UPDATE ON TOXOCARA BIOLOGY, DIAGNOSIS AND HUMAN INFECTION

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Hany Elsheikha considers the risks posed by toxocariasis both to cats and dogs and to humans, stressing the importance of a one health approach

Summary

Toxocariasis continues to be one of the most important enteric parasitic diseases caused by roundworm parasites of the genus *Toxocara* in dogs and cats. Despite the availability of efficient anthelmintics for the treatment of dogs and cats, toxocariasis still persists in many parts around the world. Besides their significant animal health and welfare impacts these roundworms can be transmitted from pets to humans without the involvement of vectors or intermediate hosts, leading to public health problems. A good understanding of the parasite's biology and epidemiology, including the transmission to animals and humans, is required for planning and implementation of effective control strategies. Tackling toxocariasis requires a one health approach and, in this respect, the collaboration between veterinary and medical health professionals in educating the public on modes of transmission, at-risk populations and methods of prevention, and in providing uniform recommendations to pet owners is essential. In this article, recent data on the biology, epidemiology, clinical relevance, diagnostics and control of *Toxocara* in pets and humans are summarised.

Key words

pets, toxocariasis, animal health, zoonoses, parasite control

***TOXOCARA* species (Figure 1) are ascarid nematodes in the family Toxocaridae, order Ascaridida. The two main species in genus *Toxocara* are *T canis* (infects dogs) and *T cati* (infects cats). Dogs and cats are the definitive hosts in which *Toxocara* worms live as adults within the lumen of the small intestine.**

Other species of *Toxocara* infecting cats and other felids have been reported (Despommier, 2003). Despite the availability of efficient anthelmintics, *Toxocara* worms still represent the most prevalent intestinal nematodes in dogs and cats. The importance of *Toxocara* worms is emphasised by its global distribution and high prevalences in some developed countries.

Toxocara has been recognised as a companion animal parasite with a well-documented zoonotic potential for a long time. However, many aspects of its biology and epidemiology, including the spectrum of parasite species causing human infection, different clinical syndromes and dynamic geographic distribution, are still poorly known.

A better understanding of the pathobiology and epidemiology of *Toxocara* would be expected to provide further opportunities to improve treatment strategies and refine infection control measures.

Therefore, an updated overview of the current state of knowledge is presented, with focus on biology, transmission characteristics and epidemiology (infective sources) of toxocariasis in the natural definitive host (dogs and cats) and in the incidental host (humans).

A further aim of this article is to highlight gaps in our understanding of some aspects of toxocariasis to promote future research and attract the attention of public health authorities.

Acquisition and transmission

• Dogs

The canine roundworm *T canis* has a complicated life cycle and can be transferred by four different routes.

– **Ingestion of eggs**

After a dog eats viable, embryonated eggs from the environment, the eggs hatch and the larvae enter the wall of the small intestine. The larvae migrate through the circulatory system and either go to the respiratory system or other organs/tissues in the body. If they enter body tissues, they encyst, especially in older dogs and pregnant bitches. In very young puppies, larvae move from the circulation to the respiratory system, are coughed up and swallowed.

The larvae mature into adults. The adult worms lay eggs that pass out of the animal in the faeces four to five weeks post-infection.

The eggs mature in the environment within two weeks to several months, depending on the soil type and environmental conditions such as temperature and humidity. Eggs become infectious and can remain viable for at least one year under optimal circumstances.

– **Ingestion of larvae in transport/ paratenic host**

If a dog ingests a transport host having encysted larvae, the migration is similar to that of ingesting infective eggs. Larvae are released from the transfer host when it is eaten and digested.

– **Larvae through the uterus**

The dormant larvae in the tissues of pregnant bitch can migrate through the uterus and placenta and infect the fetal pup. This is called in-utero transplacental transmission. The intra-uterine infection is the most important mode of transmission in pups resulting in egg excretion after a minimum period of 16 days.

– **Lactogenic transmission of larvae through the milk**

Larvae can also enter the female's mammary tissues. The puppies can become infected through the milk while nursing. The swallowed larvae mature in the pup's intestine. Larvae have been found to pass in the bitch's milk for at least five weeks postpartum.

• **Cats**

In cats, transmission occurs by three mechanisms.

– **Ingestion of eggs**

– **Ingestion of larvae in paratenic hosts**

– **Transmammary transmission**

Transmammary passage of larvae occurs in the colostrum and throughout the first three weeks of lactation. This mode of transmission is the most important source of infection in kittens. Unlike *T canis* , prenatal infection via the placenta does not occur with *T cati* .

• **Humans**

Humans are infected by the accidental ingestion of infective embryonated *Toxocara* eggs present in contaminated soil (sapro-zoonosis), unwashed hands or raw vegetables, or by ingestion of larvae present in the raw/undercooked tissues of paratenic hosts, such as cattle, sheep or chickens.

Risks of toxocariasis in humans are particularly high in:

• children with pica because they are more likely to ingest embryonated eggs from soil than those not exhibiting this behaviour;

• children between two and four years of age; and

• individuals growing up in a poor neighbourhood.

The fur of dogs has been seen as an important source of *Toxocara* eggs for human infection by direct contact with infected dogs (Aydenizöz-Ozkayhan et al, 2008). However, contact with pets harbouring patent *Toxocara* infection is usually not considered a risk because the eggs need to embryonate during several weeks before becoming infectious. Also, *Toxocara* eggs are very sticky and difficult to remove from the coat of the animal, rendering the ingestion of a sufficient number of eggs less likely.

Parasite epidemiology

T canis and *T cati* are among the few parasites that have a worldwide distribution. The prevalence rates in western Europe vary from 3.5 per cent to 34 per cent for *T canis* and from eight per cent to 76 per cent for *T cati.*

Worm burden and prevalence of *Toxocara* infection are highest in puppies and young dogs less than six months of age and in kittens. Mean egg density is highest in faeces from pups less than eight weeks old. Hence, having a litter of puppies in the home has been considered as a risk factor.

Foxes are also commonly infected, with prevalences usually higher in young cubs (younger than six months old). Growing fox populations, especially in urban areas, with prevalences of *T canis* above 30 per cent, cause a high environmental contamination and maintain parasite cycles independent from pet populations. Surveillance programmes are needed to determine the incidence of *Toxocara* in dogs, cats and foxes.

Environmental contamination

Toxocara eggs (Figure 2) are common environmental contaminants of public parks, due largely to the high density of freely roaming dogs and cats in urban areas, which maintain a constant infection pressure of *Toxocara* and other parasites.

Developing effective control programmes will require better understanding of the effect of the soil's physical environment on the survivability and distribution of *Toxocara* eggs.

Infective ascarid eggs can last for months to years outside the host under optimal conditions, due to a resistant outer shell composed of ascarosides. This acellular layer enables eggs to withstand extreme temperatures and various harsh chemicals (for example, high concentrations of formalin and acids).

Future strategies for reducing the number of infectious eggs in soil must find novel ways of breaching the eggshell barrier that protects the juvenile worm from external environment. Some soil fungi have been shown under experimental conditions to have larvicidal activity against the juvenile worm within its egg's shell. However, the application of fungi doesn't seem a feasible approach to control *Toxocara* eggs in soil.

Earthworms, small mammals and birds have all been reported to play a role in dispersing *Toxocara* eggs from the original source. Viable eggs ingested by earthworms become incorporated into their faeces and are distributed in the local environment by the effect of rain and wind. Cats, dogs, chipmunks and squirrels can play a role similar to that of earthworms in the dispersal of *Toxocara* eggs (Dubinsky et al, 1995). Birds that feed on the ground, such as sparrows and pigeons, can serve as paratenic hosts, carrying eggs from one place to another on their feet and beaks, and may deposit eggs in places distant from the point source.

Toxocara eggs have been found in recreational water, and can potentially contaminate municipal drinking water supplies (Beer et al, 1999).

Clinical relevance to humans

Human toxocariasis is caused by the larval stage of *T canis* and less frequently *T cati* (Fisher et al, 2003).

In contrast to dogs and cats (the natural definitive hosts), infection in humans (accidental host) remains occult, often resulting in disease caused by the migrating larval stages. Within humans, *Toxocara* larvae don't complete their life cycle and fail to mature to adult worms. Instead, they migrate throughout the body for a long time, causing damage to tissues they encounter.

The clinical manifestations of human toxocariasis vary from asymptomatic infection to severe organ injury, depending on the parasite load, the sites of larval migration and the host's inflammatory response.

Four different clinical syndromes have been reported. The two main clinical syndromes associated with toxocariasis in humans are visceral larva migrans (VLM), which includes pathologies associated with the major visceral organs, and ocular larva migrans (OLM), in which toxocariasis disease effects on the host are limited to the eye and the optic nerve (Magnaval et al, 2001). Both syndromes are serious health problems and their diagnosis and treatment are difficult.

Two less severe syndromes have also been reported: "covert toxocariasis", observed mainly in children and characterised by headache, fever, behavioural and sleep disturbances, anorexia, cough, abdominal pain, hepatomegaly and vomiting; and “common toxocariasis”, seen mainly in adults with pruritus, rash, difficult breathing and abdominal pain. Clinical involvement of the central nervous system (CNS) in VLM has been reported. The CNS migration may lead to a variety of neurological disorders, such as meningo-encephalitis, optic neuritis and cognitive/ behavioural disorders.

A study reported a positive association between *Toxocara* seropositivity and epilepsy (Quattrocchi et al, 2012), suggesting toxocariasis could play a role in the incidence of epilepsy.

Human toxocariasis seems to be rare in England and Wales because fewer than 10 newly diagnosed cases are reported to the Health Protection Agency (HPA) Centre of Infections each year. This prevalence might, however, be underestimated because the disease is not noti fiable and source of the data is based on voluntary reporting by microbiology laboratories.

Diagnostics

• Pets

Toxocariasis in dogs and cats is diagnosed primarily on the basis of clinical criteria during clinical examination. The parasite results in gastrointestinal manifestations, such as diarrhoea, emesis, stunted growth, abdominal discomfort, and, in severe cases, intestinal obstruction and distended abdomen (pot-bellied appearance).

Laboratory diagnosis of patent *Toxocara* infections is achieved by the detection and specific identification of *Toxocara* species eggs in the faeces following a flotation technique. Molecular (PCRbased) techniques are available as an alternative or complement to morphology-based diagnostic techniques. However, these methods are not part of the routine diagnostic procedures adopted by clinical laboratories. The development of rapid, highly sensitive and specific diagnostic tests that can be executed in the field is an essential element in any future control programmes.

• Humans

Diagnosis of human toxocariasis is based on clinical presentation, blood abnormalities (for example, peripheral eosinophilia and elevated total-IgE) and serodiagnostic techniques to detect antibodies and circulating antigens. Anti-*Toxocara* antibodies can persist for up to 2.8 years in infected individuals; thus, their presence does not distinguish between current and past infections and does not allow a definitive diagnosis of clinical toxocariasis. Regarding OLM, intraocular antibodies appear to have more diagnostic value compared to serum antibodies.

Treatment and control

An integrated control approach consisting of chemotherapy, improved hygiene, and public health education is needed to prevent the continued upsurge in toxocariasis, especially in endemic areas.

• **Chemotherapy**

Various anthelmintics can be used for the treatment of *Toxocara* infection in dogs and cats with emphasis on puppies, kittens, nursing bitches and queens.

Periodic treatments with anthelmintics, or treatments based on the results of faecal examinations, are of great value for the control of enteric helminths in dogs and cats. Based on the prepatent period in dogs, a regular treatment every four to six weeks would prevent most patent infections. Monthly administration of macrocyclic lactones suppresses nearly all canine nematodes. However, anthelmintics at the normal doses are not highly effective against encysted somatic larvae.

The most serious and concentrated source of *Toxocara* infection are a bitch nursing a litter and puppies aged between three weeks and six months because milk transmission can occur for at least five weeks postpartum.

As a prophylactic measure, a multidose schedule has been used to suppress *T canis* egg output during puppyhood. Puppies should be treated with appropriate anthelmintics at two, four, six and eight weeks of age and then monthly until six months of age.

Because prenatal infection does not occur in kittens, this bi-weekly treatment can begin at three weeks of age. Nursing bitches and queens should be treated concurrently with their offspring, since they may develop patent infections.

A treatment schedule should be individually tailored for pets based on certain infection risks, such as free roaming, uncontrolled access to rodents or offal, contact to other animals and so on.

• **Additional measures**

Since no practical methods exist for reducing environmental egg burdens, prevention of initial contamination of the environment is the key point in the management of *Toxocara*. In practice, measures should be focused on the following two principal points:

• restriction of free-roaming dogs and cats, and limiting access of dogs and cats to public areas frequented by small children, especially children’s playgrounds; and

• pet owners’ education to prevent defaecation of pets in public areas and to clean up faeces from soil and on pavements.

Local authorities have implemented a variety of interventions to tackle dog fouling, including placing notices in public areas, leaflet distribution, enforcement, media coverage, provision of free poop scoops and siting of dog waste bins (Atenstaedt and Jones, 2011).

One factor we think is absolutely essential for the control and prevention of toxocariasis is public awareness.

Pet owners' lack of understanding of parasites and their zoonotic implications underpin many of the potential public health problems we face.

Uniform guidelines for the control and treatment of parasites in pet animals have been developed and published by the Companion Animal Parasite Council in the US (www.capcvet.org) and the European Scientific Counsel Companion Animal Parasites in Europe (www.esccap.org). These guidelines provide an overview on worm species, their clinical and zoonotic significance, and enable pet owners and veterinarians to make informed decisions on the selection of rational control measures to mitigate the risk of *Toxocara* infection.

• **Treatment of infected people**

Treatment of humans with toxocariasis will not have any impact on the disease prevalence in dogs or cats because a human is a dead-end host and doesn't pass infection to any other mammalian hosts.

However, for very obvious reasons, people who suspect they may be infected with *Toxocara* should seek medical attention. Standard treatment of VLM using albendazole, and management of OLM using a combination of surgery, anthelmintic therapy and corticosteroids have been reported to be effective (Small et al, 1989; Sturchler et al, 1989).

Conclusion and outlook

Despite the implementation of deworming programmes, *Toxocara* still prevails, highlighting the challenges in toxocariasis control and prevention. Good hygiene should be encouraged and further strategies to prevent *Toxocara* transmission should be identified and implemented.

A radically new approach is needed to eliminate *Toxocara* eggs from contaminated soil. Molecular vaccines could aid in the control of infection in domestic dogs and cats. The search so far has identified *Toxocara* myosins as potential candidates. To date, however, no molecular vaccines are available. The development of effective vaccines offering the possibility of long-term protection is needed.

The presence of different *Toxocara* species that infect humans besides their main animal hosts (dogs and cats), resulting in different pathologies, and the presence of wild reservoirs potentially interacting with the anthropogenic environment, confer a high level of biological, clinical, and epidemiological complexity to human toxocariasis.

Further in-depth studies of the genome, proteome, metabolism, pathogenesis, and survival mechanisms of *Toxocara* species may provide information on novel therapeutic and infection control targets and explain the differences in the relationships between *Toxocara* parasites and their different hosts.

KEY CONCEPTS

• Toxocariasis remains a common parasitic infection worldwide, impacting on the health and welfare of dogs and cats.

• *Toxocara canis* and *T cati* are too common parasites of dogs and cats, particularly puppies and kittens.

• The parasite has a complex life cycle, including infection via ingestion of either embryonated eggs from the environment or larvae from infected paratenic hosts, or infection via vertical transplacental transmission or lactogenic route.

• Any preventive and control measures must aim to break the life cycle of the parasite.

• Wherever toxocariasis exists, there is a public health risk, especially among children exhibiting pica and in public parks and playgrounds, which are common areas for *Toxocara* egg acquisition.

• *Toxocara* eggs are very resistant to adverse environmental conditions and can remain viable for at least one year.

• People should ensure their owned dogs and cats are routinely checked and treated.

• Veterinarians can play an important role in combating the spread of *Toxocara* infection. Recommending routine monitoring of infection (faecal examinations) and the proper use of chemotherapeutic compounds should be effective in controlling infection via reducing worm burdens and limiting the environmental contamination with *Toxocara* eggs.

• More awareness and research are required to improve control strategies in pets and to prevent transmission to humans.

References

- Atenstaedt R L and Jones S (2011). Interventions to prevent dog fouling: a systematic review of the evidence, *Public Health* **125**: 90-92.
- Aydenizöz-Ozkayhan M, Yaðci B B and Erat S (2008). The investigation of Toxocara canis eggs in coats of different dog breeds as a potential transmission route in human toxocariasis, *Veterinary Parasitology* **152**: 94-100.
- Beer S A, Novosilítsev G I and Melínikova L I (1999). The role of the water factor in the dissemination of Toxocara eggs and the spread of toxocariasis in a megalopolis, *Parasitology* **33**: 129-135.
- Despommier D (2003). Toxocariasis: clinical aspects, epidemiology, medical ecology, and molecular aspects, *Clinical Microbiology Review* **16**: 265-272.
- Dubinsky P, Havasivoa-Reiterova K and Petko B (1995). Role of small mammals in the epidemiology of toxocariasis, *Parasitology* **110**: 187-193.
- Fisher M (2003). Toxocara cati: an underestimated zoonotic agent, *Trends in Parasitology* **19**: 167-170.
- Magnaval J F, Glickman L T, Dorchies P and Morassin B (2001). Highlights of human toxocariasis, *Korean Journal of Parasitology* **39**: 1-11.
- Quattrocchi G, Nicoletti A, Marin B, Bruno E, Druet– Cabanac M et al (2012). Toxocariasis and epilepsy: systematic review and meta-analysis, *PLoS Neglected Tropical Diseases* **6** (8): e1775.
- Small K W, McCuen B W, De Juan E and Machemer R (1989). Surgical management of retinal retraction caused by toxocariasis, *American Journal of Ophthalmology* **108**: 10-14.
- Sturchler D, Schubarth P and Gualzata M (1989). Thiabendazole v. albendazole in treatment of toxocariasis: a clinical trial, *Annals of Tropical Medicine and Parasitology* **83**: 473-478.