Chapter

Toxocariosis: From a One Health Perspective

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Abstract

Toxocariosis is a neglected zoonotic infection caused by the nematodes *Toxocara canis* or *Toxocara cati*. The distribution of the disease is worldwide and mainly affects dogs and cats, and its larval stage can cause human infection with serious repercussions on the health of its hosts. The infection causes a delay in the development, digestive disorders, nonspecific nervous manifestations, and occasionally death of some puppies and kittens associated with hyperparasitosis. In humans, the infection produces clinical syndromes known as *visceral larva migrans* (VLM), *ocular larva migrans* (OLM), neurotoxocariosis and covert toxocariosis. The close contact of people with their pets and the environmental conditions that favor the transmission of this diseased place it within the context of one health. The One Health concept is defined as the collaborative efforts of multiple disciplines (medical personnel, veterinarians, researchers, etc.) that work locally, nationally, and globally to achieve optimal health for people, animals, and the environment, from this perspective, toxocariosis is a study model in which classic and recent knowledge of the medical and veterinary area must be combined for its full understanding, with a goal of establishing integrative criteria for its treatment, control, and prevention.

Keywords: *Toxocara*, one health, toxocariosis, zoonosis, visceral larva migrans, ocular larva migrans

1. Introduction

Toxocariosis is a neglected zoonotic disease transmitted from dogs and cats to humans. This is mainly caused by the presence and action of the nematode *Toxocara canis* (*T. canis*) and less frequently by *Toxocara cati* (*T. cati* syn. *T. mystax*). *T. canis* uses canines, mainly puppies, as its definitive host, and *T. cati* uses kittens. In addition, they use a wide variety of paratenic hosts, including pigs, sheep, rabbits, rats, mice, other mammals, chickens, and other birds. In humans, the infection is accidental, and the parasite behaves similarly as it does in paratenic hosts. Some invertebrates, such as earthworms and cockroaches, can also have *Toxocara* larvae in their tissues or their gut [1, 2].

Adult *T. canis* worms live in the small intestine of puppies. The females measure from 10 to 18 cm, and the males measured from 4 to 10 cm. At the anterior end, they have three small lips that do not protrude beyond the diameter of the body.

A dentigerous border can be seen on the inner surface of each lip. Behind the lips are a pair of cervical fins that give the anterior end of the worm an arrowhead appearance. The posterior end in males ends coiled toward the ventral part and has a terminal narrowing in the form of an appendix, and a pair of small and symmetrical spicules (0.75–0.95 mm) are observed. In females, the vulva is located approximately in the middle of the body, and the posterior end ends at a straight, blunt point. *T. cati* adults are very similar to *T. canis*; the cervical fins are broader and convex, giving the anterior end a more marked arrowheaded appearance; males are 3–6 cm long, and females are 4–10 cm long [3].

2. Biological cycle

Embryonated *T. canis* eggs are shed in the feces of puppies. In the environment, a first-stage larva develops inside the egg, which molts twice until it becomes larva 3 (L3). Larvated eggs (passive L3 inside) are the infective stage. Depending on humidity and temperature, the development of the infective stage requires 2–5 weeks in the environment. In susceptible hosts after ingestion of the infective stage, L3 hatches (active L3) in the duodenum and traverses the intestinal wall; the larvae pass into the lymphatic flow or blood capillaries. From this moment on, the development and migration of the larvae vary depending on whether the host is a young dog (<3 months), an adult dog, a pregnant bitch, or a paratenic host (rats, mice, birds, and humans, among others) [4].

In puppies, L3 migrate via blood or lymph to the liver, where they remain for 1 to 2 days. Subsequently, they migrate through blood, pass through the lumen of the atrium and right ventricle of the heart and via the pulmonary artery, reach the lungs, and cross the capillaries to reach the alveoli. The larvae migrate through the lumen of the bronchioles, bronchi, trachea, larynx, and pharynx (tracheal migration), where they are swallowed; during this tracheal migration, the larvae molt to L4. The larvae remain in the stomach for some time (up to Day 10 postinfection), return to the duodenum, and molt to L5 or preadult to finally become adults (19–27 days postinfection). The prepatent period is 4–5 weeks [4].

In paratenic hosts and adult dogs, L3 larvae migrate through the blood and are distributed throughout the body, mainly to the striated muscle, liver, lungs, kidneys, and brain, where they remain for years in a state of latency or dormancy as infective somatic larvae (dormant larvae) until they die and calcify.

In pregnant bitches, on approximately Day 20 of gestation, many of their dormant larvae are reactivated by the influence of progesterone. Between Days 43 and 47 of gestation, under the influence of progesterone and prolactin, the larvae cross the placenta and infect the fetuses. The larvae remain in the fetal liver until birth; later, by blood, they migrate to the lungs where they remain during the first week of life, molting to L4 occurs during this stage or later when the larva arrives in the stomach by tracheal migration. By the end of the third week, the larvae molt at L5 and develop rapidly into adult worms. After copulation, the females produce eggs that are passed in the feces of the pups at 15 days of age. In recently delivered bitches, some reactivated larvae arrive by the influence of prolactin on the mammary gland and are excreted in the colostrum and milk to be ingested by the puppies, constituting another important source of infection for the litter. The larvae ingested in this way molt at L4 and L5 in the intestinal lumen, where they develop into adult worms without tracheal migration [5].

In recently delivered bitches, some larvae may reactivate during gestation migrate to the intestine, molt to L4 and L5 and become adult worms. Bitches can remain up to 60 days passing eggs in feces until the adult worms are eliminated spontaneously. This is one of the ways adult worms can develop in adult dogs [1].

Dormant larvae in the tissues of paratenic hosts can be reactivated when they are predated. If the predator is another paratenic host, the ingested reactivated larvae undergo a new somatic migration and become dormant in this new host. On the other hand, if the predator is an adult dog, the ingested reactivated larvae molt at L4 and L5 and develop into adult worms in the lumen of the small intestine without further somatic migration. In this way, dogs can spend a short time excreting eggs in the feces until the adult worms are eliminated spontaneously. This is another way that adult worms can develop in adult dogs [1].

The life cycle of *T. cati* is similar to that of *T. canis* except that prenatal transplacental infection in this parasite does not occur [6].

3. Epidemiology

3.1 Dogs and cats

T. canis is the most common nematode in dogs in many regions of the world and *T. cati* in cats. In a meta-analysis study where data from more than 13 million dogs from 60 countries were included, the overall prevalence of *Toxocara* infection in dogs was found to be 11.1%. The prevalence was estimated in different World Health Organization regions: Eastern Mediterranean (19.2%), Africa (18.5%), South-East Asia (11.9%), North America (11.1%), South America (10.9%), Europe (10.8%) and Western Pacific (6.4%) [7].

In a second meta-analysis where data from 2,158,069 cats from 51 countries were included, an overall prevalence of *T. cati* of 17% was found. The prevalence was estimated in different World regions: African (43.3%), Eastern Mediterranean (21.6%), North America (18.3%), Europe (17.8%), Western Pacific (17.3%), South-East Asia (14.9%),and South American (12.6%)[8].

Transplacental transmission from bitches to their puppies is the most important form of *T. canis* infection in dogs. Not all somatic larvae in bitches are reactivated during the same gestation; thus, reactivation of larvae occurs in subsequent gestations. In addition, bitches become reinfected by ingesting persistent larvated eggs in an environment contaminated with fecal matter from their puppies. Transplacental transmission does not appear to occur in cats with *T. cati*, making lactogenic infection the most common form of infection in kittens [4, 6].

Puppies are the main source of environmental contamination; they can excrete eggs in feces from 15 days of birth, and the greatest egg shedding occurs between 1 and 3 months of age, when they can eliminate more than a million eggs per day. Gradually, the worm burden in the intestine tends to decrease, and they stop shedding eggs before reaching 6 months of age. In addition, the larvae ingested by the lactogenic route gradually increase the worm burden and the elimination of eggs in the puppies. Puppies under three months of age are the only hosts that can develop adult worms in the intestine by ingesting larvated eggs, although apparently, this is not their main route of infection [9].

Adult *Toxocara* females are very prolific, producing between 25,000 and 85,000 eggs per day, and the presence of many females in the intestine of a puppy can mean the

elimination of enormous numbers of eggs in the feces (>100,000/g). In the environment, when eggs are protected from direct sunlight and desiccation, they develop to the infective stage (L3 passive) 2–4 weeks after shedding. In earthen soils, the eggs can remain viable for many months, accumulating in the environment. Therefore, the soil in areas where dogs with toxocariosis commonly defecate is considered a permanent source of infection for animals and humans. In addition, rainwater can carry the eggs to distant places and accumulate them in large concentrations in some places [1]. A study that included 42,797 soil samples in 40 countries showed a global prevalence of *Toxocara* eggs in public places of 21%. The estimated prevalence rates in the different regions ranged from Western Pacific (35%), Africa (27%), South America (25%), South-East Asia (21%), the Middle East and North Africa (18%), Europe (18%) and the North and Central Americas (13%) [10].

Paratenic hosts infected by ingesting larvated eggs present in soil, food or water accumulate L3 in their tissues. If these are predated, they can be a source of infection for adult dogs. If predated by another paratenic host, the larvae can infect the new host, bypassing a definitive host.

3.2 Humans

Due to the great difficulty of identifying the physical presence of somatic larvae, the most common way to identify *Toxocara* infection in humans is by serological tests (ELISA and Western blot). Serologically, it is not possible to distinguish between a *T. canis* infection and a *T. cati* infection, and although *T. canis* infection has generally been considered to be the predominant infection in humans, the seroprevalence of *T. cati* has not been determined, which could have been underestimated [11].

The seroprevalence of *Toxocara* in humans varies in different regions of the world. A meta-analysis carried out in 2019 that included 265,327 participants in 71 countries showed an estimated global *Toxocara* seroprevalence rate of 19.0%. The pooled seroprevalence for regions was as follows: African (37.7%), South-East Asia (34.1%), Western Pacific (24.2%), American regions (22.8%), European regions (10.5%), and Eastern Mediterranean region (8.2%) [12]. Seroprevalence has been associated with different risk factors, such as age, contact with young dogs and kittens, socioeconomic level, consumption of vegetables, and unboiled water, ethnicity, educational level, living in a rural area and pet ownership [13, 14]. The serological differences associated with the different ethnic groups in some countries may be the result of different contextual exposures linked, among other factors, to their socioeconomic level, segregation, and the environmental conditions in which the different ethnic groups live, and not necessarily due to a genetic predisposition [15].

The most common way of infection in humans occurs through the accidental ingestion of *Toxocara* larvated eggs, which can be found on soil in public parks, gardens, dirt floors, sandboxes, and vegetables irrigated with sewage, among others. Although people of any age can be infected, children are more frequently affected due to their habits of playing with pets and dirt, geophagia, and pica, in addition to their commonly poor hygiene habits [16–18]. Infection can also occur through the ingestion of somatic larvae present in raw or undercooked meat and viscera of cattle, pigs, and poultry, among others, which act as paratenic hosts (**Figure 1**) [19–22]. *Blattella germanica* and *Periplaneta americana* cockroaches have recently been shown to be able to ingest and shed larvated *T. canis* eggs in their feces, suggesting that they could carry infective eggs from dog feces to kitchens where human food is prepared [2].

There are multiple reports of the presence of *Toxocara* eggs in the hair of dogs and cats, which is why it has been proposed that they are a source of infection for their

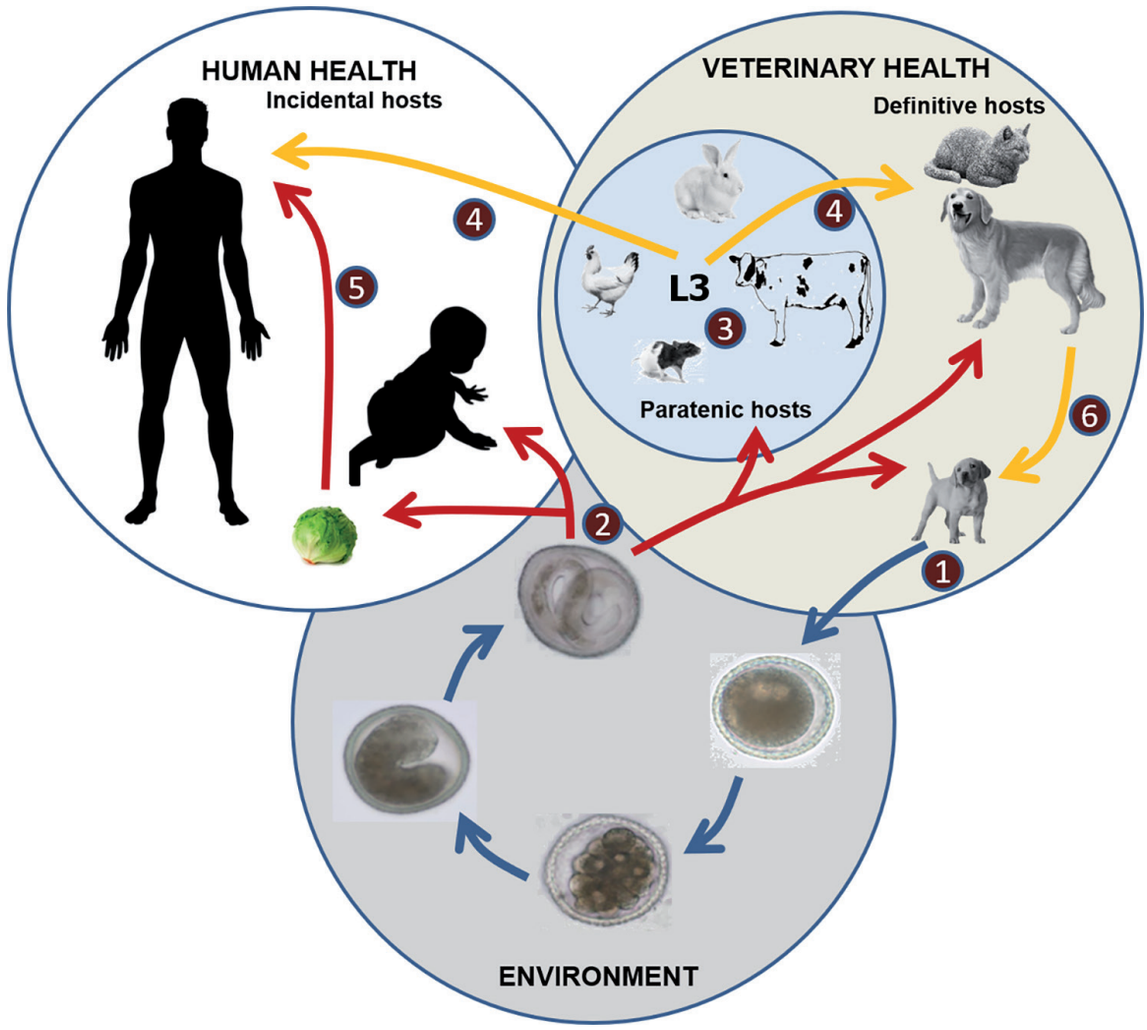

Figure 1.
Epidemiology of toxocariosis from the one health approach. The biological cycle of Toxocara *sp. involves definitive (dogs and cats), paratenic (several species of mammals and birds), and incidental (human) hosts. Puppies are the main eliminators of immature eggs into the environment (1). In optimal environmental conditions of humidity and temperature, passive larvae 3 develop inside the eggs, which are the main infective stage for all hosts (2). Paratenic or incidental hosts that ingest larvated eggs maintain somatic larvae in their tissues (3) that are infective to predators of the infected paratenic host. Human infection occurs mainly by ingestion of larvated eggs or by ingestion of raw animal meat or viscera (chicken, pig, beef) with infective somatic larvae (4). The ingestion of larvated eggs can be facilitated by the consumption of contaminated vegetables (5). Somatic larvae present in the definitive host are transmitted to puppies by transplacental (dog) and lactogenic (dog and cat) routes (6). Blue arrows show the dynamics of egg development in the environment, red arrows show transmission from larvated eggs, and yellow arrows show transmission from somatic larvae.*

owners [23–26]. However, the presence of larvated infective eggs in the hair is very low, probably due to poor temperature and humidity conditions [27], suggesting a low risk of infection for humans when petting the hair of their pets, although the possibility exists.

4. Canine and feline toxocariosis

4.1 Pathogenesis and clinical picture

The adult worms of *T. canis* and *T. cati* feed on intestinal content, compete with the host for nutrients and, depending on the worm burden, can produce different

degrees of malnutrition. The presence of adult worms causes intestinal irritation, which induces decreased absorption of nutrients and is responsible for diarrhea and vomiting observed in some young animals. The presence of adult worms in the intestinal lumen exerts a mechanical obstructive action on the normal flow of intestinal content. Microscopically, the presence of adult worms produces mucosal muscular hypertrophy, intestinal villus atrophy, and crypt hyperplasia [1].

Larval migration in mild or moderate infections in puppies generally does not produce obvious clinical signs; however, larval migration in severe infections produces respiratory signs such as tachypnea, cough, and runny nose. Nervous signs such as incoordination or convulsions are occasionally observed in puppies due to the passage of the larvae through the brain. In puppies with intense prenatal infection, the lesions produced by the passage of the larvae in the liver, lungs, or central nervous system can cause the death of the puppies in the first 2 weeks of life [28].

Mild to moderate adult worm infections in puppies are usually asymptomatic or cause mild digestive symptoms and growth retardation. In severe infections, dirty-looking bristly hair, rough skin, painful intestinal distention, vomiting (frequently with adult worms), bulging abdomen (mainly when they have just eaten), presence of large amounts of gas produced by intestinal dysbiosis, alternating periods of constipation and diarrhea with profuse mucus, decreased appetite and growth retardation, can be observed. The blood count shows eosinophilia and anemia. Occasionally, there may be the death of puppies due to aspiration of vomit and intestinal obstruction or rupture. The presence of large numbers of adult worms as a result of massive prenatal infections in puppies can cause complete obstruction of the intestinal lumen, intussusception of the small intestine, and death of the entire litter [9, 29, 30].

In kittens, there is no transplacental transmission; therefore, the development of adult worms occurs until almost 30 days of age and the beginning of the elimination of eggs at approximately 50 days of age. The clinical picture is similar to that described in dogs but less severe, diarrhea, vomiting, and loss of appetite predominate, and deaths are very rare. The highest incidence of *T. cati* in cats occurs between 2 and 6 months of age; in general, the worm burden is lower in kittens than in puppies and occurs when the kittens are older and therefore have a higher degree of development [9, 31].

4.2 Diagnosis of toxocariosis in dogs and cats

Sporadically, shed adult worms can be observed macroscopically in the vomit or feces of puppies. The detection of *Toxocara* eggs in feces is performed by coproparasitoscopic techniques, such as Faust or McMaster; however, this can only be done when there are adult stages in the intestine, mainly in puppies [3]. In the eggs, three external layers are observed, forming the shell; the outermost layer is albuminous, the middle layer is lipoid, and the inner layer chitinous. The shell has depressions on the surface, called pits, which give it an appearance similar to a golf ball. The egg measures 75–85 μm and has a protoplasmic mass that occupies the entire interior.

In adult dogs and paratenic hosts, infection by somatic larvae can be demonstrated by the detection of specific antibodies against excretion-secretion antigens using immunological techniques such as ELISA or Western blot; however, due to their cost, difficulty in obtaining the antigens, and their difficult implementation, these techniques are not widely used in the veterinary field [32].

5. Human toxocariosis

Human toxocariosis is a neglected worldwide zoonosis caused by nematodes of the genus *Toxocara* (*T. canis* and *T. cati*). Current data indicate that toxocariosis is an infection of global distribution whose importance has been significantly underestimated [12, 15, 33, 34]. Human toxocariosis occurs in four clinical forms: *visceral larvae migrans* (VLM) syndrome, *ocular larvae migrans* (OLM) syndrome, neurotoxocariosis and covert toxocariosis.

5.1 VLM syndrome

In the 1950s, second-stage larvae of *T. canis* (now known to be third-stage larvae) were identified in the tissues of several children associated with the presence of clinical signs and a pathology that has since been known as VLM [35]. The associated syndrome in these children was characterized by extensive eosinophilia, hepatomegaly, splenomegaly, hypergammaglobulinemia, and chronic cough with eosinophilic pulmonary infiltration. VLM is more common in children (1–5 years) than in adults because they are more exposed to the infection through the ingestion of larvated eggs of *T. canis*, favored by factors such as living with puppies, poor hygienic habits, and pica [14, 36].

In humans, after ingestion of infective eggs, the larvae hatch in the small intestine and penetrate the intestinal wall, from which they are transported by the blood circulation to various organs, mainly the liver, heart, lungs, brain, muscle, and eyes [37]. In these organs, the larvae actively migrate, aided by proteases with which they cause tissue damage and exert a histophagous spoliating action (traumatic action). The migrating larvae do not continue their development; however, they remain dormant for several years, but they continue to secrete excretion-secretion antigens that induce an inflammatory response in some organs, such as the liver and spleen (hepatosplenomegaly), or are mediators of immunopathological alterations in other organs, such as the lung, where they produce eosinophilic pulmonary infiltration related to cough and persistent secretion [38].

Given the impossibility of carrying out studies in humans, experimental models have been developed in different species of paratenic hosts, such as primates [39], rabbits [40], rats [41], mice [42], and gerbils [43], where the sequence of pathophysiological and immunological events of VML have been studied. In these models, it has been observed that organ injuries can be acute or chronic. The acute phase is characterized by a severe inflammatory response that causes multifocal lesions with necrosis and vacuolization with polymorphonuclear infiltrate, mainly neutrophils with the presence of eosinophils in the liver and lungs. The chronic phase is characterized by the presence of granulomatous lesions with infiltrates of mononuclear cells, fibroblasts, and eosinophils, as well as the presence of fibrosis around the lesion with traces of calcification in the center of the lesions, which in some cases can be extensive. The main organs affected are the liver, lung, kidney, and brain (**Figure 2**). These lesions can be seen with or without the presence of the larva, which suggests the importance of the antigenic excretion-secretion products released by the larva in the tissues.

The clinical picture of VLM includes hyperleukocytosis (30,000–60,000 cells/mm3), eosinophilia (14–90%), abdominal pain, enlargement of lymph nodes, hepatomegaly, splenomegaly, increased ishemagglutinins and liver enzymes, intermittent fever, cough, and bronchospasm, among others [44–47]. The severity of the condition

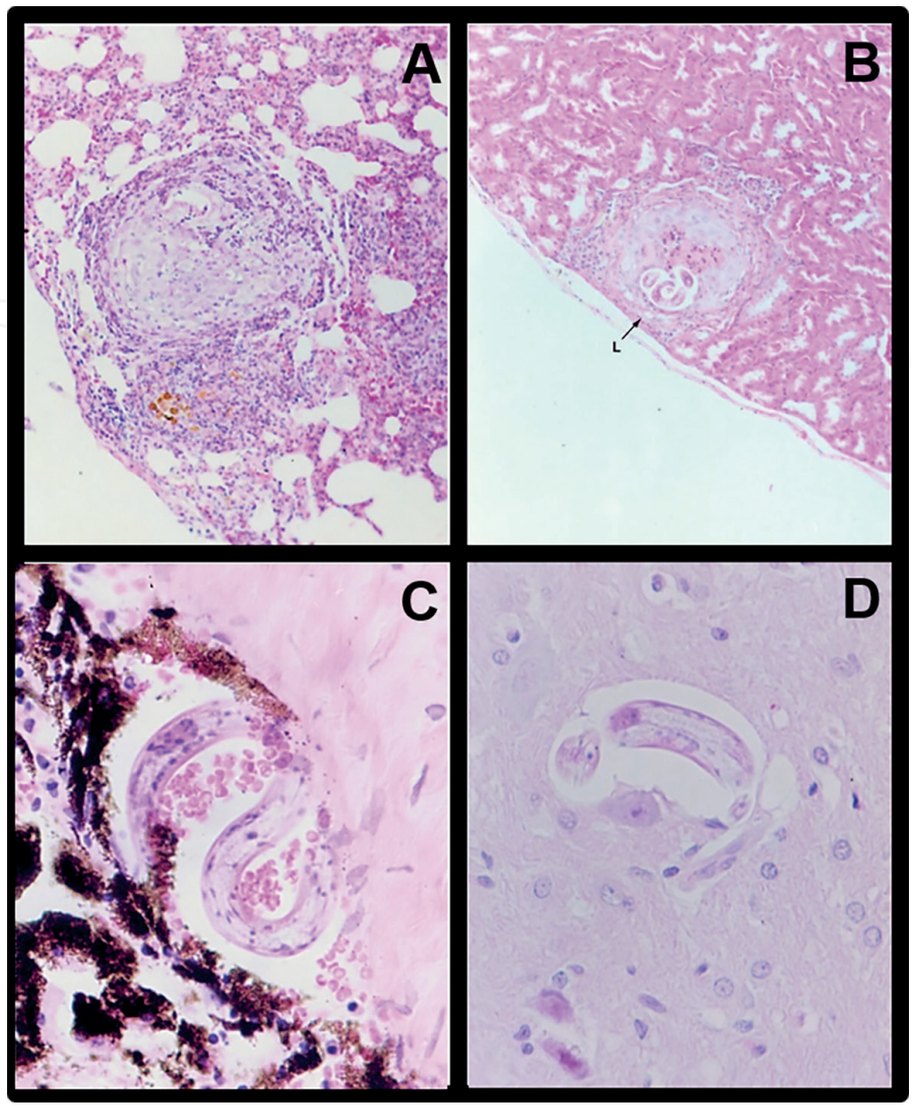

Figure 2.
Lesions produced by Toxocara canis *larvae in Mongolian gerbils (*Meriones unguiculatus*). A: lung with chronic granuloma. B: kidney with chronic granuloma with a larva trapped inside (L). C: larva in the pigmented layer of the retina with rupture of blood capillaries. D: larva the in brain with no apparent tissue reaction (photo credits: Dr. Alba-Hurtado).*

depends on the number of eggs ingested and the presence of larvae in critical places; although most patients recover and the signs subside with anthelmintic treatment, deaths from this infection have been reported [48, 49].

The diagnosis of VLM is based on the initial detection of antibodies against excretion-secretion antigens of *T. canis* by ELISA and its confirmation by Western blot in patients with eosinophilia, with high concentrations of serum IgE or with suggestive clinical manifestations. [50–52]. It has been proposed that the confirmatory diagnosis can be validated with the identification of a larva from a biopsy or by some molecular tests, such as PCR, DNA hybridization and restriction fragment length polymorphism, or sequencing of *Toxocara* ribosomal DNA; however, it is still in the of experimentation in animal models and is not available for humans [53]. Different tools, such as ultrasound (US), contrast-enhanced ultrasound (CEUS), contrast-enhanced computed tomography (ceCT), contrast-enhanced magnetic resonance imaging (ceMRI) and positron emission tomography (PET), are currently used to obtain suggestive images of the main lesions in different human organs [49, 54].

5.2 OLM syndrome

This syndrome was first described by Wilder in 1950, who found nematode larvae (unidentified at the time) in 24 of 46 pseudogliomas in eyes enucleated for endophthalmitis with apparent retinoblastoma [55]. Nichols later identified the larvae as *T. canis* in sections from four out of five of the eyes examined by Wilder [56]. Although, it is currently accepted that *T. canis* larvae are the main etiologic agent of OLM, it has also been shown that T. cati can cause ocular infections in humans [57–59].

OLM is a disease that generally occurs in young patients. In a systematic review and meta-analysis of studies published internationally, it was observed that the highest infection rate was detected in the 1–25 mean age group; within this range, the highest prevalence occurred between 11 and 20 years of age and was higher in men than in women [34]. It has been shown that having contact with dogs, ownership of dogs or cats, exposure to soil, and consuming raw/undercooked meat can be risk factors for OLM [12, 26, 34, 60].

OLM is generally observed in the absence of clinical signs and symptoms of VLM; it is considered to occur in people initially exposed to a small number of larvae, so they do not mount a significant immune response (many patients with a clinical diagnosis of OLM are seronegative to *Toxocara*), and the larvae migrate freely through various organs and accidentally reach the eye [61, 62]. Observations in experimental models and some clinical evidence indicate that *Toxocara* larvae infect the eye by migrating through capillaries or directly from the brain through the optic nerve [63–66].

The lesions detected in the eyes of patients diagnosed with OLM have been granulomas located near the optic disc or intraretinal (see **Figure 2C**), posterior and peripheral retinochoroiditis, panuveitis, optic papillitis, uveitis, retinal deformation or detachment, idiopathic epiretinal membranes, infiltration of inflammatory cells in the humor vitreous, hemorrhagic lesions and neuroretinitis as a sequel to migration of larvae in the retina [60, 67–69]. The main clinical manifestations include poor visual acuity, vision loss, strabismus, leukorrhea, eye irritation, and endophthalmitis [58, 70]. In most cases, lesions occur in only one eye, although there are reports of bilateral conditions [70].

The initial diagnosis of OLM is based on clinical signs and observation of lesions with an ophthalmoscope in the fundus examination. Confirmation of the diagnosis can be made by the detection of antibodies against excretion-secretion antigens of *T. canis* by ELISA in the vitreous humor of the affected eye and the study of the lesions by ultrasound biomicroscopy (UBM) and optical coherence tomography (OCT) [71, 72].

5.3 Neurotoxocariosis

The first report of the presence of an encapsulated larva of *T. canis* in the brain of a child was in 1951; originally, the larva was identified as probably *Ascaris lumbricus* [73]; later, this larva was identified as *T. canis* [74]. The damage produced by *Toxocara* larvae in the central nervous system (CNS) of humans has been widely discussed by many authors. The pathology depends on the number of larvae, the location of the larvae in the nervous system, the time postinfection, the immune response, and some intrinsic factors of the host. Most cases of neuro toxocariosis have been attributed to the presence of *T. canis* and, less frequently, to *T. cati*; however, the latter cannot be

ruled out in some neurological infections. In experimental models, a greater tendency for *T. canis* to migrate to the CNS than *T. cati* has been observed [75].

In humans, many *Toxocara* infections in the CNS can go unnoticed and do not produce manifestations; therefore, their frequency is unknown. Some autopsy studies have shown the presence of larvae in the leptomeninges, gray and white matter of the cerebrum, cerebellum, thalamus, and spinal cord, unrelated to previous neurological signs [76].

In experimental models, it has been shown that *T. canis* larvae in the CNS can produce areas of necrosis, loss of Purkinje cells, glial nerve fibers and nerve sheaths, granulomatous lesions, emorrhagic and exudative lesions, vasculitis with eosinophilic and lymphocytic infiltration, gliosis and hemosiderosis. Some larvae can be observed without any response around them (see **Figure 2D**) [76, 77].

The clinical pictures of neurotoxocariosis in humans rarely occur simultaneously with signs of VLM. Most clinical manifestations occur in adult men with an average age of 35–42 years. Clinical signs associated with neurotoxocariosis may be indicators of different neurological disorders, such as myelitis (sensation disorders such as tingling sensation or hypoesthesia to specific dermatomes; motor disorders such as sphincter disturbances and conus medullaris syndrome; autonomic disturbances such as bladder and bowel dysfunction, and erectile failure), encephalitis (focal deficits, confused state, seizure and cognitive disorders) or meningitis (headaches, stiff neck/neck pain, nausea or vomiting, and Kernig's/Brudzinski's sign). Fever may occur on some occasions, although this is not a constant sign [76, 78].

The association between *T. Canis* seropositivity and cognitive development is controversial and has been widely discussed by several authors. Some authors, such as Magnaval et al. [79], found no association between seropositivity and any recognizable neurological syndrome; however, other authors have shown an association between seropositivity and lower cognitive development in children; however, due to incomplete controls and low sample size, the results are not clear [80–83].

In this context, Walsh and Haseeb [84], conducted one of the most conclusive studies; they analyzed a sample of 3,949 children representative of the US child population. Seropositive to *T. canis* children scored significantly lower on the Scale for Children-Revised (WISC-R) and Wide Range Achievement Test-Revised (WRAT-R) than seronegative children. Moreover, this relationship was independent of socioeconomic status, ethnicity, sex, rural residence, cytomegalovirus infection and blood lead levels. These results show another facet of the importance of toxocariosis as a neglected infection.

The diagnosis of neurotoxocariosis is difficult because there is no characteristic clinical syndrome. Due to the lack of confirmatory diagnostic tests and the nonspecific nature of its symptoms, neurotoxocariosis is probably underdiagnosed. As there is no universally accepted criterion for the diagnosis of this syndrome, a comprehensive diagnosis must be considered that must include the broad spectrum of neurological manifestations (signs of meningitis, encephalitis, myelitis, and/or cerebral vasculitis), together with high titers of antibodies against *Toxocara* in cerebrospinal fluid and/or blood, eosinophilia in blood and/or cerebrospinal fluid, suggestive radiological images, the presence of risk factors and clinical and radiological improvement after anthelmintic therapy [54, 78, 85].

5.4 Covert toxocariosis

Taylor et al. [86] proposed the term covert toxocariosis to describe a new clinical entity of human toxocariosis. It is currently considered that covert toxocariosis is

characterized by nonspecific symptoms and signs that are not associated with the VLM, OLM,or neurotoxocariosis. Clinical manifestations include asthma, acute bronchitis, pneumonia, wheezing with or without Loeffler's syndrome, chronic urticaria or eczema, lymphadenopathy, myositis, and pseudorheumatoid syndrome, with or without eosinophilia.

The excretion-secretion antigens produced by *T. canis* during migration are strong stimulants of Th2-associated immune responses and the consequent induction of IL-4, IL-5, IL10, and IL-13. This cytokine profile induces an increase in the level of specific IgE-antibodies and eosinophilia, which are effectors to kill some larvae. These same effectors contribute to airway hypersensitivity and inflammation, associating chronic *T. canis* infection with allergic disorders such as asthma, allergic rhinitis, atopic dermatitis, and urticaria [87–89].

Asthma is a lung disease characterized by an exacerbation of the immune response in the airways to a variety of external stimuli, which produces inflammation, bronchospasm, and obstruction of the airways, which are reversible spontaneously or with treatment. Since years ago, several epidemiological and experimental studies have shown a significant relationship between *Toxocara* infection and the development of asthma, mainly in children [90–92]. Meta-analysis studies, where extensive collections of published data were made, have confirmed this association. Li et al. [93] using data from 723 asthmatic patients and 807 controls found a significantly higher prevalence of *T. canis* infection in patients with asthma than in controls (OR 3.36, $P < .001$). Aghaei et al. [87] using data from 872 asthmatics and 4597 non-asthmatics children, found an increased risk for asthma in children with *Toxocara* infection seropositivity (OR, 1.91; 95% CI, 1.47–2.47).

The exact mechanisms by which *Toxocara* infection induces asthma and other allergic disorders remain unclear. *Toxocara* larval migration has been associated with an intense immune response, which causes strong allergic inflammation involving the intestine, muscle, liver, kidney, and lung [43, 94]. An animal model study (mice) showed that previous infection with *T. canis* intensified the ovalbumin-induced allergic airway inflammatory response associated with elevated eosinophil counts and IgE antibody levels in bronchoalveolar fluid and increased expression of IL-4 mRNA in the lung [92]. Several authors have described skin manifestations associated with toxocariosis and the risk of seropositive patients presenting skin lesions [95]. Significant associations have been observed between *Toxocara* seropositivity and pruritus (OR = 4.1, $P < 0.1$) and chronic urticaria (OR = 6.9, $P < 0.0001$) [96, 97]. Some of these patients presented with symptoms of VLM or OLM; however, the majority had no signs of previous *Toxocara* infection. Similar to neurotoxocariosis, there is no specific diagnosis for the clinical symptoms of cutaneous toxocariosis, so the participation of *T. canis* as a producer of skin alterations has probably been underestimated.

6. Comprehensive control of toxocariosis

The main role in the control of toxocariosis falls on the veterinarian, who is responsible for the diagnosis and deworming programs in dogs and cats, as well as the awareness and health education of pet owners so that they are aware of the threat of this and other infectious diseases from pets to humans. Periodic deworming of dogs and cats is an effective strategy to reduce the worm burden and, therefore, the number of eggs in the environment [98]. Puppies and kittens must be dewormed (piperazine, ivermectin, mebendazole, pyrantel, and febantel, among others) at

one month of age, and the treatment should be repeated at least twice in 15 days. In adult dogs, coproparasitoscopic examinations (Faust technique) should be carried out every 6 months, and positive dogs should be dewormed, with special care for dogs with known predatory habits. There are no effective antiparasitic agents against somatic larvae of *Toxocara* sp. In adult female dogs and cats, therefore, to reduce transplacental and/or lactogenic transmission to their puppies, it is necessary to reduce the number of infective eggs in the environment where they live.

The main way of infection in humans is the ingestion of infective eggs (L3 passive) that contaminate their environment. The fecal of dogs and, to a lesser extent, of cats in the soil of public parks, gardens, ridges, and rural areas, among others, is the cause of the gradual accumulation of infective eggs of *Toxocara* sp. in these places. Due to its high resistance, there are no chemical products capable of inactivating these eggs in the soil without seriously affecting other organisms and damaging the ecosystem. Therefore, one of the most important strategies for the control of environmental contamination is the immediate collection of dog feces eliminated during walks and its subsequent disposal in the drainage. It should always be considered that puppies and kittens are the main egg eliminators; however, adult dogs can also eventually eliminate eggs [99].

One of the risk factors most frequently associated with human toxocariosis is ownership of dogs or cats. For this reason, it is necessary to wash the floors daily with soap and water inside the houses or patios where the dogs live and defecate to detach the infective eggs from the surfaces and achieve their mechanical dragging to the drainage, considering that the infective eggs resist most commercial disinfectants. In addition, due to the possible presence of infective eggs attached to pet hair, it is necessary to periodically bathe and brush dogs and cats to avoid the presence of *Toxocara* eggs or other parasites in the hair.

Drainage water contaminated with *Toxocara* eggs can reach places where vegetables are grown or there may be dogs that defecate in these places, so vigorous washing of vegetables with drinking water is essential, especially those that are eaten raw and are grown at ground level (lettuce, cabbage, carrots, and strawberries, among many others) to reduce the risk of ingestion of infective eggs by humans. Another source of infection in humans is the ingestion of raw or undercooked meat or viscera of paratenic hosts infected with somatic larvae (chickens, pigs, cattle, and ducks, among others) in traditional dishes, so it is suggested that this type of dish is cooked with meat from animals raised in conditions free of the parasite. Cooking meat kills somatic larvae. At the government level, it is necessary to implement educational campaigns for the management of pet feces, knowledge of this and other zoonotic diseases, and the control of feral dogs and cats.

7. Health professionals involved

In summary, toxocariosis is a complex disease that, for its comprehensive control from a one health perspective, requires the knowledge of researchers and different health professionals. The veterinarian is the professional responsible for the diagnosis, control, and prevention of toxocariosis in pets that act as definitive hosts of the parasite (dogs and cats), as well as in domestic species that can act as paratenic hosts (chickens, pigs, beef, rabbits, etc.).

From the perspective of human health, the joint work of a very wide variety of health professionals is required to achieve an early and accurate diagnosis of the

disease or at least a firm suspicion of the condition. Among these are parasitologists, infectologists, pediatricians, allergists, ophthalmologists, neurologists, dermatologists, imaging specialists, and epidemiologists, who are sensitized and trained to cover the entire clinical spectrum that human toxocariosis can produce. In addition, highly trained laboratory personnel are required for the parasitological, immunological, and molecular diagnosis of toxocariosis in animals and humans.

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Conflict of interest

The authors declare no conflict of interest.

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References

[1] Deplazes P, Eckert J, Mathis A, Samson-Himmelstjerna GV, Zahner H. Parasitology in Veterinary Medicine. Wageningen Academic Publishers: Wageningen; 2016. p. 652

[2] González-García T, Muñoz-Guzmán MA, Sánchez-Arroyo H, Prado-Ochoa MG, Cuéllar-Ordaz JA, Alba-Hurtado F. Experimental transmission of *Toxocara canis* from *Blattella germanica* and *Periplaneta americana* cockroaches to a paratenic host. Veterinary Parasitology. 2017;**246**:5-10

[3] Alba-Hurtado F. Parasitología Veterinaria. Ciudad de México: UNAM; 2020. p. 184

[4] Schnieder T, Laabs EM, Welz C. Larval development of *Toxocara canis* in dogs. Veterinary Parasitology. 2011;**175**:193-206

[5] Muñoz-Guzmán MA, Alba-Hurtado F. Progesterone and prolactin: Hormones important for the reactivation of *Toxocara canis* larvae in bitches. Advances in Neuroimmune Biology. 2018;**7**:67-78

[6] Coati N, Schnieder T, Epe C. Vertical transmission of *Toxocara cati* Schrank 1788 (Anisakidae) in the cat. Parasitology Research. 2004;**92**:142-146

[7] Rostami A, Riahi SM, Hofmann A, Ma G, Wang T, Behniafar H, et al. Global prevalence of *Toxocara* infection in dogs. Advances in Parasitology. 2020;**109**:561-583

[8] Rostami A, Sepidarkish M, Ma G, Wang T, Ebrahimi M, Fakhri Y, et al. Global prevalence of *Toxocara* infection in cats. Advances in Parasitology. 2020;**109**:615-639

[9] Overgaauw PA, Nederland V. Aspects of *Toxocara* epidemiology: Toxocarosis in dogs and cats. Critical Reviews in Microbiology. 1997;**23**:233-251

[10] Fakhri Y, Gasser RB, Rostami A, Fan CK, Ghasemi SM, Javanian M, et al. *Toxocara* eggs in public places worldwide-A systematic review and meta-analysis. Environmental Pollution. 2018;**242**:1467-1475

[11] Fisher M. *Toxocara cati*: An underestimated zoonotic agent. Trends in Parasitology. 2003;**19**:167-170

[12] Rostami A, Riahi SM, Holland CV, Taghipour A, Khalili-Fomeshi M, Fakhri Y, et al. Seroprevalence estimates for toxocariasis in people worldwide: A systematic review and metaanalysis. PLoS Neglected Tropical Diseases. 2019;**13**:e0007809

[13] Gyang PV, Akinwale OP, Lee YL, Chuang TW, Orok AB, Ajibaye O, et al. Seroprevalence, disease awareness, and risk factors for *Toxocara canis* infection among primary schoolchildren in Makoko, an urban slum community in Nigeria. Acta Tropica. 2015;**46**:135-140

[14] Holland CV. Knowledge gaps in the epidemiology of *Toxocara*: The enigma remains. Parasitology. 2017;**144**:81-94

[15] Hotez PJ, Wilkins PP. Toxocariasis: America's most common neglected infection of poverty and a helminthiasis of global importance? PLoS Neglected Tropical Diseases. 2009;**3**:e400

[16] Manini MP, Marchioro AA, Colli CM, Nishi L, Falavigna-Guilherme AL. Association between contamination of public squares and seropositivity for *Toxocara* spp. in children. Veterinary Parasitology. 2012;**188**:48-52

[17] Hernández SA, Gabrie JA, Rodríguez CA, Matamoros G, Rueda MM, Canales M, et al. An integrated study of *Toxocara* infection in Honduran children: Human seroepidemiology and environmental contamination in a coastal community. Tropical Medicine and Infectious Disease. 2020;**5**:135

[18] Wang S, Li H, Yao Z, Li P, Wang D, Zhang H, et al. *Toxocara* infection: Seroprevalence and associated risk factors among primary school children in central China. Parasite. 2020;**27**:30. DOI: 10.1051/parasite/2020028

[19] Hoffmeister B, Glaeser S, Flick H, Pornschlegel S, Suttorp N, Bergmann F. Cerebral toxocariasis after consumption of raw duck liver. The American Journal of Tropical Medicine and Hygiene. 2007;**76**:600-602. DOI: 10.1.1.318.4997&rep=rep1&type=pdf

[20] Yoshikawa M, Nishiofuku M, Moriya K, Ouji Y, Ishizaka S, Kasahara K, et al. A familial case of visceral toxocariasis due to consumption of raw bovine liver. Parasitology International. 2008;**57**:525-529

[21] Choi D, Lim JH, Choi DC, Lee KS, Paik SW, Kim SH, et al. Transmission of *Toxocara canis* via ingestion of raw cow liver: A cross-sectional study in healthy adults. The Korean Journal of Parasitology. 2012;**50**:23-27. DOI: 10.3347/kjp.2012.50.1.23

[22] Karaca I, Menteş J, Nalçacı S. *Toxocara* neuroretinitis associated with raw meat consumption. Turkish Journal of Ophthalmology. 2018;**48**:258. DOI: 10.4274/tjo.27085

[23] Roddie G, Holland C, Stafford P, Wolfe A. Contamination of fox hair with eggs of *Toxocara canis*. Journal of Helminthology. 2008;**82**:293-296

[24] da Cunha-Amaral HL, Rassier GL, Pepe MS, Gallina T, Villela MM, de Oliveira-Nobre M, et al. Presence of *Toxocara canis* eggs on the hair of dogs: A risk factor for visceral larva migrans. Veterinary Parasitology. 2010;**174**:115-118

[25] Bakhshani A, Maleki M, Haghparast A, Shirvan SP, Borji H. A survey on *Toxocara cati* eggs on the hair of stray cats: A potential risk factor for human toxocariasis in Northeastern Iran. Comparative Immunology, Microbiology and Infectious Diseases. 2019;**64**:10-13

[26] Maurelli MP, Santaniello A, Fioretti A, Cringoli G, Rinaldi L, Menna LF. The presence of *Toxocara* eggs on dog's fur as potential zoonotic risk in animal-assisted interventions: A systematic review. Animals. 2019;**9**:827. DOI: 10.3390/ani9100827

[27] Keegan JD, Holland CV. A comparison of *Toxocara canis* embryonation under controlled conditions in soil and hair. Journal of Helminthology. 2013;**87**:78-84

[28] Miller AD. Pathology of larvae and adults in dogs and cats. Advances in Parasitology. 2020;**109**:537-544

[29] Parsons JC. Ascarid infections of cats and dogs. The Veterinary Clinics of North America: Small Animal Practice. 1987;**17**:1307-1339

[30] Epe C. Intestinal nematodes: Biology and control. Veterinary Clinics of North America: Small Animal Practice. 2009;**39**:1091-1107. DOI: 10.1016/j.cvsm.2009.07.002

[31] Ursache AL, Györke A, Mircean V, Dumitrache MO, Codea AR, Cozma V. *Toxocara cati* and other parasitic enteropathogens: More commonly found in owned cats with gastrointestinal signs than in clinically healthy ones. Pathogens. 2021;**10**:198

[32] Muñoz-Guzmán MA, Alba-Hurtado F. Secretory-excretory antigens of *Toxocara canis* recognized by puppies of the Mexico City metropolitan area. Vet Méx. 2010;**41**:59-64

[33] Ma G, Holland CV, Wang T, Hofmann A, Fan CK, Maizels RM, et al. Human toxocariasis. The Lancet Infectious Diseases. 2018;**18**:14-24

[34] Badri M, Eslahi AV, Olfatifar M, Dalvand S, Houshmand E, Abdoli A, et al. Keys to unlock the enigma of ocular toxocariasis: A systematic review and meta-analysis. Ocular Immunology and Inflammation. 2021;**29**:1-12

[35] Beaver PC, Snyder CH, Carrera GM, Dent JH, Lafferty JW. Chronic eosinophilia due to visceral larva migrans: Report of three cases. Pediatrics. 1952;**9**:7-19

[36] Carvalho EA, Rocha RL. Toxocariasis: Visceral larva migrans in children. The Journal of Pediatrics. 2012;**87**:100-110

[37] Lim JH. Toxocariasis of the liver: Visceral larva migrans. Abdominal Imaging. 2008;**33**:151-156

[38] Morsy TA. Toxocariasis: Visceral and ocular larva migrans. Journal of the Egyptian Society of Parasitology. 2020;**50**:41-48

[39] Aljeboori TI, Ivey MH. *Toxocara canis* infection in baboons. The American Journal of Tropical Medicine and Hygiene. 1970;**19**:249-254

[40] Morales OL, Lopez MC, Nicholls RS, Agudelo C. Identification of *Toxocara canis* antigens by Western blot in experimentally infected rabbits. Revista do Instituto de Medicina Tropical de São Paulo. 2002;**44**:213-216

[41] Del Río-Araiza VH, Nava-Castro KE, Alba-Hurtado F, Quintanar-Stephano A, Muñoz-Guzmán MA, Cuenca-Micò O, et al. Endocrine immune interactions during chronic toxocariasis caused by *Toxocara canis* in a murine model: New insights into the pathophysiology of an old infection. Veterinary Parasitology. 2018;**252**:173-179

[42] Kavitha KT, Sreekumar C, Latha BR, Gowri AM, Nagarajan B, Azhahianambi P, et al. Migratory behaviour and pathological changes of *Toxocara canis* in organs and tissues of experimentally infected Balb/c mice. J Entomol Zool St. 2018;**6**:2388-2392

[43] Alba-Hurtado F, Muñoz-Guzmán MA, Valdivia-Anda G, Tórtora JL, Ortega-Pierres MG. *Toxocara canis*: Larval migration dynamics, detection of antibody reactivity to larval excretory–secretory antigens and clinical findings during experimental infection of gerbils (*Meriones unguiculatus*). Experimental Parasitology. 2009;**122**:1-5

[44] Snyder CH. Visceral larva migrans Ten years'experience. Pediatrics. 1961;**28**:85-91

[45] Baldisserotto M, Conchin CF, Soares MDG, Araujo MA, Kramer B. Ultrasound findings in children with toxocariasis: Report on 18 cases. Pediatric Radiology. 1999;**29**:316-319. DOI: 10.1007/s002470050596.pdf

[46] Wiśniewska-Ligier M, Woźniakowska-Gęsicka T, Sobolewska-Dryjańska J, Markiewicz-Jóźwiak A, Wieczorek M. Analysis of the course and treatment of toxocariasis in children-a long-term observation. Parasitology Research. 2012;**110**:2363-2371. DOI: 10.1007/s00436-011-2772-y

[47] Desai SN, Pargewar SS, Agrawal N, Bihari C, Rajesh S. Hepatic visceral larva

migrans with atypical manifestations: A report of three cases. Tropical Gastroenterology. 2020;**39**:211-221. DOI: 10.7869/tg.507

[48] Rugiero E, Cabera ME, Ducach G, Noemi I, Viovy A. Systemic toxocariasis in the adult patient. Revista Médica de Chile. 1995;**40**:1097-1099

[49] Kuenzli E, Neumayr A, Chaney M, Blum J. Toxocariasis-associated cardiac diseases—A systematic review of the literature. Acta Tropica. 2016;**154**:107-120

[50] Mohamad S, Azmi N, Noordin R. Development and evaluation of a sensitive and specific assay for diagnosis of human toxocariasis by use of three recombinant antigens (TES-26, TES-30USM, and TES-120). Journal of Clinical Microbiology. 2009;**47**:1712-1717. DOI: 10.1128/JCM.00001-09

[51] Fillaux J, Magnaval JF. Laboratory diagnosis of human toxocariasis. Veterinary Parasitology. 2013;**193**: 327-336

[52] Mazur-Melewska K, Mania A, Sluzewski W, Figlerowicz M. Clinical pathology of larval toxocariasis. Advances in Parasitology. 2020; **109**:153-163

[53] Özbakış G, Doğanay A. Visceral larva migrans detection using PCR–RFLP in BALB/c mice infected with *Toxocara canis*. Journal of Helminthology. 2020;**94**:1-8

[54] Dietrich CF, Cretu C, Dong Y. Imaging of toxocariasis. Advances in Parasitology. 2020;**109**:165-187

[55] Wilder HC. Nematode endophthalmitis. Transactions of the American Academy of Ophthalmology and Otolaryngology. 1950;**55**:99-109

[56] Nichols RL. The etiology of visceral larva migrans: I. Diagnostic morphology of infective second-stage *Toxocara* larvae. Journal of Parasitology. 1956;**42**:349. DOI: 10.2307/3274518

[57] MRH T. Ocular toxocariasis. In: Holland CV, Smith HV, editors. Toxocara: The Enigmatic Parasite. Pondicherry: Cromwell Press Ltd; 2006. pp. 127-144

[58] Pivetti-Pezzi P. Ocular toxocariasis. International Journal of Medical Sciences. 2009;**6**:129-130. DOI: 10.7150/ijms.6.129

[59] Zibaei M, Sadjjadi SM, Jahadi-Hosseini SH. *Toxocara cati* larvae in the eye of a child: A case report. Asian Pacific Journal of Tropical Biomedicine. 2014;**4**:S53-S55. DOI: 10.12980/APJTB.4.2014C1281

[60] Ahn SJ, Woo SJ, Jin Y, Jin Y, Chang YS, Kim TW, et al. Clinical features and course of ocular Toxocariasis in adults. PLoS Neglected Tropical Diseases. 2014;**8**:e2938. DOI: 10.1371/journal.pntd.0002938

[61] Sharkey JA, McKay PS. Ocular toxocariasis in a patient with repeatedly negative ELISA titre to *Toxocara canis*. The British Journal of Ophthalmology. 1993;**77**:253-254. DOI: 10.1136/bjo.77.4.253

[62] Fata A, Hosseini SM, Woo SJ, Zibaei M, Berenji F, Farash BRH, et al. Frequency of *Toxocara* antibodies in patients clinically suspected to ocular toxocariasis in the northeast of Iran. Iranian Journal of Parasitology. 2020;**16**:305-311

[63] Alba-Hurtado F, Tortora PJL, Tsutsumi V, Ortega-Pierres MG. Histopathological investigation of experimental ocular toxocariasis

in gerbils. International Journal for Parasitology. 2000;**30**:143-147

[64] Taylor MRH. The epidemiology of ocular toxocariasis. Journal of Helminthology. 2001;**75**:109-118

[65] Hayashi E, Akao N, Fujita K. Evidence for the involvement of the optic nerve as a migration route for larvae in ocular toxocariasis of *Mongolian gerbils*. Journal of Helminthology. 2003;**77**:311-315

[66] Choi KD, Choi JH, Choi SY, Jung JH. *Toxocara* optic neuropathy: Clinical features and ocular findings. International Journal of Ophthalmology. 2018;**11**:520-523

[67] Yokoi K, Goto H, Sakai JI, Usui M. Clinical features of ocular toxocariasis in Japan. Ocular Immunology and Inflammation. 2003;**11**:269-275

[68] Stewart JM, Cubillan LD, Cunningham JR, Emmett T. Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. Retina. 2005;**25**:1005-1013. DOI: 10.1097/00006982-200512000-00009

[69] Bae KW, Ahn SJ, Park KH, Woo SJ. Diagnostic value of the serum anti-toxocara IgG titer for ocular toxocariasis in patients with uveitis at a tertiary hospital in Korea. Korean Journal of Ophthalmology. 2016;**30**:258-264

[70] Shields JA. Ocular toxocariasis. A review. Survey of Ophthalmology. 1984;**28**:361-381

[71] Campbell JP, Wilkinson CP. Imaging in the diagnosis and management of ocular toxocariasis. International Ophthalmology Clinics. 2012;**52**:145-153

[72] Inchauspe S, Echandi LV, Dodds EM. Diagnosis of ocular toxocariasis by detecting antibodies in the vitreous humor. Archivos de la Sociedad Española de Oftalmología. 2018;**93**:220-224

[73] Beautyman W, Woolf AL. An *Ascaris* larva in the brain in association with acute anterior poliomyelitis. The Journal of Pathology and Bacteriology. 1951;**63**:635-647

[74] Beautyman W, Beaver PC, Buckley JJ, Woolf AL. Review of a case previously reported as showing an ascarid larva in the brain. The Journal of Pathology and Bacteriology. 1966;**91**:271-273

[75] Springer A, Heuer L, Janecek-Erfurth E, Beineke A, Strube C. Histopathological characterization of *Toxocara canis*-and *T. cati*-induced neurotoxocarosis in the mouse model. Parasitology Research. 2019;**118**:2591-2600

[76] Meliou M, Mavridis IN, Pyrgelis ES, Agapiou E. Toxocariasis of the nervous system. Acta Parasitologica. 2020;**65**:291-299

[77] Cardillo N, Rosa A, Ribicich M, López C, Sommerfelt I. Experimental infection with *Toxocara cati* in BALB/c mice, migratory behaviour and pathological changes. Zoonoses and Public Health. 2009;**56**:198-205

[78] Deshayes S, Bonhomme J, de La Blanchardière A. Neurotoxocariasis: A systematic literature review. Infection. 2016;**44**:565-574. DOI: 10.1007/s15010-016-0889-8

[79] Magnaval JF, Galindo V, Glickman LT, Clanet M. Human *Toxocara* infection of the central nervous system and neurological disorders: A case control study. Parasitology. 1997;**115**:537-543

[80] Worley G, Green JA, Frothingham TE, Sturner RA, Walls KW, Pakalnis VA, et al. *Toxocara* canis infection: Clinical and epidemiological associations with seropositivity in kindergarten children. The Journal of Infectious Diseases. 1984;**149**:591-597

[81] Jarosz W, Mizgajska-Wiktor H, Kirwan P, Konarski J, Rychlicki W, Wawrzyniak G. Developmental age, physical fitness and *Toxocara* seroprevalence amongst lower secondary students living in rural areas contaminated with *Toxocara* eggs. Parasitology. 2010;**137**:53-63

[82] Marmor M, Glickman L, Shofer F, Faich LA, Rosenberg C, Cornblatt B, et al. *Toxocara canis* infection of children: Epidemiologic and neuropsychologic findings. American Journal of Public Health. 1987;**77**:554-559. DOI: 10.2105/AJPH.77.5.554

[83] Nelson S, Greene T, Ernhart CB. *Toxocara canis* infection in preschool age children: Risk factors and the cognitive development of preschool children. Neurotoxicology and Teratology. 1996;**18**:167-174

[84] Walsh MG, Haseeb MA. Reduced cognitive function in children with toxocariosis in a nationally representative sample of the United States. International Journal for Parasitology. 2012;**42**:1159-1163

[85] Fan CK. Pathogenesis of cerebral toxocariasis and neurodegenerative diseases. Advances in Parasitology. 2020;**109**:233-259

[86] Taylor MR, Keane CT, O'connor P, Girdwood ARW, Smith H. Clinical features of covert toxocariasis. Scandinavian Journal of Infectious Diseases. 1987;**19**:693-696

[87] Aghaei S, Riahi SM, Rostami A, Mohammadzadeh I, Javanian M, Tohidi E, et al. *Toxocara* spp. infection and risk of childhood asthma: A systematic review and meta-analysis. Acta Tropica. 2018;**182**:298-304

[88] Maizels RM. *Toxocara canis*: Molecular basis of immune recognition and evasion. Veterinary Parasitology. 2013;**193**:365-374

[89] Mazur-Melewska K, Figlerowicz M, Cwalińska A, Mikoś H, Jończyk-Potoczna K, Lewandowska-Stachowiak M, et al. Production of interleukins 4 and 10 in children with hepatic involvement in the course of *Toxocara* spp. infection. Parasite Immunology. 2016;**38**:101-107. DOI: 10.1111/pim.12303

[90] Hakim SL, Thadasavanth M, Shamilah RR, Yogeswari S. Prevalence of *Toxocara canis* antibody among children with bronchial asthma in Klang Hospital, Malaysia. Transactions of the Royal Society of Tropical Medical and Hygiene. 1997;**91**:528-528

[91] Muñoz-Guzmán MA, del Río-Navarro BE, Valdivia-Anda G, Alba-Hurtado F. The increase in seroprevalence to *Toxocara canis* in asthmatic children is related to cross-reaction with *Ascaris suum* antigens. Allergologia et Immunopathologia. 2010;**38**:115-121

[92] Pinelli E, Brandes S, Dormans J, Gremmer E, Van Loveren H. Infection with the roundworm *Toxocara canis* leads to exacerbation of experimental allergic airway inflammation. Clinical and Experimental Allergy. 2008;**38**:649-658

[93] Li L, Gao W, Yang X, Wu D, Bi H, Zhang S, et al. Asthma and toxocariasis. Annals of Allergy, Asthma & Immunology. 2014;**113**:187-192

[94] Cooper PJ. *Toxocara canis* infection: An important and neglected

environmental risk factor for asthma? Clinical and Experimental Allergy. 2008;**38**:551-553

[95] Gavignet B, Piarroux R, Aubin F. Millon L, Humbert P. Cutaneous manifestations of human toxocariasis. Journal of the American Academy of Dermatology 2008;59:1031-1042

[96] Wolfrom E, Chene G, Boisseau H, Beylot C, Geniaux M, Taieb A. Chronic urticaria and *Toxocara canis*. Lancet. 1995;**345**:196

[97] Wolfrom E, Chene G, Lejoly-Boisseau H, Beylot C, Geniaux M, Taieb A. Chronic urticaria and toxocara canis infection. A case-control study. Annales de Dermatologie et de Venereologie. 1996, January;**123**(4):240-246

[98] Palmer CS, Thompson RA, Traub RJ, Rees R, Robertson ID. National study of the gastrointestinal parasites of dogs and cats in Australia. Veterinary Parasitology. 2008;**151**:181-190

[99] Lee AC, Schantz PM, Kazacos KR, Montgomery SP, Bowman DD. Epidemiologic and zoonotic aspects of ascarid infections in dogs and cats. Trends in Parasitology. 2010;**26**:155-161