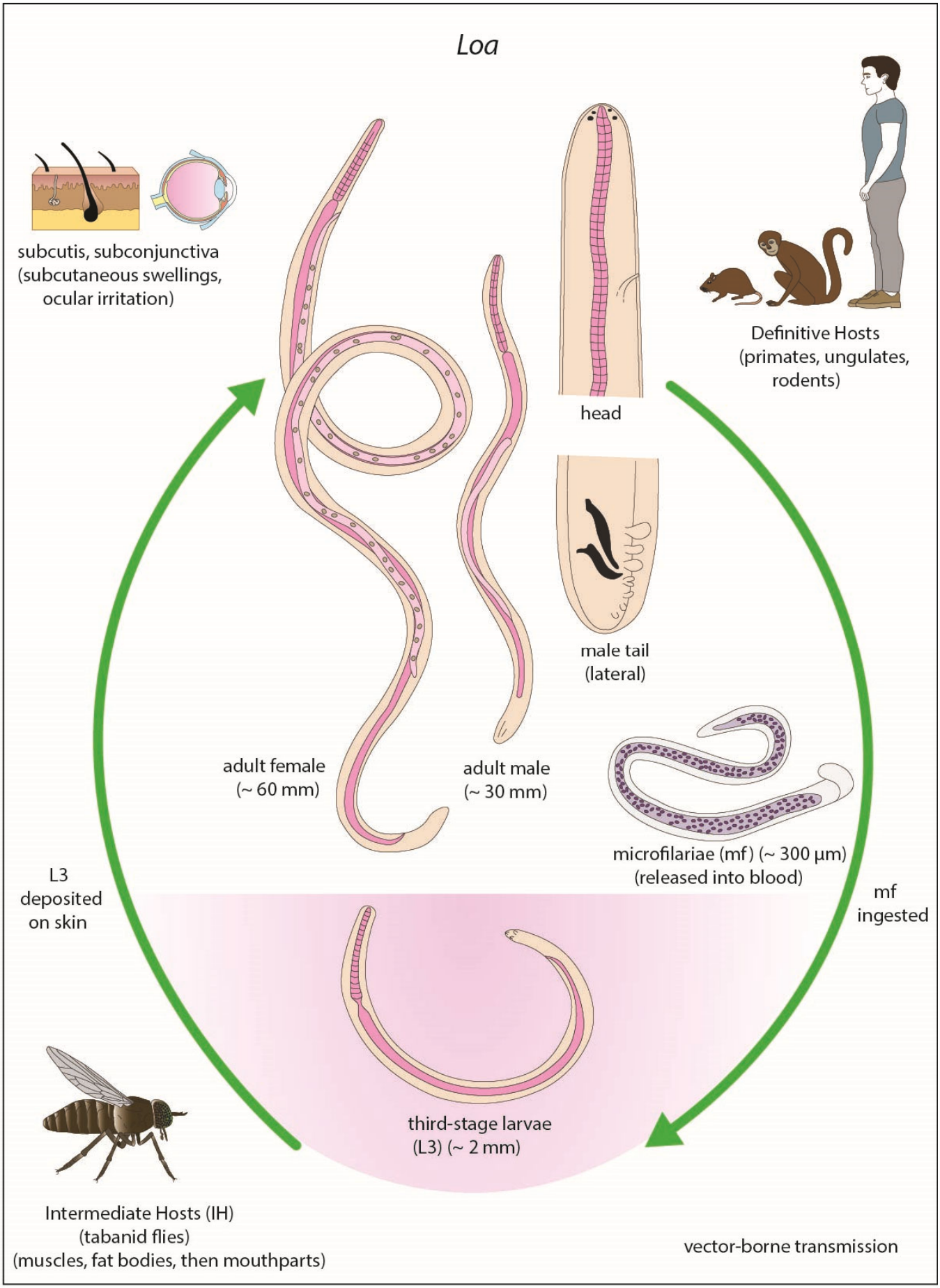
Pathogenesis: *L. loa* infections are frequently asymptomatic, but some may cause a mild disease (loiasis) in which symptoms may appear within a few months of infection, but often not for more than a decade. Many cases are therefore latent or occult, and the absence of circulating microfilariae appears to be due to their destruction by the host immune system and/or their possible sequestration within tissues. The pathogenesis of infections also varies according to exposure, with residents indigenous to endemic areas often having high blood microfilarial counts without symptoms, and non-indigenous people often having low or no microfilarial counts but with massive hypersensitivity responses, involving peripheral eosinophilia, hypergammaglobulinaema (esp. IgE) and systemic symptoms. Most symptoms are caused by the extensive migrations of worms in subcutaneous tissues, sometimes moving at rates up to 1.5 cm/min, resulting in 3 principal manifestations: cutaneous; ocular; and cerebral signs. While many worm migrations may go unnoticed, others may trigger localized inflammatory (hypersensitive) responses resulting in transient angioedematous swellings on the body (known as Calabar swellings). The swellings develop rapidly and last from 1-3 days, usually accompanied by localized pain, urticaria and pruritus. They can be found anywhere on the body, usually involving the face and limbs, and those near joints make movement difficult and painful. Occasionally, developing larvae or young adult worms may migrate across the surface of the eye under the conjunctiva (condition commonly known as eyeworm) resulting in inflammatory swelling of the orbit, congestion, itching, pain, photophobia and psychosomatic manifestations. Subconjunctival migration may take anywhere from 15 min to a full day to be completed. Rarely, worms may invade the interior of the eye, causing severe inflammation, ocular irritation and occasionally leading to blindness. Ectopic infections of deeper tissues may also sometimes occur leading to severe complications, including endomyocardial fibrosis, pleural effusion, nephropathy, neurological problems (ranging from headache to loss of sensation and motor deficiencies) and sometimes fatal encephalitis. Infection can also induce fatigue and sudden bouts of popular or vesicular rash. Loiasis is confined to sub-Saharan Africa (it was introduced into the Caribbean during the slave trade era, but did not persist) and those most at risk reside or work near rainforests, savannahs and areas near streams or rivers. The prevalence of infection increases with age, and Calabar swellings occur more frequently in women than men, with greater recurrences. This mild disease was neglected for many years in favour of more severe infectious diseases, but this changed when mass eradication programs for onchocerciasis were conducted in regions endemic for *Loa*. It was found that ivermectin drug treatment led to severe neurological complications (termed serious adverse events, SAEs), such as encephalitis and coma, in patients with concomitant *Loa* infections (esp. those with heavy microfilaraemias). It is estimated that some 30 million people live in areas where both infections co-exist.

Developmental cycle and mode of transmission: All filarial worms have indirect heteroxenous life-cycles involving vector-borne transmission. Gravid *Loa* worms produce microfilariae which demonstrate a circadian (daily) rhythm to their concentration in host blood. Microfilariae in humans exhibit diurnal periodicity, whereby they occur in peripheral blood during daylight hours (5 am to 7 pm, but peak concentrations from 10 am to 2 pm) and are sequestered in capillaries of the skin, lungs and other organs at night (Note: some workers have reported a variant *Loa* strain in monkeys which apparently demonstrates a nocturnal periodicity). Nonetheless, the characteristic diurnal periodicity of loiasis distinguishes it from Bancroftian and Brugian filariasis which are nocturnally periodic. The occurrence of *Loa* microfilariae in blood during the day corresponds well to the peak feeding times (9 am to 4 pm) of the tabanid fly vectors, *Chrysops* spp. (known as deer flies, mango flies or mangrove flies). Female flies require a blood meal for egg production and they use specialized scissor-like mouthparts to cut the skin, thus inflicting painful bites which often cause allergic reactions in humans. They breed in swamps, muddy ponds and slow-moving waters impeded by rotting vegetation. The main vectors for human infections are *C. silacea, C. dimidiata* and *C. distinctipennis* which are found in tropical rainforests and gallery forests of West and Central Africa, particularly during rainy seasons. In contrast, the nocturnal variant strain found in monkeys is transmitted mainly by *C. centurionis* and *C. langi* which feed on animals in the forest canopy at night. Ingested microfilariae exsheath in the gut and migrate through the haemocoel to the thoracic cavity (infected tissues become disorganized and syncytial). Here they moult to second-stage larvae (L2) in 3-5 days, to third-stage larvae (L3) in 6-9 days and then migrate to the mouthparts by 9-14 days. Infective L3 larvae emerge from the proboscis when the labium is bent (kinked) during feeding. Transmission is contaminative (rather than inoculative) as the larvae are deposited onto the host skin and invade the bite wound into subcutaneous tissues. They moult to fourth-stage larvae (L4) in 18-30 days and then to sub-adult stages around 50 days. Developing worms migrate extensively through the connective tissues and become sexually mature over several months. Female worms are ovoviviparous and may produce thousands of microfilariae per day. The prepatent period (time from infection to first appearance of microfilariae) may be as short as 4-5 months, but is often extended to 12 months. Adult worms have been found to live as long as 15-17 years in infected patients.

Differential diagnosis: Infections may be suspected on the basis of clinical manifestations (e.g. Calabar swellings or wandering eyeworm) in patients with a history of residency or travel to endemic areas, but similar swelling may arise due to other conditions (such as hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency) and other worms may undertake subconjunctival migration (e.g. *Dirofilaria repens, Thelazia californiensis*). In some cases, worms may be surgically removed from the subconjunctiva, or from accessible subcutaneous locations, and examined microscopically for distinctive features (size, cuticular protrusions, transverse striations, simple heads with 8 cephalic papillae, and blunt tails). Generally, infections are confirmed by the microscopic examination of blood samples for microfilariae, taking care to differentiate those of *Loa* from other filarial worms often found in the same geographic locations (such as *Onchocerca volvulus* and *Wuchereria bancrofti*). It is recommended that blood be collected around 1 pm as the microfilaraemia associated with loiasis exhibits diurnal periodicity. Microfilariae may be found in thick or thin blood smears stained with Giemsa or haematoxylin, or in concentrates obtained by membrane filtration (3-5 μm pore size) or by centrifugation after haemolysis (treatment with formalin, saponin or hypotonic saline). *Loa* microfilariae are identified by

their large faintly-staining sheath and tapering tail with nuclei extending to the tip. It should be remembered, however, that infections undergo a long incubation period before becoming microfilaraemic (months to years) and some infections remain amicrofilaraemic with or without symptoms. A range of immunological tests have been developed to detect host antibodies against infection, including class-specific fluorescent or enzyme immunoassays, but many have demonstrated poor sensitivity, cannot differentiate recent infection from previous exposure and sometimes cross-react with other filarial infections. Studies are currently examining immunological techniques to detect parasite antigens in blood samples, and promising results have been obtained with enzyme immunoassays and luciferase immunoprecipitation assays. Molecular biological techniques have also been used to detect parasite DNA in both occult and regular loiasis following the polymerase chain reaction (PCR) amplification of specific gene sequences, particularly the repeat 3 region of a 15 kDa polyprotein allergen (15r3).

Treatment and control: Infections may be treated with filaricidal anthelmintics, including diethylenediamine (diethylcarbamazine (DEC)), macrocyclic lactones (ivermectin) and benzimidazole-methylcarbamate (albendazole and mebendazole). Chemotherapy was found to significantly reduce microfilariaemia, but only DEC was effective against adult worms, with some minor side-effects (headache, rash, fever). Mass treatments for onchocerciasis with single or combination anthelmintics had been undertaken in many endemic areas, but it quickly became evident that treatment of patients with high *Loa* microfilarial counts caused serious adverse events (SAEs), including shock, encephalitis and retinal haemorrhage coincident with massive antigen release from dying microfilariae. While such events may be ameliorated through the concurrent application of steroids and other anti-inflammatory drugs, treatment programs were curtailed or closely monitored in areas where both loiasis and onchocerciasis occurred. *Loa* is one of the few filarial worms that does not have endosymbiotic *Wolbachia* bacteria, so it is not susceptible to treatment with tetracycline antibiotics. In eyeworm cases, worms may often be surgically removed after local anaesthesia, but it is chemotherapy is still required to treat microfilariae or any remaining adults. Surgery may also be used to extract worms from subcutaneous tissues when infections are superficial, easily accessible and are not threaded through joints. The prevention of infections relies on avoiding vector bites rather than on vector control. Deer flies are active during the day and rarely enter buildings (houses, barns), so the use of residual insecticides on dwellings and impregnated bed nets has limited efficacy. Flies also breed in wet and wild locations not particularly suited to intervention strategies (physical, chemical or biological). Instead, people should practise personal protection to avoid fly bites through the use of personal repellents (esp. DEET), impregnated clothing (esp. permethrin) and wearing long-sleeved shirts and long pants when working outdoors.


Loa
subcutis, subconjunctiva
(subcutaneous swellings,
ocular irritation)
Definitive Hosts
(primates, ungulates,
rodents)
head
male tail
(lateral)
adult female
(~ 60 mm)
adult male
(~ 30 mm)
microfilariae (mf) (~ 300 µm)
(released into blood)
L3
deposited
on skin
mf
ingested
third-stage larvae
(L3) (~ 2 mm)
Intermediate Hosts (IH)
(tabanid flies)
(muscles, fat bodies, then mouthparts)
vector-borne transmission

	
Loa adult worm	*Loa* microfilaria