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Nemata

Ascaridoidea (Superfamily): Large Intestinal Nematodes

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Phylum Nemata

Superfamily Ascaridoidea

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Chapter 50

Ascaridoidea (Superfamily): Large Intestinal Nematodes

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Introduction

Ascaridomorpha includes a diverse group of parasites that live in the alimentary tract of their definitive hosts, and includes species that are of veterinary, medical, and economic importance. The life cycles of these parasites are quite variable, ranging from species with simple direct patterns involving the ingestion of eggs containing infective juveniles, to others that use invertebrates or vertebrates as intermediate or paratenic hosts. Species of Ascaridomorpha are familiar to biologists and laypersons alike as the large intestinal roundworms (although, here preferentially called nematodes) that infect pet dogs and cats; however, a much wider range of vertebrates serves as definitive hosts, including elasmobranchs, teleost fishes, amphibians, reptiles, birds, and mammals.

Ascaridomorpha occurring in mammals are typically large, stout nematodes with 3 large lips; however, there is substantial variation in body size and morphological characteristics among genera and species, even though different taxa are superficially similar in structure. Phylogenetic analysis of SSU rDNA sequences has shown that species allocated to this group are not monophyletic (Nadler et al., 2007), whereas certain families and subfamilies in this group are strongly supported as clades by molecular data (Nadler and Hudspeth, 2000). Of several families in this infraorder, this chapter will emphasize Ascarididae (subordinate within the superfamily Ascaridoidea), which includes many species of medical importance. Representative members of certain other superfamilies will be discussed briefly.

Superfamily Ascaridoidea

Family Ascarididae Baird, 1853

Ascaridids are among the largest nematodes, some species achieving a length of 45 cm or more. They are distinguished by having large rounded or trapezoidal **lips**, and cervical, lateral, and caudal **alae** may be present. **Spicules** are equal in length and rodlike or alate. This family contains the cosmopolitan human intestinal parasite, *Ascaris lumbricoides* Linnaeus 1758 (Crompton, 2001).

Ascaris lumbricoides

Because of their great size and high prevalence, these nematodes may well have been among the first parasites known to humans. The ancient Greeks and the Romans were familiar with them and they were mentioned in the Ebers Papyrus, the 16th century book of medical knowledge from Egypt (Hallman-Mikołajczak, 2004). It is probable that *Ascaris lumbricoides* was either a parasite of pigs that adapted to humans when swine were domesticated and began to live in close association with humans—or perhaps it was a human parasite that humans gave to pigs. Populations of *Ascaris* spp. exist in both humans and pigs, but the extent of genetic isolation between these putative species (*A. lumbricoides* and *A. suum*, respectively) has been the subject of much recent research (Leles et al., 2012).

The two forms are so close morphologically that they are now considered to be the same species. Slight differences in the tiny denticles (small "teeth") on the inner edge of the lips were described between these species (Sprent, 1952), but were later found to reflect age-related wear rather than serve as reliable taxonomic characters (Madden and Tromba, 1976). None of the genetic markers examined to date consistently discriminate between pig- and human-source *Ascaris* spp. Experimental cross-transmission studies show that both putative species can reach maturity in humans and pigs. Genetic studies based on microsatellite markers reveal that there is a low level of hybridization between these species that occurs during co-infection. The distribution of maternally in-

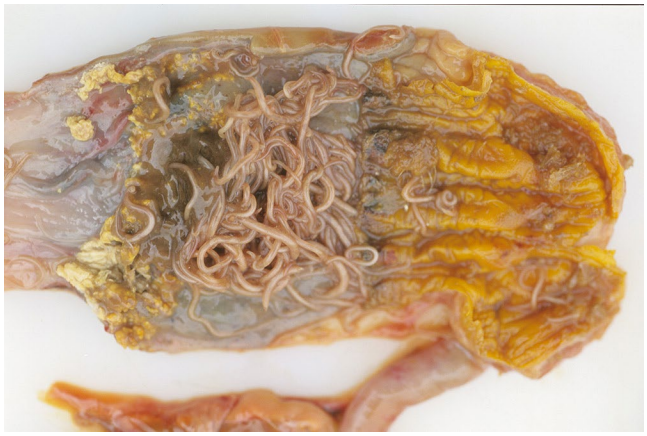

Figure 1. *Contracaecum* sp. (Rhabditida: Anisakidae) in proventriculus and gizzard of a guillemot (*Cepphus* sp.) collected from Scotland, United Kingdom between 1994 and 2013. Source: T. Pennycott, available at Edinburgh DataShare, 2013. License: CC BY 4.0.

herited mitochondrial DNA (mtDNA) haplotypes also reveals patterns that are consistent with low levels of cross-infection, but this interpretation is complicated by the possible retention of ancestral mtDNA polymorphisms between these very recently diverged taxa (Anderson and Jaenike, 1997; Criscione et al., 2007). Leles and colleagues (2012) showed that there are essentially no differences between these two species,so they should be considered to be one species: *A. lumbricoides* Linnaeus 1758.

Morphology

In addition to their great size (Figure 1), *Ascaris lumbricoides* is characterized by having 3 prominent lips each with a dentigerous ridge and no alae. Lateral hypodermal cords are visible with the unaided eye.

Males are 15–31 cm-long and 2–4 mm in diameter at the greatest width. The posterior end is curved ventrally and the tail tip is blunt. Spicules are simple, nearly equal, and measure 2.0–3.5 mm-long. No gubernaculum is present.

Females are 20–49 cm-long and 3–6 mm in diameter. The vulva is about one-third the body length from the anterior end. The ovaries are extensive and uteri may contain up to 27 million eggs with 200,000 being laid per day. When transferred to parasite-naive pigs, female *Ascaris* cease producing eggs after 2–3 weeks (Jungersen et al., 1997). They resume egg production when male worms are transferred into the pig with the females.

Fertilized eggs (Figure 2) are oval to round, 45–75 µm-long by 35–50 µm-wide, with a thick, lumpy outer shell (comprising a mammillated, uterine, or proteinaceous layer) that is contributed by the uterine wall. When eggs are passed in the host's feces, the mammillated layer is bile-stained a

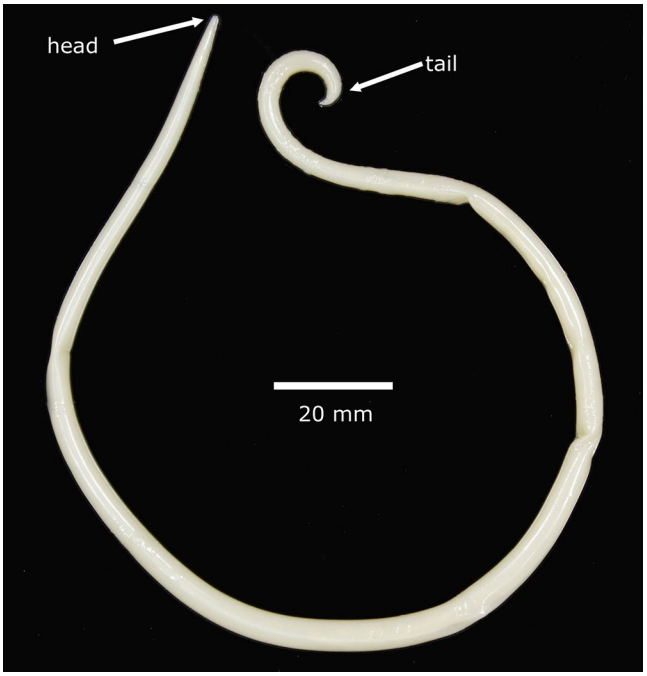

Figure 2. *Ascaris lumbricoides* (Nemata: Ascaridida: Ascarididae), adult male from a human host. Note the tapered head end and the tail that is reflexed (curved) ventrad (meaning, in the ventral direction). These nematodes commonly come out of the anus or the nose of the human host at inopportune times. Source: S. L. Gardner, HWML. License: CC BY.

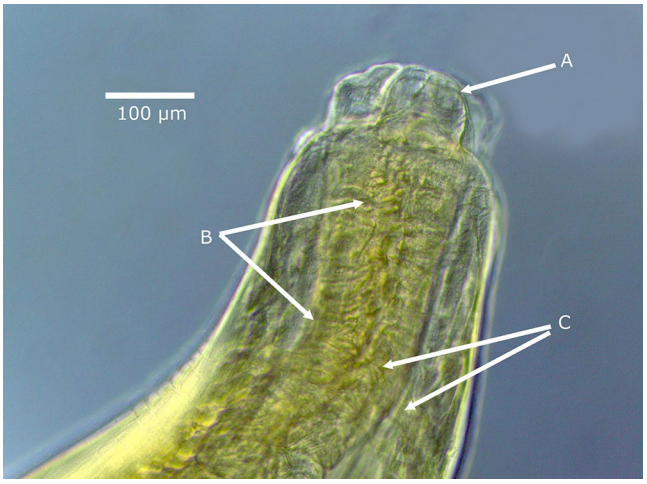

Figure 3. Close up view of the anterior end of an ascarid (Nemata: Ascaridida: Ascarididae) (*Toxascaris procyonis*) showing well, 1 of the 3 lips on the anterior end (A), the anterior part of the esophagus (B), and the nerve ring is seen in arrows pointing from (C). Source: S. L. Gardner, HWML. License: CC BY.

golden brown. The embryos within are usually uncleaved when eggs are passed. An uninseminated female, or one in early stages of oviposition, commonly deposits unfertilized eggs (Figure 3) that are longer and narrower than fertilized ones, measuring 88–94 µm-long by 44 µm-wide. Only the

proteinaceous layer can be distinguished in unfertilized eggs because the vitelline, chitinous, and lipid layers of the eggshell are formed only after sperm penetration of the oocyte.

Biology

A period of 9–13 days is the minimal time required for embryos to develop into active first-stage juveniles (J_1s). Embryos are extremely resistant to low temperature, desiccation, and strong chemicals; however, sunlight and high temperatures are lethal in a relatively short time (for example, 2 days at 47 °C). Human ascariasis does not occur where average land temperatures exceed 37–40 °C. Clearly, global warming may change the distribution of ascariasis and other parasitic diseases (Weaver et al., 2010). Juveniles must molt to the third stage to be infective (Geenen et al., 1999) .

Infection occurs when host animals swallow unhatched juveniles with contaminated food and water. They hatch in the duodenum through an indistinct operculum (Figure 4), where the juveniles penetrate the mucosa and submucosa and enter lymphatic tissue or venules (Figure 5). After passing through the right heart of a pig, they enter the pulmonary circulation and break out of capillaries into air spaces. Many worms get lost during this migration and accumulate in almost every organ of the body, causing acute tissue reactions. In contrast to this classical pattern, Murrell and colleagues (1997) report that juvenile *Ascaris* do not penetrate the mucosa immediately after hatching but rather rapidly transit the small intestine and penetrate the mucosa of the cecum and upper colon. Juveniles then accumulate in the liver for up to 48 hours. Incidentally, this research on *Ascaris* in pigs strongly suggests that the actual migration pattern of these nematodes in humans involves the liver, rather than the pattern observed in experiments with abnormal hosts such as guinea pigs and rats (Crompton, 2001).

While migrating through tissues, juveniles molt to the fourth stage (J_4), and during a period of about 10 days grow to a length of 1.4–1.8 mm. They then move up the respiratory tree of the host to the pharynx, where they are swallowed. Many juveniles make this last step of their migration before molting to the fourth stage, but these J_3s cannot survive gastric juices in the stomach. Fourth-stage juveniles (J_4) are resistant to such a hostile environment and readily pass through the stomach to the small intestine, where they molt again and mature. Within 60–65 days of being swallowed, they begin producing eggs. Genetic markers show that *Ascaris* females may be inseminated by more than 1 male in producing offspring (Zhou et al., 2011).

It seems curious that these worms embark on such a hazardous migration only to end up where they began. One hypothesis to account for it suggests that migration simulates an intermediate host, which normally would be required during juvenile development for species with indirect life cycles. Indeed, molecular phylogenetic hypotheses confirm that indirect life cycles are ancestral for ascaridoids, and that the direct (1-host) life cycle of *Ascaris* sp. and *Parascaris* sp. is the derived condition (Nadler and Hudspeth, 2000). After comparing many nematode taxa having tissue migration with closely related taxa that remain in the gut, Read and Skorping (1995) conclude that tissue migration enables faster growth and larger size, thus increasing reproductive capacity.

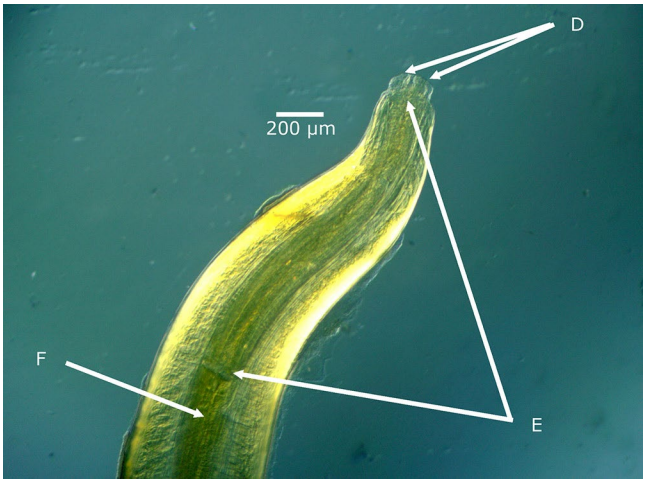

Figure 4. Anterior end of *Toxascaris procyonis* (Nemata: Ascaridida: Ascarididae) showing the three lips on the anterior end (D), the esophagus (E), and the proximal end of the intestine where it attaches to the esophagus (C). Source: S. L. Gardner, HWML. License: CC BY.

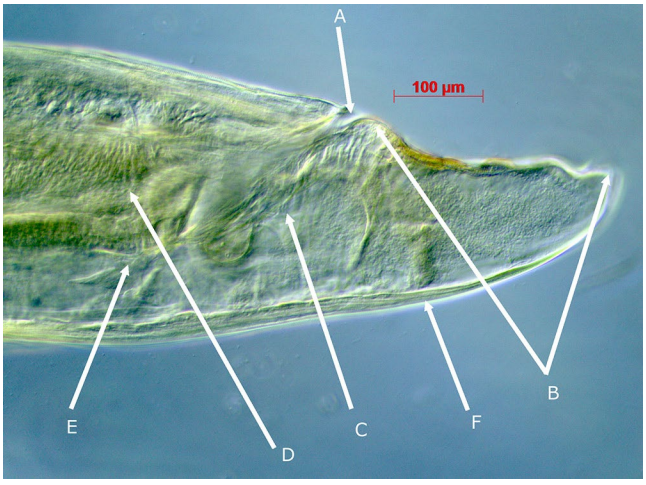

Figure 5. Posterior end of a female *Toxascaris procyonis*. Anus (A), tail (B), muscles that control the rectum and anus (C and E), posterior end of the intestine (D), cuticle (F). Source: S. L. Gardner, HWML. License: CC BY.

Epidemiology

The dynamics of *Ascaris* spp. infection are similar to those of *Trichuris trichiura*. Indiscriminate defecation by hosts, particularly near human or other animal habitations, seeds the soil with eggs that may remain viable for years. Resistance of *Ascaris* spp. eggs to chemicals is in fact legendary. They can embryonate successfully in 2% formalin, in potassium dichromate, and in 50% solutions of hydrochloric, nitric, acetic, and sulfuric acid, among other similar inhospitable substances (Schwartz, 1960). Eggs can survive in anaerobic sewage lagoon sludge for more than 10 years (Rosypal et al., 2007). This extraordinary chemical resistance is a result of the lipid layer of their eggshell, which contains ascarosides.

Longevity of *Ascaris* spp. eggs also contributes to success of the parasite. Brudastov and colleagues (1971) infected themselves with eggs kept for 10 years in soil at Samarkand, Uzbek SSR, Soviet Union. Of these eggs, 30–53% were still infective after all that time. Because of such longevity, it is impossible to prevent reinfection when yards have been liberally seeded with eggs, even when proper sanitation habits are initiated later.

Contamination, then, is the typical means of infection. Children are the most likely to become infected by eating soil or placing fingers and toys in their mouths. Chickens can serve as paratenic hosts (Permin et al., 2000). In regions in which night soil (that is, human excrement) is used as fertilizer, uncooked vegetables become important mechanical vectors of *Ascaris lumbricoides* eggs (Weidong et al., 1998). Experimental support for this hypothesis came from Mueller (1953), who seeded a strawberry plot with eggs. He and volunteers ate unwashed strawberries from this plot every year for 6 years and became infected each year. Cockroaches can carry and disseminate *A. lumbricoides* eggs (Burgess, 1984). Similarly, in some areas, dogs acquire *A. lumbricoides* eggs by coprophagy and spread viable eggs in their feces (Traub et al., 2002). Even windborne dust can carry eggs when conditions permit. Bogojawlenski and Demidowa (1928) found *A. lumbricoides* eggs in the nasal mucus of 3.2% of school children examined in the Soviet Union. Dold and Themme (1949) found *A. lumbricoides* eggs on 20 German banknotes in actual circulation.

Worldwide, 1.27 billion people, about one-quarter of the world population, are infected at any given time (Chan, 1997). Most infections occur in east Asia, China, sub-Saharan Africa, South America, and Central America (WHO, 2006). Morbidity as assessed by disability-adjusted life years (DALYs) totals ~ 10.5 million (Chan, 1997). Severe morbidity occurs in > 100 million cases each year (Chan, 1997); intestinal obstruction, mainly in children, occurs in roughly 1 out of 1,000 infections.

Worms are commonly aggregated in local populations, with a small number of people harboring infections of high intensity. These individuals seem to be predisposed to infection; when they are cured, they tend to become reinfected with large numbers of worms. The reasons for predisposition may be social, behavioral, environmental, and genetic, either alone or in combination. Members of a household tend to have similar infection intensities (household clustering), and individual household risk factors account for much of the variation in household worm counts (Walker et al., 2011).

Pathogenesis

Little damage is caused by penetration of intestinal mucosa by newly hatched worms. Juveniles that become lost and wander and die in anomalous locations, such as the host's spleen, liver, lymph nodes, or brain, often elicit an inflammatory response. Symptoms may be vague and difficult to diagnose and may be confused with those of other diseases. Transplacental migration into a developing fetus is also known. Allergy and immunopathology of ascariasis was reviewed by Coles (1985). The polyprotein allergens (lipid binding proteins) of *Ascaris* spp. are known to elicit IgE antibody responses and appear to be a contributing factor in *Ascaris* pneumonitis (sometimes referred to as Loeffler's pneumonia).

When juveniles break out of lung capillaries into the respiratory system, they cause a small hemorrhage at each site. Heavy infections will cause small pools of blood to accumulate which then initiate edema (swelling) with resultant clogging of air spaces. Accumulations of eosinophils and dead epithelium add to the congestion, which is known as *Ascaris* pneumonitis. Large areas of lung can become diseased, and, if bacterial infections become superimposed, death can result. Once, a student vented his ire on his roommates by seeding their breakfast with embryonated *Ascaris suum* eggs. One roommate almost died before his malady was diagnosed (Newsday, 1970; Phills et al., 1972; Jack Morrison, personal communication, 2023).

Pathogenesis from "normal worm activities"

The main food of *Ascaris* spp. is liquid contents of the small intestinal lumen. In moderate and heavy infections, the resulting theft of nourishment from the host can cause malnutrition, underdevelopment, and cognitive impairment in small children (Crompton, 2001; Levav et al., 1995). Abdominal pains and sensitization phenomena—including rashes, eye pain, asthma, insomnia, and restlessness—often result as allergic responses to metabolites produced by the worms.

A massive infection can cause fatal intestinal blockage (Baird et al., 1986) (Figure 6). Why in one case do large numbers of worms cause no apparent problem, whereas in

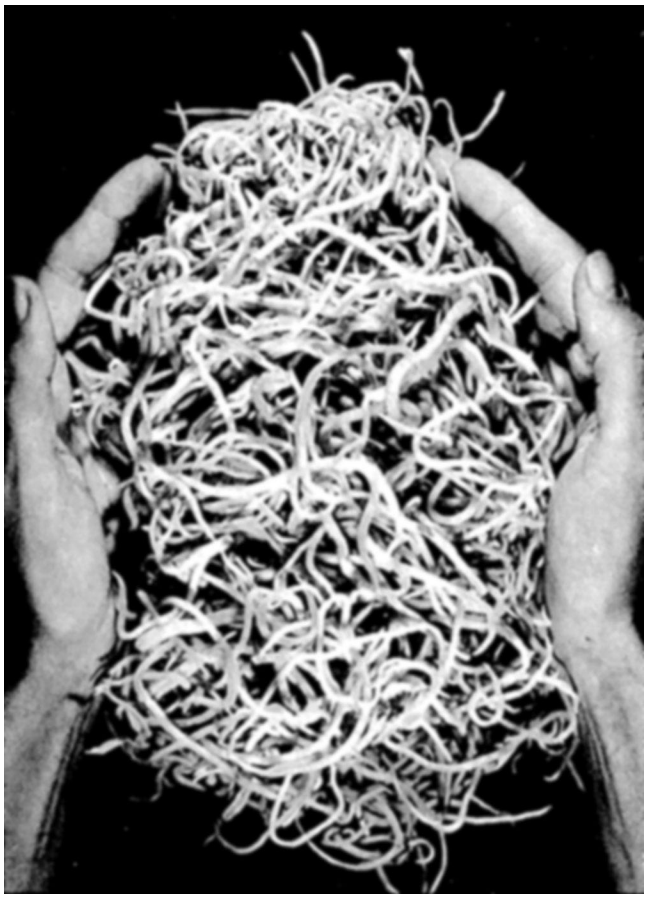

Figure 6. Worms recovered from necrotic small intestine, stomach, esophagus, intrahepatic and extrahepatic bile ducts, and gallbladder of a 2-year-old South African girl. Source: Baird et al., 1986. United States public domain.

another worms knot together to form a mass that completely blocks the intestine? The drug tetrachloroethylene, which was formerly used to treat hookworm, can cause *Ascaris* to knot up, but other factors remain unknown. Penetration of the intestine or appendix is not uncommon. The resulting peritonitis is usually quickly fatal. According to Louw (1966), at one time, 35.5% of all deaths in acute abdominal emergencies of children in Cape Town, South Africa were caused by *Ascaris lumbricoides*.

Wandering worms

Overcrowding in high-intensity infections may lead to wandering of adult worms. Downstream wandering may lead to the host's appendix, which can become inflamed or penetrated, or to the anus, with an attendant surprise found in the toilet of an unsuspecting host. Upstream wandering may lead to the pancreatic and bile ducts, possibly occluding them with subsequent grave results. Multiple liver abscesses have resulted from such invasion (Rossi and Bisson, 1983). Worms reaching the stomach are aggravated by the acidity and writhe around, often causing nausea. The psychological trauma induced in someone who vomits up a 45-cm ascarid is difficult to quantify. Aside from any psychological effects, aspiration of a vomited worm can result in death (Darby and Westphal, 1972). Worms that reach the esophagus, usually while the host is asleep, may crawl into the trachea, causing suffocation or lung damage; they may crawl into eustachian tubes and middle ears, causing extensive damage; or they may simply exit through the nose or mouth.

Diagnosis and treatment

Accurate diagnosis of migrating juveniles is impossible at this time. Demonstration of juveniles in sputum is definitive, provided a technician can identify them. Most diagnoses are made by identifying the characteristic, mammillated eggs in feces or by an appearance of the worm itself. Adults can also be diagnosed by ultrasound and other noninvasive radiographic methods (Goyal et al., 2010). So many eggs are laid each day by one worm that direct fecal smears are usually sufficient to demonstrate eggs. *Ascaris lumbricoides* should be suspected when any of the previously listed pathogenic conditions are noted. Most light infections are asymptomatic, and such infections are typically diagnosed only following spontaneous elimination of adults from the anus.

Benzimidazole-based drugs (for example, mebendazole or albendazole) are often effective in a single dose. Benzimidazoles bind to tubulin in the worm's intestinal cells and body wall muscles (Bughio et al., 1994). Emodepside, a novel anthelminthic so far licensed in combination with praziquantel for use in cats, causes relaxation of body-wall muscle of *Ascaris* and inhibits contraction (Willson et al., 2003). Nitazoxanide and ivermectin are also effective (Doumbo et al., 1997; Marti et al., 1996). In regions endemic for many different soil-transmitted nematodes, certain drugs may be preferable to others due to their broader spectrum of efficacy in cases of multiple-species infections.

Toxocara canis

This species is a cosmopolitan intestinal parasite of domestic dogs and wild canids and it is the chief cause of visceral migrans (VM) in humans, discussed later.

As a result of prenatal infections, even puppies in well-cared-for kennels are typically infected at birth and require anthelminthic treatment. It is not uncommon for 100% of puppies to be infected. The owner of a brand new puppy is likely to be startled by the pet's vomiting up several large, active worms. Puppies tend to have the highest infection prevalence. The infective dose of eggs has a large impact on the success of infection in adult dogs where protective immu-

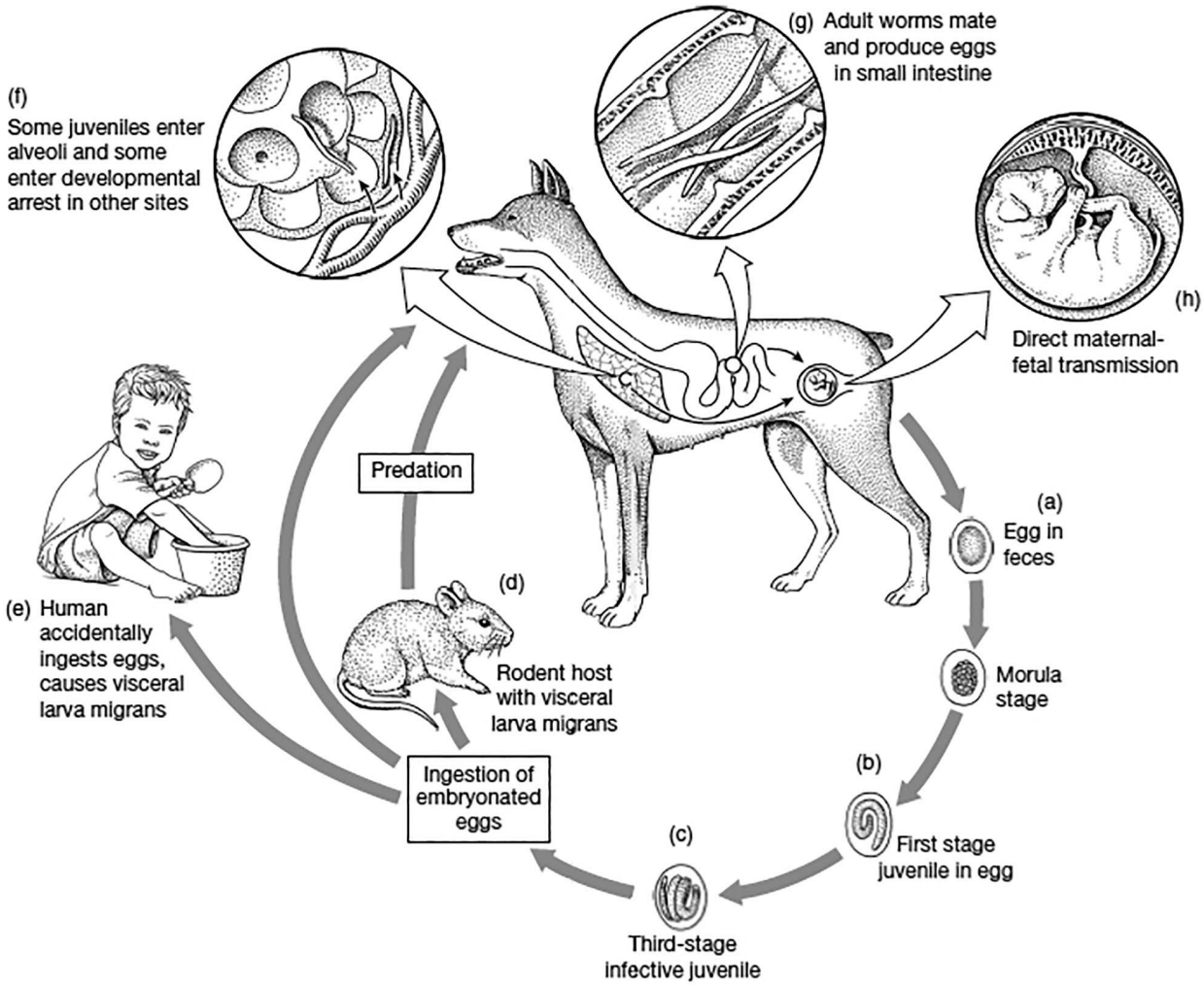

Figure 7. Life cycle of *Toxocara canis*. (a) Shelled embryo passed in feces. (b) J_1 in egg. (c) Infective J_3 in egg. (d) Eggs hatch in rodent host, and juveniles enter developmental arrest in viscera. (e) Eggs hatch in human and juveniles cause visceral larva migrans. (f) After penetration of intestinal wall, some juveniles break out into alveoli, ascend trachea, and finally mature in small intestine. Other juveniles (especially in mature dogs) enter developmental arrest in other sites. (g) Adult worms mate and produce eggs in small intestine. (h) Direct maternal-fetal transmission. Source: W. Ober and C. Garrison in Roberts et al., 2014. License: CC BY 4.0.

nity may have a larger role in the fate of juveniles; a smaller number of eggs administered is more likely to lead to patent infection (Dubey, 1978).

Adult *Toxocara canis* resemble *Ascaris* spp., only are much smaller. Three lips are present. Unlike *Ascaris* spp., however, *T. canis* has cervical alae in both sexes. Males are 4–6 cm-long, and females are 6.5 cm- to more than 15.0 cm-long. The brownish-colored eggs are almost spherical and roughly 75 µm × 85 µm, with surface pits, and are unembryonated when laid.

Biology

Adult worms live in the small intestine of their host, producing prodigious numbers of eggs, which are passed with the host's feces (Figure 7). Development of J_3 within eggs takes 9 days under optimal conditions.

The fate of ingested J_3s depends on host age and immunity. If a puppy is young and has had no prior infection, worms hatch and migrate through the portal system and lungs and back to the intestine, as in *Ascaris lumbricoides*. If the host is an older dog, J_3 fate is variable. Most J_3s will not complete the tracheal migration to become adults, but instead will enter the capillaries and undergo a somatic migration, eventually entering developmental arrest, with most individuals residing in the skeletal muscles.

If a dog harboring encysted, arrested juveniles becomes pregnant, those juveniles are reactivated late in the pregnancy and reenter the circulatory system, where they are carried to

the placenta. There they penetrate through to the fetal bloodstream and migrate to the liver where they reside until birth. Juveniles begin migration to the lungs within 30 minutes following birth, and then undergo a tracheal migration. Thus, a puppy can be born with an infection of *Toxocara canis*, even though its mother has shown no sign of patent infection (meaning, not producing eggs). The puppy may also become infected by the transmammary route (that is, in the mother's milk), but this is probably less common than the transplacental route (Gillespie, 1988). If a lactating dog ingests infective juveniles, they can complete migration to the intestine and produce a patent infection.

Another option in the life cycle of *Toxocara canis* is offered when a rodent or other mammal ingests embryonated eggs. In this host the juvenile begins to migrate but then becomes dormant with arrested development. If the rodent is eaten by a dog, the worms promptly migrate through the lungs to the intestine or into tissues to continue their wait, depending on the dog's age. Thus, rodents are paratenic hosts. Although this adaptability favors survival of the parasite, it bodes ill for paratenic hosts, which may undergo behavioral changes as a result of infection that increases their risk of predation (Hamilton et al., 2006).

Visceral migrans

When nematode juveniles gain access to the wrong host species they do not complete the normal migration but undergo developmental arrest and may begin an extended, random wandering through various organs and soft tissues of the body. The resulting disease is known as visceral migrans (VM), in contrast to cutaneous migrans (CM), which occurs only in skin. Visceral migrans can be caused by a variety of spirurid, strongylid, and other nematodes in addition to ascaridoids. However, *Toxocara canis* is the most common species causing VM in humans.

Epidemiology

Many years ago, it was assumed that dog and cat ascaridoids could not infect humans or were not dangerous to them. In the early 1950s it was discovered that this assumption is not true, particularly for nematodes such as *Toxocara canis*. At any one time, about 2.2% of adult dogs and 98% of puppies in the United States are infected with *T. canis*; with the population of pet dogs in the United States, this means that more than 1 million dogs are currently shedding *T. canis* eggs. Thus, risk of human exposure to infective eggs is very high. However, most human infections are covert, and even overt symptoms may go unrecognized and unreported.

Development of a specific immunodiagnostic test, an ELISA using secretory-excretory antigens collected from cultured juveniles, has been a boon to epidemiological studies of VM (Schantz, 1989). This test can distinguish between *Ascaris lumbricoides* and *Toxocara canis*, but does not distinguish *T. canis* from *T. cati* (see Lynch et al., 1993). In the United States, an extensive survey showed an overall seroprevalence of 13.9% (in people > 6 years-old), but was higher for non-Hispanic blacks (21.2%). Other risk factors included low socioeconomic status, living in rural areas, and geographic region (Hotez and Wilkins, 2009; Overgaauw, 1997). A seroprevalence of 34% has been found among Irish school children, and 31% of the children from Croatia with eosinophilia (Holland et al., 1995; Sviben et al., 2009). Seroprevalence among children in developing tropical countries has been much higher, from 50–80%. Visceral migrans is predicted to have a substantial impact on individuals living in poverty worldwide.

Dogs and cats defecating on the ground seed an area with eggs, which embryonate and become infective to any mammal or bird ingesting them. Small mammals are important paratenic hosts; infected mice undergo behavioral changes that increase their risk of predation, which increases the chance to complete the life cycle (Cox and Holland, 1998; 2001; Dold and Themme, 1949; Hamilton et al., 2006). Considering that the crawling-walking age of small children is a time when virtually every available object goes into the mouth for a taste, it is not surprising that the disease is common in children between 1 and 3 years old. In an urban setting, dog owners look upon the city park as the perfect place to walk a dog, while parents bring young children there to play on egg-seeded grass. Thus, of note is the high risk to children by exposure to the environment of puppies (Schantz, 1989). Finally, a factor to contemplate in light of the foregoing is the durability and longevity of *Toxocara canis* eggs, which are comparable to those of *Ascaris* (discussed above).

Pathogenesis

Juvenile *Toxocara canis* provoke a delayed-type hypersensitivity reaction in paratenic hosts and the degree and timing of the reaction depend on the infecting dose (Schantz, 1989). In experimental hosts, most juveniles eventually end up in the brain; it is unclear whether this is because juveniles have a predilection for the brain or because they are destroyed in other sites but remain in the brain. In sites other than the brain, juveniles may be encapsulated by a granulomatous reaction (Figure 8). The most common site of juvenile residence is the liver (as shown in Figure 8), but any organ will do.

Characteristic symptoms of VM include fever, pulmonary symptoms, hepatomegaly, and eosinophilia. The extent of damage usually is related to numbers of juveniles present

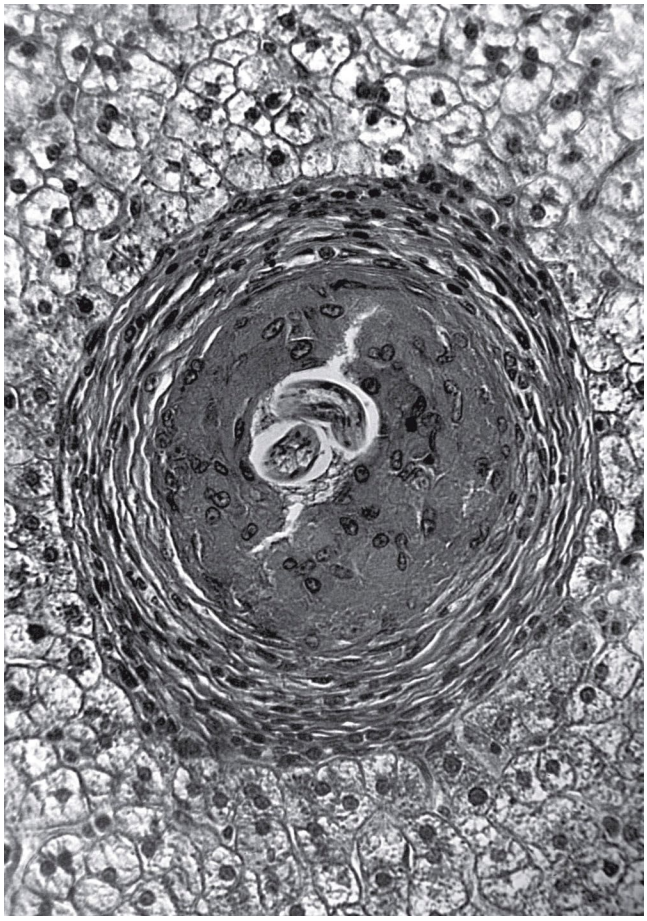

Figure 8. *Toxocara canis* juvenile section in liver of a monkey at 9 months' infection. The juvenile rests in a matrix of epithelioid cells surrounded by a fibrous capsule lacking intense inflammatory reaction. Source: Beaver, 1969 in Roberts et al., 2014. License: CC BY-NC-SA 4.0.

and their ultimate homestead in the host's body. Various neurological symptoms have been reported and deaths have occurred when juveniles were especially abundant in the brain. Presence of juveniles in the spinal cord can lead to inflammatory lesions and sensory or motor dysfunction; treatment with albendazole can yield neurologic improvement in such patients (Jabbour et al., 2011). Rarely, juveniles of *Toxocara canis* cause eosinophilic meningoencephalitis (Vidal et al., 2003). While dire consequences such as these can result from infection, most cases result in rather minor, transient symptoms such as abdominal pain, headache, and cough. This subacute condition is known as covert or common toxocariasis, which is commonly either undiagnosed or misdiagnosed.

Juveniles in a host's eye may cause chronic inflammation of the inner chambers or retina or provoke dangerous granulomas of the retina. These reactions can lead to blindness in the affected eye. The frequency of ocular toxocariasis in the United States is difficult to assess. Ocular toxocariasis was diagnosed in 1% of patients examined for vision loss in Alabama eye clinics in 1987 (Maetz et al., 1987). Generally, ocular damage is the result of invasion of only a single juvenile (Schantz, 1989). It may be that, because heavy infections stimulate a much stronger immune response with low survival rates, juveniles survive longer in light infections, giving them more time to wander into an eye. Other lesions destroy lung, liver, kidney, muscle, and nervous tissues.

Diagnosis and treatment

An ELISA using secretory-excretory antigens has facilitated clinical diagnosis enormously. This test is more sensitive for detecting covert toxocariasis and VM than ocular disease. A high eosinophilia is suggestive of infection with *Toxocara canis*, especially if the possibility of other parasitic infections can be eliminated.

Usually, only patients with severe symptoms are treated (Gillespie, 1988). Diethylcarbamzine and mebendazole appear to be effective treatments (Magnaval, 1995; Smith et al., 2009). An excellent summary of current therapies and preventative measures is given by Magnaval and colleagues (2022). Control consists of periodic deworming of household pets, especially young animals, and proper disposal of the animals' feces. Thus, for toxocariasis, veterinary medicine practices are important to mitigate disease transmission to humans. Some anthelminthics have been reported to be effective against all stages in dogs, including juveniles in arrested development (Altreuther et al., 2009), which presents new options for reducing transmission among dogs. Dogs and cats should be restrained, if possible, from eating available transport hosts. Sandpits in public parks can be protected from contamination by covering them with vinyl sheets when not in use (Uga and Kataoka, 1995; Uga et al., 1996).

Other *Toxocara* Species

Toxocara cati is widely prevalent among domestic cats and other felids (Figure 9). The cervical alae (Figure 10) of *T. cati* are shorter and broader than those of *T. canis*, and the eggs of the two species are slightly different in size. Life cycles are similar, including the use of paratenic hosts, but kittens are infected with *T. cati* only by the transmammary route if mothers are infected during late gestation (Gillespie, 1988). *Toxocara cati* may be an important cause of visceral migrans (VM), but it is difficult to determine the relative importance of each species because the current ELISA test for human infection does not distinguish between *T. canis* and *T. cati*. Adult *T. cati* have occasionally been reported from humans (Eberhard and Alfano, 1998).

Toxocara vitulorum is the only ascaridid that occurs in cattle. Its life cycle is similar to that of *T. cati*, with the young

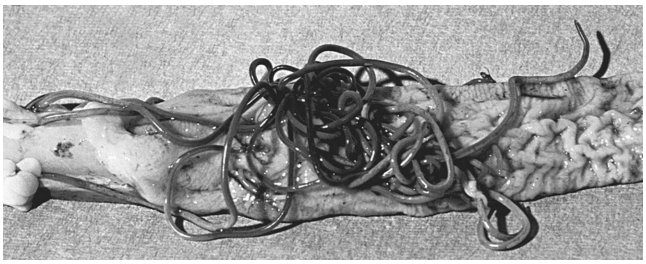

Figure 9. Intestine of a domestic cat, opened to show numerous *Toxocara cati*. Source: R. E. Kuntz in Roberts et al., 2014. License: CC BY-NC-SA 4.0.

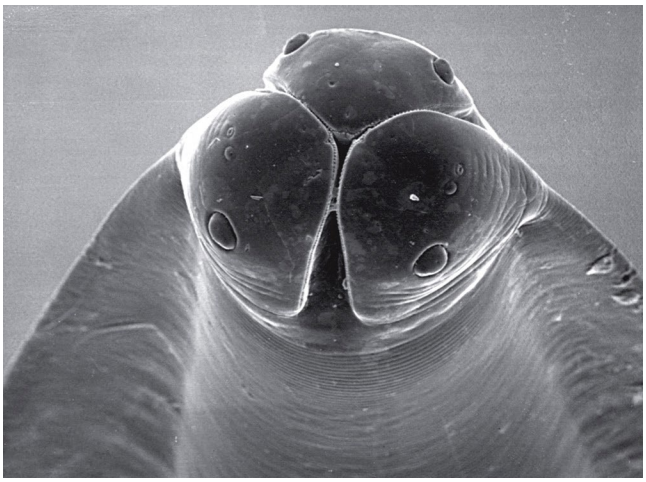

Figure 10. Scanning electron micrograph of *Toxocara cati* en face view. Note the 3 lips with sensory papillae and broad cervical alae on each side. Source: J. Ubelaker in Roberts et al., 2014. License: CC BY 4.0.

being infected by their mother's milk (Roberts, 1990). Adult hosts are refractory to intestinal infection. Young calves may succumb to verminous pneumonia during migratory stages of the parasites. Diarrhea or colic results in economic losses to the animal's human owner.

Parascaris equorum

This large nematode and its congener *Parascaris univalens* are the only ascaridoids found in horses and other equids. *Parascaris equorum* is a cosmopolitan species. It is very similar in gross appearance to *A. lumbricoides* but is easily differentiated by its huge lips, which give it the appearance of having a large, round head. In addition, *Parascaris* spp. individuals are white, whereas fresh *Ascaris* spp. specimens have a reddish color due to their characteristic muscle hemoglobin.

The life cycle is similar to that of *Ascaris lumbricoides*, involving a lung migration. Foals are often infected soon after birth; however, there is no evidence of prenatal or transmammary transmission. Resulting pathogenesis is especially important in young animals, with pneumonia, bronchial hemorrhage, colic, and intestinal disturbances resulting in unthriftiness and morbidity. Intestinal perforation or obstruction is common. Prevalence and intensity of infection decrease with horse age, presumably due to acquired immunity. In several regions *Parascaris equorum* shows strong resistance to the drug ivermectin, although certain other compounds remain viable alternatives for treatment (Lyons et al., 2008). The development and spread of drug resistance in nematodes is of concern because relatively few new anthelminthic drugs are being developed.

Baylisascaris procyonis

This is a very common intestinal parasite of raccoons in North America. Other related species in this genus occur in bears, skunks, badgers, and other carnivores. When embryonated eggs are ingested by a young raccoon, they will hatch in the small intestine, burrow into the intestinal wall, and mature. Older raccoons are typically infected when they eat infected rodent, lagomorph, or bird paratenic hosts that have juveniles encysted in their tissues. More than 90 species of birds and mammals have been reported to be infected (Kazacos, 1986). In these animals, parasite juveniles wander, often invading the central nervous system, resulting in neurological damage and debilitation, or death. This makes infected hosts vulnerable to predation or scavenging by raccoons. Unfortunately, juveniles affect humans in the same way. Neural (juvenile) migrans (NM) caused by *Baylisascaris procyonis* occurs almost exclusively in children younger than 2 years old; risk factors for egg ingestion include geophagia and pica. A substantial fraction of NM cases are fatal. Ocular migrans may occur in association with NM, or independently when it occurs in adult humans. Serological diagnosis of infection in humans has been difficult, but a new ELISA method based on a recombinant DNA antigen appears promising (Dangoudoubiyam et al., 2011).

An important epidemiological factor is close contact between humans and raccoons or raccoon feces. Scavenging raccoons may prowl and feed on pet dog or cat food near human dwellings and outbuildings. Their preferred communal defecation sites are dangerous sources of infection to humans and other animals (Page et al., 1999). Infected raccoons shed approximately 25,000 eggs per gram of feces, and communal raccoon latrines almost always contain infective eggs. Eggs can remain infective for years under ideal conditions, so once an area is contaminated it is nearly impossible to decontaminate using chemical treatments. Methods using heat such as steam generators or a propane flame gun can be effective for small areas (Kazacos, 2001) because juveniles within eggs are killed at 62 °C (Kazacos, 1982; Shafir et al., 2011). Pet kinka-

jous (another procyonid) sold in the United States have been reported to be infected with *Baylisascaris procyonis* (see Kazacos, 2001). Domestic dogs can also serve as hosts of adult *B. procyonis*, and if such infections were to become prevalent, this could alter factors influencing human infection.

Other species of *Baylisascaris* may have similar pathogenicity, but most hosts are not as likely to come in close contact with humans. Skunks infected with *B. columnaris* are potential hazards, however.

Toxascaris leonina

Toxascaris leonina is a cosmopolitan parasite of dogs and cats and related canids and felids. It is similar in appearance to *Toxocara* spp., being recognized in the following ways: 1) The body tends to flex dorsally in *T. leonina* and ventrally in *Toxocara* spp.; 2) alae of *T. cati* are short and wide, whereas they are long and narrow in *T. canis* and *T. leonina* (Figure 11); 3) the egg surface is smooth in *T. leonina* but pitted in *Toxocara* spp.; and 4) the tail of male *Toxocara* spp. constricts abruptly behind the cloaca, whereas it gradually tapers to the tail tip in *T. leonina*.

The life cycle of *Toxascaris leonina* is simple. Ingested eggs hatch in the host's small intestine, where juveniles penetrate the mucosa. After a period of growth, they molt and return directly to the intestinal lumen, where they mature. Alternatively, juveniles in intermediate hosts such as rodents can infect definitive hosts following predation.

Like for *Toxocara* spp., the pathogenicity of *T. leonina* for the definitive host depends on infection intensity, and in severe cases can involve intestinal obstruction or rupture of the intestine. Visceral migrans involving *T. leonina* has been implicated as a possible cause of human eosinophilia on St. Lawrence Island (Bering Sea), where this nematode commonly infects Arctic foxes, working dogs, and voles (rodent genus *Microtus*) as paratenic hosts (Rausch and Fay, 2011).

Figure 11. Anterior end of *Toxascaris leonina*, an intestinal parasite of dogs, cats, and other canids and felids. Note the narrow cervical alae (arrow) as compared with the broad alae of *Toxocara cati*. Source: J. Georgi in Roberts et al., 2014. License: CC BY-NC-SA 4.0.

***Lagochilascaris* species**

Relatively little is known about the natural definitive host ranges of the 5 described species in *Lagochilascaris*, a genus mainly reported from North America, Central America, and South America. The genus name is derived from the prominent cleft on the inner margin of each lip (Figure 12). These nematodes normally mature in the host's gastrointestinal tract but seem to have a tendency to develop in abscesses outside the gut. The life cycle is indirect, with juveniles developing to the infective stage within rodent intermediate hosts that ingest the eggs. Embryonated eggs are not directly infective for definitive hosts. *Lagochilascaris minor* and *L. major* have often been reported from domesticated cats; *L. minor* is typically found in subcutaneous abscesses in the head or neck of such hosts whereas it localizes in the stomach, esophagus, and trachea of wild cats in South America and the Caribbean. Domestic cats have been experimentally infected with the third-stage juveniles (J_3) of *L. minor* from mice (Barbosa et al., 2007). Experimental infections were patent, suggesting that domestic cats may serve as a reservoir for zoonotic infection. The pharynx of domestic cats appears to be the preferred site for *L. major*; this species has also been reported from wild and domestic canids, and raccoons. Wild cats are believed to represent the natural definitive host for both *L. minor* and *L. major* in South America, but host records are few. In North

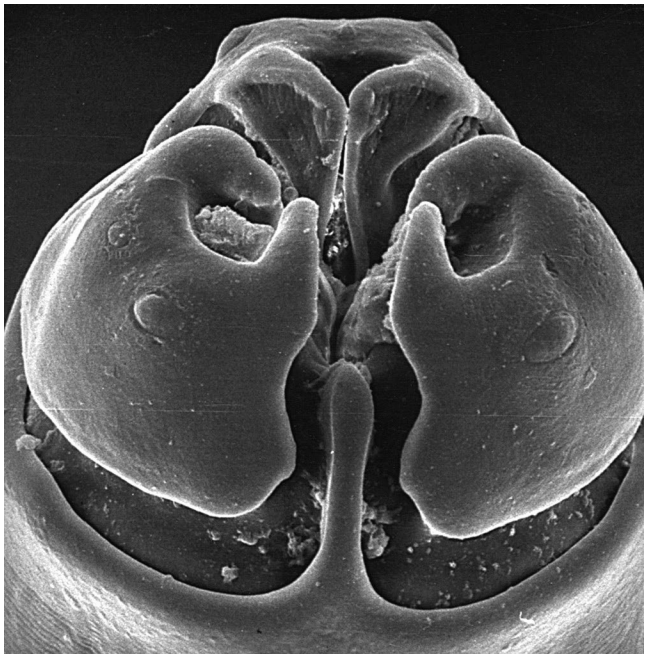

Figure 12. *Lagochilascaris turgida.* Note the prominent cleft in the tip of each lip, typical of the genus (lagos (Greek) = hare; cheilos (Greek) = lip). Source: J. Sprent in Roberts et al., 2014. License: CC BY 4.0.

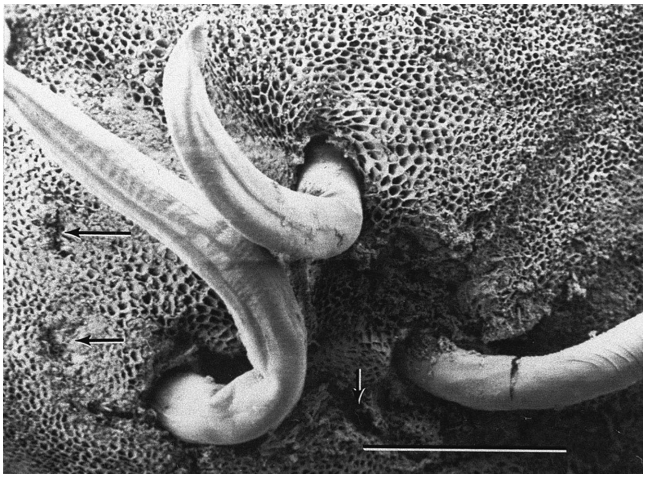

Figure 13. Scanning electron micrograph of *Terranova* sp. juveniles (family Anisakidae) penetrating the stomach of a rat on day three postinfection. Arrows indicate acute lesions caused by juveniles. Scale bar = 1 mm. Source: Deardorff et al., 1983 in Roberts et al., 2014. License: CC BY-NC-SA 4.0.

America, *L. sprenti* uses opossums as its definitive host.

Lagochilascaris minor has been reported in humans at least 8 times, usually found in the tonsils, nose, or neck (Sprent, 1971; Volcan et al., 1982). A fatal brain infection has been reported (Rosemberg et al., 1986). When present, worms cause abscesses that may contain from 1 to more than 900 individuals. Juveniles can mature in these locations, and they produce pitted eggs, much like those of *Toxocara* spp. Human infections may last many years or may kill infected people rapidly. How humans become infected is unknown. Humans are unnatural, accidental hosts for this zoonotic infection.

Family Anisakidae Railliet & Henry, 1912

The many species in the family Anisakidae are stomach parasites of fish-eating birds and marine mammals. Species in the genus *Anisakis*, have a life cycle that involves passage of eggs in feces of their definitive hosts, embryogenesis and hatching of J_3s, ingestion of J_3s by a crustacean, development in the hemocoel of the crustacean, and then either, 1) Ingestion by a definitive host, or 2) ingestion by a fish paratenic host, which is ultimately consumed by a definitive host (Deardorff et al., 1991; Sakanari, 1990). Definitive hosts of *Anisakis* spp. are marine mammals.

Living *Anisakis* spp. juveniles can produce pathological conditions in humans who eat them in raw, salted, marinated, smoked, or pickled fish in preparations such as ceviche, sushi, sashimi, lomilomi, and rollmops. Such conditions may be asymptomatic, mild, or severe (Bier et al., 1987). Symptoms generally commence when juveniles begin to penetrate the stomach lining or intestinal mucosa (Figure 13). Gastric involvement may manifest from 1 to 12 hours after ingestion of infected seafood or after up to 14 days in the case of intestinal penetration. Symptoms may include severe epigastric pain, nausea, vomiting, diarrhea, and hives, but the disease may be confused with other disorders, such as peptic ulcers. Sometimes severe IgE-mediated hypersensitivity reactions occur, and because the allergenic substances present may be heat resistant, even cooking may not render them harmless (Caballero and Moneo, 2004).

Diagnosis of gastric anisakiasis by endoscope and removal of worms with biopsy forceps is effective, although catching lively worms with forceps may be challenging (Deardorff et al., 1991). In intestinal anisakiasis, or cases in which the worm has fully penetrated into submucosa or migrated beyond the gastrointestinal tract, diagnosis is more problematic, and symptoms can mimic a number of other, more common conditions. In such cases serodiagnosis can be helpful and recombinant antigens have made detection of IgE antibodies highly specific (Anadón et al., 2010; Sakanari et al., 1988).

Most cases have been reported from Japan, South Korea, Spain, and Scandinavian countries, where raw or marinated fish is consumed regularly. Approximately 2,000 cases per year have been reported from Japan, where it is a major

foodborne disease, and the number of cases reported from the United States is increasing (Deardorff et al., 1991; Kagei and Isogaki, 1992). Fatalities due to peritonitis have been recorded (Bier et al., 1987).

Anisakis spp. juveniles are the most frequent cause of anisakiasis, but the name of this disease is a misnomer because other anisakid genera, and even species from other families (such as Raphidascarididae), can be responsible. A common feature of the causative organisms is that they are transmitted through aquatic food chains that involve invertebrates and most typically fish paratenic hosts; these paratenic hosts can be infective for humans.

Cooking kills juveniles, but continued popularity of raw or undercooked fish dishes (some examples of which are listed above) ensures a continued risk of human infection. In many cases, commercial blast freezing causes little change in the texture or taste of fish while effectively killing *Anisakis* sp. juveniles (Deardorff and Throm, 1988).

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