

Special Issue: Zoonoses of people and pets in the USA

Hookworms of dogs and cats as agents of cutaneous larva migrans

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Dogs and cats are hosts to hookworms that may cause zoonotic disease, most notably, cutaneous larva migrans. *Ancylostoma braziliense* is most often implicated in dermatological lesions, and *Ancylostoma caninum* has been associated with eosinophilic enteritis and suggested as a possible cause of diffuse unilateral subacute neuroretinitis in humans. Other manifestations include eosinophilic pneumonitis, localized myositis, folliculitis, erythema multiforme, or ophthalmological manifestations. *Ancylostoma* eggs are morphologically indistinguishable, which complicates epidemiological studies. Surveys of dermatologists, gastroenterologists, and ophthalmologists would help to define the incidence of these zoonotic infections. Improved diagnostic tests are needed to identify the causative species involved and understand the epidemiology of hookworm disease. This review describes the discovery of the disease, the biology of the agents, and how that biology may impact disease.

Dog and cat hookworms and zoonotic disease

The common hookworms of dogs, *Canis familiaris*, are: *Ancylostoma caninum*, *A. braziliense*, *A. ceylanicum* and *Uncinaria stenocephala*; and of cats, *Felis catus*, are: *Ancylostoma tubaeforme*, *A. braziliense*, *A. ceylanicum* and *U. stenocephala* [1]. Larval infection in humans can lead to hookworm associated cutaneous larva migrans (CLM) [1] and, less commonly, eosinophilic pneumonitis [2–5], localized myositis [6,7], folliculitis [8–12] erythema multiforme [13] or ophthalmological manifestations [14]. Of these species, only *A. ceylanicum* will readily develop to adults in people, but *A. caninum* has, on occasion, reached adulthood in people, causing eosinophilic enteritis [1,15].

The geographical distribution of each species is imperfectly known because ranges overlap, hosts can harbor several species simultaneously, and only the larger *U. stenocephala* egg can be morphometrically distinguished [16]. *Uncinaria stenocephala* occurs in dogs and cats in the colder climates of North America, South America, Europe, Asia, Australia and New Zealand [17,18]. Recently, mol-

ecular methods were developed to distinguish *Ancylostoma* eggs in feces [19,20], but most older surveys were based on necropsy results. *A. caninum* and *A. tubaeforme*, the most common species, are found throughout the warmer ranges of dogs and cats [1,19,20]. *Ancylostoma ceylanicum* is found in Asia (India, Taiwan, Thailand, Malaysia, Borneo, Indonesia), Australia and South America (Surinam)

Glossary of terms

Bulla: a large blister (plural – bullae). Some bullae associated with CLM have been several inches in diameter.

Colitis: inflammation of the large intestine

Enteritis: inflammation of the intestine, usually the small intestine.

Eosinophilia: increase in the type of white blood cells called eosinophils in the peripheral blood. Such increases often accompany infections with helminths and arthropods. The numbers in the peripheral blood will also often increase in allergic reactions.

Folliculitis: inflammation of hair follicles

Gasterophilus: This is a genus of flies, called botflies, which lay eggs on the hairs of horses (and a few other animals). The adults are free living, but the larvae, the maggots, live and develop only in the stomach of the horse.

Hookworm: These are small nematode parasites of the intestinal tract of vertebrates; hookworms suck blood to various degrees, depending on the species. They are called hookworms because the anterior end is bent backwards giving the worm a 'hooked' appearance.

Myiasis: Infection with maggots. The term maggot is typically reserved for the larvae of flies, more specifically dipteran flies lacking a distinct head capsule. Apart from the *Gasterophilus* mentioned in the text, other genera of maggots such as *Hypoderma* of cattle have also been responsible for serpiginous track lesions in the skin of people.

Myositis: Inflammation of the muscle.

Papule/papular: Small, solid nodule in the skin, which may be intensely pruritic.

Paratenic host: This is a host in which a parasite can persist, without major developmental change, but which is not required for the life cycle to be completed. In the case of *A. caninum*, the larvae can infect and persist in cockroaches. They can also persist in the muscles of small rodents following infection by skin penetration, ingestion of larvae from soil, or by eating a cockroach. Dogs can get infected by ingesting larvae on grass, the skin penetration of larvae, or the ingestion of either the cockroach or mouse paratenic hosts.

Pruritus: an unpleasant sensation that induces someone to scratch or rub the skin

Transmammary transmission: Transmission via the milk/mammary gland. Puppies become infected with the larvae of *A. caninum* while nursing. Some percentages of larvae that enter a dog persist in the dog's muscles. These larvae are reactivated (probably hormonally) towards the end of gestation and make their way to the mammary glands where they are transferred to the suckling puppies.

Vesicle: small circumscribed fluid-filled elevations on the skin, also called blisters. Bullae are large vesicles.

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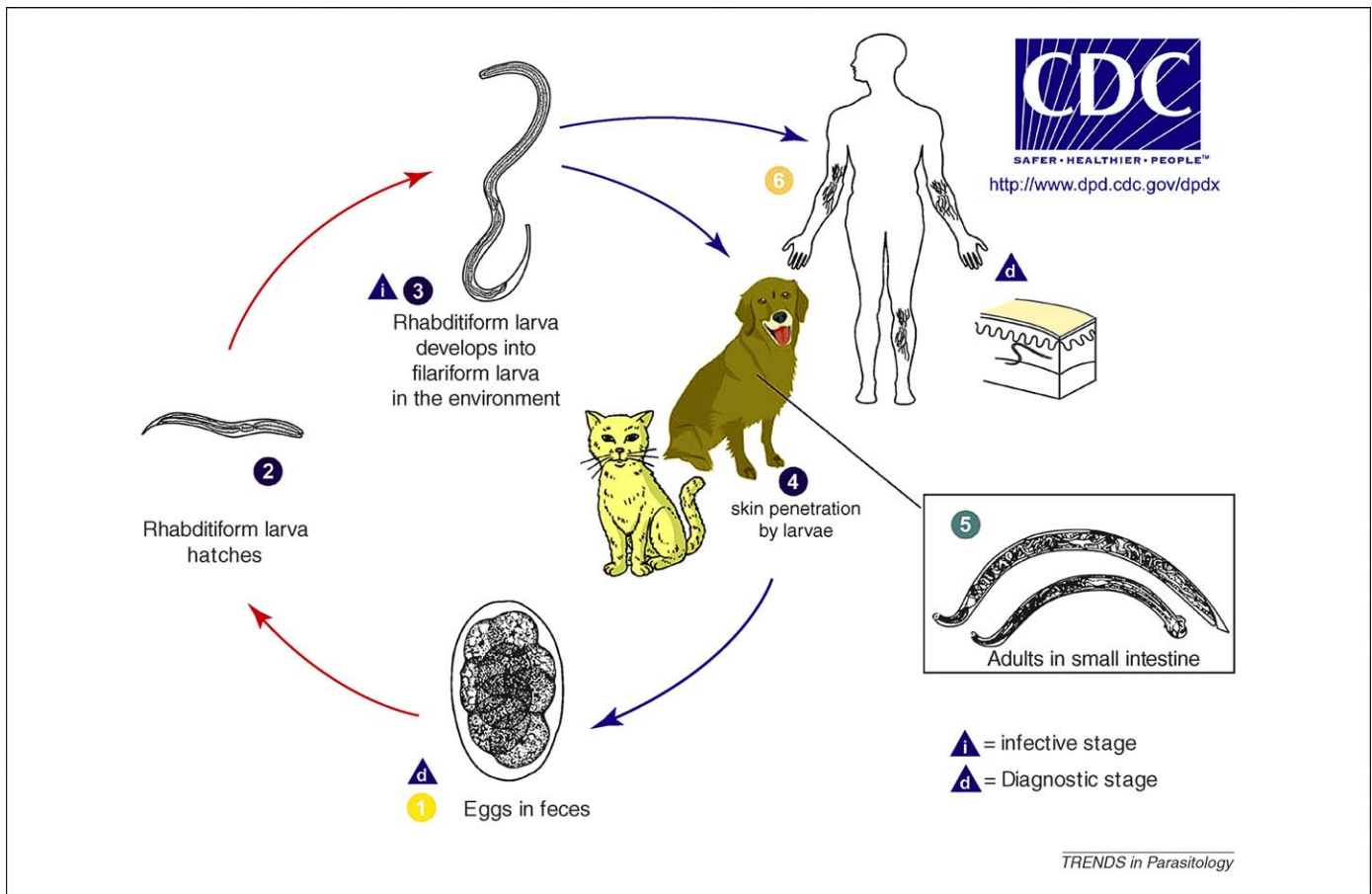


Figure 1. Cutaneous larval migrans (also known as ‘creeping eruption’) is a zoonotic infection with hookworm species that do not use humans as a definitive host, the most common being *A. braziliense* and *A. caninum*. The normal definitive hosts for these species are dogs and cats. The cycle in the definitive host is very similar to the cycle for the human species. Eggs are passed in the stool (1), and, under favorable conditions (moisture, warmth, shade), larvae hatch in 1–2 days. The released rhabditiform larvae grow in the feces and/or the soil (2), and after 5–10 days (and two molts) they become filariform (third-stage) larvae that are infective (3). These infective larvae can survive 3–4 weeks in favorable environmental conditions. On contact with the animal host (4), the larvae penetrate the skin and are carried through the blood vessels to the heart and then to the lungs. They penetrate into the pulmonary alveoli, ascend the bronchial tree to the pharynx, and are swallowed. The larvae reach the small intestine, where they reside and mature into adults. Adult worms live in the lumen of the small intestine, where they attach to the intestinal wall and suck blood. Some larvae become arrested in the tissues, and serve as source of infection for pups via transmammmary (and possibly transplacental) routes (5). Humans may also become infected when filariform larvae penetrate the skin (6). With most species, the larvae cannot mature further in the human host, and migrate aimlessly within the epidermis, sometimes as much as several centimeters a day. Some larvae may persist in deeper tissue after finishing their skin migration and a few species may enter the human intestine and develop further.

[19,10]. *A. braziliense* is found along the southeastern Atlantic coast of North America, the Gulf of Mexico and the Caribbean Sea, down to Uruguay in South America, in Africa (South Africa, Somalia, Democratic Republic of Congo, Sierra Leone), Australia and Asia (Malaysia and Indonesia, and based on humans cases, also in Thailand) [3,5,19,20]. In India, *A. braziliense*-like lesions are reported in humans, with adults being described from animals [21,22], but the necropsy literature is confusing because of the morphologic similarity of *A. ceylanicum* and *A. braziliense* [19].

Hookworm life cycle and pathogenicity

The life cycle of these nematodes begins with hookworm larvae hatching from eggs passed in the host’s feces, developing to the infective stage (filariform larva) in soil, and gaining access to the definitive host most commonly through skin penetration (Figures 1 and 2) [1]. Infective larvae can also establish infections if ingested [1]. In adult dogs, a large proportion of *A. caninum* infective larvae undergo somatic migration, and puppies are often infected by the transmammmary route [1,23]. Transmammmary transmission does not occur in cats or with the other species in

dogs. *Ancylostoma* spp. are capable of being sequestered in the tissues of vertebrate paratenic hosts (Box 1) where they persist without development (Figure 3); thus, infection via hunting is a possibility [1,23]. For several species (*A. caninum*, *A. tubaeforme*, *A. ceylanicum*), the adult worms cause blood loss and anemia. Peracute and acute disease from blood loss is particularly important and sometimes fatal in young puppies and kittens. Other hookworms such as *U. stenocephala* and *A. braziliense* cause negligible blood loss, but can sometimes induce disease [23].

CLM in humans

When humans, dogs and cats are infected percutaneously with larvae of their own host-adapted hookworms, the lesion at the penetration site varies from nil to an erythematous papular or vesicular rash (Box 1) with varying levels of pruritus (Box 1). This rash on people in human-hookworm endemic areas is called ‘ground itch’ [1]. In the early 1900 s, a lesion distinct from ground itch was found to occur within the USA (Figure 4). This lesion had a characteristic serpiginous track that could grow for weeks to months, was intensely pruritic and was ultimately self-limiting.

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