

Neglected Parasitic Infections in the United States: Toxocariasis

Dana M. Woodhall,* Mark L. Eberhard, and Monica E. Parise

Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract. Toxocariasis is a preventable parasitic disease that is caused by the dog and cat roundworms *Toxocara cani* and *T. cati*, respectively. Humans become infected when they accidentally ingest infectious *Toxocara* eggs commonly found in contaminated soil; children are most often affected. Clinical manifestations of *Toxocara* infection in humans include ocular toxocariasis and visceral toxocariasis. Although infection with *Toxocara* can cause devastating disease, the burden of toxocariasis in the United States population remains unknown. In addition, risk factors for acquiring infection need to be better defined, and research needs to be conducted to better understand the pathophysiology and clinical course of toxocariasis. Development of diagnostic tests would enable clinicians to detect active infection, and determination of optimal drug regimens would ensure patients were appropriately treated. Addressing these public health gaps is necessary to understand and address the impact of toxocariasis in the United States.

BACKGROUND

Toxocariasis, a parasitic disease caused by dog roundworms (*Toxocara canis*), cat roundworms (*T. cati*), or possibly other species of *Toxocara*, can lead to debilitating disease in humans and mainly affects children. Studies have shown that toxocariasis may be among the most common human parasitic infections in the United States.¹ It is estimated that millions of Americans have been exposed to the *Toxocara* parasite, although how many persons have become ill from the infection is unknown.² Toxocariasis is considered a neglected parasitic infection, and few resources have been devoted to increasing public and healthcare provider awareness of this preventable disease. In addition, research towards increasing epidemiologic knowledge, improving diagnostic tests, and defining optimal treatment regimens for toxocariasis remains limited.

Transmission of the *Toxocara* parasite occurs when an infected dog or cat sheds eggs in their feces into the environment; it takes 2–4 weeks for larvae to develop and for the eggs to become infectious.³ *Toxocara* eggs are typically found in soil contaminated with dog or cat feces; humans become infected when they accidentally ingest the microscopic eggs, usually through touching contaminated hands to their mouth. Children are at higher risk for infection because of their play habits and poor hygiene practices. Although less common, humans can also become infected if they eat undercooked meat from an animal that is infected with *Toxocara* larvae. Once ingested, the larvae can burrow into and travel through blood vessels to various body organs causing an inflammatory reaction; in humans, *Toxocara* larvae do not undergo further growth or maturation into adult worms.

There are three well-described clinical presentations of *Toxocara* infection in humans; visceral toxocariasis (VT) or visceral larva migrans, when body organs, such as the liver or lungs, are affected; ocular toxocariasis (OT) or ocular larva migrans, when the eye is affected; and covert or common toxocariasis, when symptoms remain mild and non-specific. Liver and pulmonary damage are the most commonly described clinical complications in VT patients; other less common disease

manifestations caused by *Toxocara* infection include neurotoxocariasis, eosinophilic meningitis, pericardial effusion, and myocarditis.^{4–8} In OT patients, inflammation caused by *Toxocara* larvae can cause severe, irreversible ophthalmologic injury, such as retinal detachment or formation of a subretinal granulomatous mass or scar; unilateral permanent vision loss develops in many OT patients.

Eosinophilia, hypergammaglobulinemia, and increased isohemagglutinin A and B titers are laboratory findings associated with acute *Toxocara* infection. Laboratory abnormalities are less likely to be found in OT patients than in VT patients. Serologic antibody tests to the *Toxocara* parasite are available in laboratories throughout the United States. The recommended test for toxocariasis is an enzyme immunoassay (EIA) using *Toxocara* excretory–secretory antigens to detect IgG against the *Toxocara* larvae. In patients with a presumptive diagnosis of toxocariasis, sensitivity of the *Toxocara* EIA is reported to be 78% and 73% for VT and OT, respectively, and the specificity of the test is > 90% for VT and OT at a titer $\geq 1:32$.⁹ EIA titers can remain elevated for years, making it difficult to determine if a positive serologic test result indicates past exposure versus active infection. Stool examination for ova and parasites is not useful in diagnosing *Toxocara* because the larvae do not mature into adult worms and therefore no eggs are shed.

Albendazole or mebendazole are the recommended treatments for *Toxocara* infection although these drugs are not approved by the Food and Drug Administration for this indication.¹⁰ To date, no randomized controlled treatment studies have been conducted in the United States and questions remain surrounding the optimum drug dose and duration of therapy; most clinicians prescribe a five-day treatment course, although there are reports of 20-day drug courses being used in patients with severe symptoms. Corticosteroids are beneficial in reducing inflammation and are often recommended as adjunctive therapy especially in severe VT cases and in most OT cases. No recommendations exist for treating asymptomatic patients who have positive serologic test results; what long-term clinical sequelae may arise from untreated *Toxocara* infection is unknown. Prevention strategies include teaching children not to eat soil, promoting good hand washing hygiene, and covering sandboxes when not in use. Pets should be regularly dewormed and communities should urge residents to keep pets away from playground areas and require pet owners to properly dispose of their pet's feces.

*Address correspondence to Dana M. Woodhall, Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop MS A-06, Atlanta, GA 30333. E-mail: dqw6@cdc.gov

PUBLIC HEALTH IMPORTANCE OF TOXOCARIASIS IN THE UNITED STATES

Toxocariasis is a completely preventable disease and although reports of devastating disease occurring in patients continue to be published in the scientific literature, little research has been devoted to understanding the extent of burden caused by infection with *Toxocara* within the United States population. Toxocariasis is not a nationally reportable disease and no surveillance systems are currently in place to track cases. In an effort to quantify how many persons have been infected with *Toxocara* in the United States, a nationally representative seroprevalence survey was conducted during 1988–1994.¹¹ Testing of samples collected during the Third National Health and Nutrition Examination Survey demonstrated that *Toxocara* seroprevalence was 13.9% in the U.S. population ≥ 6 years of age. Non-Hispanic blacks (21%) had significantly higher positive seroprevalence rates than non-Hispanic whites (12%). Multiple studies consistently report that the disease primarily affects children; the average age of VT patients is 2–7 years and the average age of OT patients is 8–16 years^{12,13} National Health and Nutrition Examination Survey data for children 6–11 years of age demonstrates a difference in *Toxocara* seroprevalence rates; 15% in black girls, 20% in black boys, and $< 5\%$ in white children. Epidemiologic research has shown associations between *Toxocara* and increased blood lead levels, lower education status, and poverty.¹¹ Other risk factors for *Toxocara* infection, such as geophagia, pet ownership, and living in warmer climates, have been identified but there is variability in the significance of these relationships among different studies.^{14,15} An association between *Toxocara* and toxoplasmosis, another neglected parasitic infection, was highlighted in one study in which infection with one of the parasites was associated with almost twice the risk of infection with the other parasite compared with those who were not dually infected.¹⁶

Determining the prevalence and incidence of VT is extremely challenging because the clinical manifestations are nonspecific, leading to under-recognition of cases by health professionals. A review of VT case reports in the literature for 1952–1972 documented 970 VT cases in western countries.¹⁷ Most current data on VT is obtained through small retrospective cohort studies and case reports; these reports highlight the wide range of clinical disease attributed to *Toxocara* infection, including respiratory, gastrointestinal, and neurologic illnesses. Although rare, *Toxocara* infection has led to death in adult and pediatric VT patients.^{18–20}

Toxocara infection has also been linked to diminished lung function, cognitive changes, and adverse neuropsychological effects.^{21,22} Questions remain surrounding the link between asthma and allergic symptoms, such as urticaria and infection with *Toxocara*. Studies have shown a decrease in forced expiratory volume in one second in persons infected with *Toxocara* compared with those without infection.²³ A separate study that tested children with asthma for *Toxocara* antibodies found no significant association between asthma and *Toxocara* infection.²⁴ Given the enormous numbers of children with asthma in the United States and its attendant economic burden, there is a strong need to clarify the association between asthma and *Toxocara* infection.

Research on the prevalence of OT is limited and has been conducted only in single ophthalmologic centers; based on a

survey of ophthalmologists in Alabama, the prevalence of OT was estimated to be 1 case/1,000 persons.²⁵ In a separate study conducted in California, the investigators estimated that 1.0% of persons with vision loss had *Toxocara* infection as the cause.¹³ In a recent national survey of ophthalmologic subspecialists, 559 respondents reported 68 cases of OT in children within one year; the median patient age was 8.5 years, and 68% of patients with reported clinical data experienced permanent vision loss.²⁶

Studies have shown that *Toxocara* is widespread in the environment and throughout the dog and cat population in the United States. Soil sample testing for *Toxocara* eggs in public parks and sandboxes, has demonstrated rates ranging from 0.3% to 39%.^{27,28} In dog and cat fecal samples tested during 2013, data collected from national laboratories showed that 1.8% of tested pet dogs were positive for *Toxocara* infection and 4.7% of tested pet cats were positive for *Toxocara* infection.²⁹ A recent survey examining more than one million canine fecal samples taken from dogs at veterinary clinics in the United States showed a *Toxocara* prevalence rate of 2.2%; rates were even higher (6.5%) in puppies less than six months old.³⁰ A separate study that examined feline fecal samples in cats residing in two shelter in New York demonstrated a *T. cati* prevalence rate of 21%, indicating that shelter animals may have higher prevalence rates than household pets.³¹

GAPS IN CURRENT KNOWLEDGE AND FUTURE DIRECTIONS

The most critical knowledge gap needing to be addressed for toxocariasis remains defining the true impact of the disease in the United States through population-based studies; without this baseline information it is difficult to determine the level of resources that should be devoted to this infection. Defining the economic costs incurred by toxocariasis would also assist in this decision-making process. Prevalence and incidence rate data also need to be monitored over time in an effort to assess the effectiveness of prevention strategies and success of treatment interventions.

Efforts also need to be focused on better defining the epidemiologic characteristics of toxocariasis cases and the demographics of affected groups. Further exploration into the differences in risk for infection among minority populations, as well as regional variations, and differences in disease prevalence in urban versus rural settings. The results of these studies will enable us to target risk behaviors and direct prevention messages to high risk groups.

Numerous questions remain surrounding the pathophysiology and clinical manifestations of the disease. Why some patients remain asymptomatic or have nonspecific self-limited symptoms and severe clinical manifestations develop in others is not fully understood. In addition, why VT develops in some patients and others have only OT remains unknown. Long-term medical consequences of *Toxocara* infection, such as asthma and neurocognitive delays, should be a research priority. Initiating large-scale prospective studies aimed at defining the spectrum of clinical disease will help us to answer these questions. One of the major barriers to collecting toxocariasis prevalence data and clinical information is that many healthcare providers are not familiar with the disease, leading

to missed diagnosis in patients infected with *Toxocara*. Education of healthcare providers regarding toxocariasis is a priority.

Presently, diagnostic testing for *Toxocara* infection is limited to antibody testing, which cannot differentiate current active disease and past infection. Development of a test that can accurately diagnose recent infection will help clinicians confirm active *Toxocara* infection in patients and potentially lead to initiation of treatment to prevent clinical disease. No randomized controlled trials of treatment medications have been conducted; current treatment guidelines are based on clinician experience and expert opinion. Drug trials to determine the optimal therapeutic agent and ideal dosage and duration of therapy are needed. Advances in ophthalmologic surgical techniques may help decrease the number of patients with permanent vision loss caused by OT. Studies need to be conducted to determine if persons who are asymptomatic but seropositive for *Toxocara* need to be treated.

Because toxocariasis is a zoonotic disease, increasing our knowledge about how the disease affects dogs and cats is crucial in preventing animal and human infection. Questions have been raised regarding anthelmintic drug resistance in dogs and cats.³² In addition, the challenge of getting pet owners to have their dogs and cats tested and treated appropriately for *Toxocara* remains.

Although further investigation is needed to guide public health and clinical recommendations, there are steps that can be taken right now. For example, coverage of programmatic interventions focused on reduction of prevalence in animals and prevention of transmission to humans should be improved. Educational campaigns directed at the general public and healthcare professionals would help to increase awareness about toxocariasis. Working with veterinarians to increase pet owners' understanding of the importance of frequent deworming and the need to properly dispose of their pet's feces will also help highlight this neglected parasitic infection. An increase in our understanding of this devastating yet preventable disease, coupled with improved disease control efforts, will ultimately lead to a decrease in disease burden in humans and animals.

Received December 10, 2013. Accepted for publication January 9, 2014.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Authors' addresses: Dana M. Woodhall, Mark L. Eberhard, and Monica E. Parise, Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, GA, E-mails: dqw6@cdc.gov, mle1@cdc.gov, and mep0@cdc.gov.

REFERENCES

- Hotez PJ, Wilkins PP, 2009. Toxocariasis: America's most common neglected infection of poverty and a helminthiasis of global importance. *PLoS Negl Trop Dis* 3: e400.
- Hotez PJ, 2008. Neglected infections of poverty in the United States of America. *PLoS Negl Trop Dis* 2: e256.
- Glickman LT, Schantz PM, 1981. Epidemiology and pathogenesis of zoonotic toxocariasis. *Epidemiol Rev* 3: 230–250.
- Marx C, Lin J, Masruha MR, Rodrigues MG, da Rocha AJ, Vilanova LCP, Gabbai AA, 2007. Toxocariasis of the CNS simulating acute disseminated encephalomyelitis. *Neurology* 69: 806–807.
- Hotez PJ, 1993. Visceral and ocular larva migrans. *Semin Neurol* 13: 175–179.
- Keller M, Pavia AT, Byington CL, 2008. Possible intrafamilial transmission of *Toxocara* causing eosinophilic meningitis in an infant. *Pediatr Infect Dis J* 27: 849–850.
- Vargo TA, Singer DB, Gillatte PC, Fernback DJ, 1977. Myocarditis due to visceral larva migrans. *J Pediatr* 90: 322–323.
- Matsuki Y, Fujii T, Nakamura-Uchiyama F, Hiromatsu K, Nawa Y, Hsyashi T, Ohtomi S, 2007. Toxocariasis presenting with multiple effusions in the pericardial space, thoracic cavity, and Morrison's pouch. *Intern Med* 46: 913–914.
- Smith HV, 1993. Antibody reactivity in human toxocariasis. Lewis JW, Maizels RM, eds. *Toxocara and Toxocariasis: Clinical, Epidemiological, and Molecular Perspectives*. London: Institute of Biology and the British Society for Parasitology, 91–109.
- Drugs for Parasitic Infections, 2010. *The Medical Letter*. New Rochelle, NY: The Medical Letter, Inc., 61.
- Won KY, Kruszon-Moran D, Schantz PM, Jones JL, 2008. National seroprevalence and risk factors for zoonotic *Toxocara* spp. infection. *Am J Trop Med Hyg* 79: 552–557.
- Magnaval JF, Glickman LT, Dorchie P, Morassin B, 2001. Highlights of human toxocariasis. *Korean J Parasitol* 39: 1–11.
- Stewart J, Cubillan LD, Cunningham E, 2005. Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. *Retina* 25: 1005–1013.
- Schantz PM, Weis PE, Pollard ZF, White MC, 1980. Risk factors for toxocaral ocular larva migrans: a case-control study. *Am J Public Health* 70: 1269–1272.
- Congdon P, Lloyd P, 2011. *Toxocara* infection in the United States: the relevance of poverty, geography and demography as risk factors, and implications for estimating county prevalence. *Int J Public Health* 56: 15–24.
- Jones JL, Kruszon-Moran D, Won K, Wilson M, Schantz PM, 2008. *Toxoplasma gondii* and *Toxocara* spp. co-infection. *Am J Trop Med Hyg* 78: 35–39.
- Ehrard T, Kernbaum S, 1979. *Toxocara canis* et toxocarose humaine. *Bull Inst Pasteur* 77: 225–287.
- Rugiero E, Cabera ME, Ducach G, Noemi I, Viovy A, 1995. Systemic toxocariasis in the adult patient. *Rev Med Chil* 40: 1097–1099.
- Khodasevich LS, Leont'ev VIa, Ladygina AS, Monastirev KB, 1988. Visceral toxocariasis. *Arkh Patol* 60: 54–55.
- Boschetti A, Kasznica J, 1995. Visceral larva migrans induced eosinophilic cardiac pseudotumor: a cause of sudden death in a child. *J Forensic Sci* 40: 1097–1099.
- Marmor M, Glickman L, Shofer F, Faich LA, Rosenberg C, Cornblatt B, Friedman S, 1987. *Toxocara canis* infection of children: epidemiologic and neuropsychologic findings. *Am J Public Health* 77: 554–559.
- Ellis GS Jr, Pakalnis VA, Worley G, Green JA, Frothingham TE, Sturmer RA, Walls K, 1986. *Toxocara canis* infestation. Clinical and epidemiological associations with seropositivity in kindergarten children. *Ophthalmology* 93: 1032–1037.
- Walsh MG, 2011. *Toxocara* infection and diminished lung function in a nationally representative sample from the United States population. *Int J Parasitol* 41: 243–247.
- Sharghi N, Schantz PM, Caramico L, Ballas K, Teague BA, Hotez PJ, 2001. Environmental exposure to *Toxocara* as a possible risk factor for asthma: a clinic-based case-control study. *Clin Infect Dis* 32: E111–E116.
- Maetz HM, Kleinstein RN, Federico D, Wayne D, 1987. Estimated prevalence of ocular toxoplasmosis and toxocariasis in Alabama. *J Infect Dis* 156: 414.
- Woodhall D, Starr MC, Montgomery SP, Jones JL, Lum F, Read RW, Moorthy RS, 2012. Ocular toxocariasis: epidemiologic, anatomic, and therapeutic variations based on survey of ophthalmic subspecialists. *Ophthalmology* 119: 1211–1217.
- Surgan MH, Colgan KB, Kennett SI, Paffman JV, 1980. A survey of canine toxocariasis and toxocaral soil contamination in Essex County, New Jersey. *Am J Public Health* 70: 1207–1208.

28. Dada BJ, Lindquist WD, 1979. Prevalence of *Toxocara* spp. eggs in some public grounds and highway rest areas in Kansas. *J Helminthol* 53: 145–146.
29. Companion Animal Parasite Council, 2013. *Parasite Prevalence Maps*. Available at: <http://www.capvet.org/parasite-prevalence-maps>. Accessed January 8, 2014.
30. Little SE, Johnson EM, Lewis D, Jaklitsch RP, Payton ME, Blagburn BL, Bowman DD, Moroff S, Tams T, Rich L, Aucoin D, 2009. Prevalence of intestinal parasites in pet dogs in the United States. *Vet Parasitol* 166: 144–152.
31. Lucio-Forster A, Bowman DD, 2011. Prevalence of fecal-borne parasites detected by centrifugal flotation in feline samples from two shelters in upstate New York. *J Feline Med Surg* 13: 300–303.
32. Traversa D, 2012. Pet roundworms and hookworms: a continuing need for global worming. *Parasit Vectors* 10: 91.