Emerging Zoonoses in the Southern United States: Toxocariasis, Bovine Tuberculosis and Southern Tick-Associated Rash Illness

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Abstract: The majority of emerging diseases in humans have been linked to zoonotic pathogens originating in domestic animals or wildlife. This is a public health concern because zoonotic infections affect several aspects of the society. The complex interactions among pathogen, host and environment also pose challenges in estimating the true burden of those infections. However, the recent development of new molecular diagnostic tools has allowed for better diagnosis of zoonotic infections. This review focuses on 3 emerging zoonoses, namely toxocariasis, bovine tuberculosis and southern tick-associated rash illness, and demonstrates that these infections may be more prevalent in the southern United States than previously recognized. This review places special emphasis on the recent epidemiologic trends, intra/interspecies transmission and clinical features of each of these zoonoses. In addition, treatment and prevention for each zoonotic pathogen are discussed. Clinicians working in the southern United States should be aware of the presence of those zoonotic infections.

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It is estimated that 75% of emerging infections are zoonotic.[1] One challenge posed by these infections is the general lack of knowledge of their combined burden in humans and animals. The purpose of this article is to provide an overview of the human and animal aspects of 3 emerging zoonoses found principally in the southern United States.

TOXOCARIASIS

Human infection with *Toxocara* species was first described by Werner in 1782. The genus was established in 1905 by Stiles, and the clinical entity known as visceral larva migrans (VLM) was described in 1952 by Beaver.[2,3] Human toxocariasis is usually caused by infection with 1 of 2 nematodes (roundworms) of the *Ascaridae* family, namely *Toxocara canis* and *Toxocara cati*, found in dogs and cats, respectively.[4,5] This soil-transmitted zoonosis was recently recognized as the most prevalent human parasitic infection in the United States.[6,7] Based on a national estimate of 72 million dogs and 83 million cats (2006) in the United States, the prospect of an increased burden of human disease is apparent.

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Interspecies Transmission

T cati and *T canis* complete their lifecycle by infecting their respective definitive hosts, with humans considered to be an accidental host.[8] The unembryonated eggs are shed in the feces of dogs and cats and survive in soil until embryonation. Embryonation may occur in as little as 3 to 6 weeks but can take up to several months depending on the soil type, humidity and temperature.[8,9] After embryonation, eggs are infectious and may be ingested by paratenic hosts (intermediate hosts that are not needed for the development of the parasite but serve to maintain the lifecycle of the parasite) such as mammals, birds, earthworms or insects. Dogs and cats ingest paratenic hosts, and the larvae migrate to host tissues.[8] The larvae of *T canis* develop into egg-producing adult worms, most often in pregnant bitches and their pups,[8] whereas cats are generally more susceptible throughout life. Humans may become infected by ingestion of contaminated soil (pica), by consumption of raw or undercooked meat of infected animals or by indirect contamination of food. Eggs hatch in either the environment or human intestinal tract, or larvae are ingested directly. The larvae migrate through human intestinal walls, enter the bloodstream and disseminate to organs, usually the liver, lung and heart, but do not multiply in the human host.[9–11] In 1998, the United States Centers for Disease Control and Prevention reported 2 cases in the southern United States (Missouri and Kansas) in children who had ingested immature worms from infected cats, suggesting alternative pathways of infection.[12] Parks, playgrounds and sandpits act as environmental sources for transmission, because these areas are often contaminated with animal feces.[8,9] Global estimates suggest that 10% to 30% of soil samples in these locations are contaminated with *Toxocara* species eggs.[7,8,10]

Epidemiology in the Reservoir Hosts

There are differences in the toxocara epidemiology of *Toxocara* between the 2 major animal hosts. In a nationwide review of medical records of 1,213,061 pet dogs seen in Banfield Veterinary Hospitals in 44 states, *T canis* prevalence increased from 3.9% (95% CI: 3.8–3.9) in 2003 to 5.3% (95% CI: 5.2–5.4) in 2006.[13] The study divided the United States into 4 regions and found the odds of infection in dogs treated in the West-South-Central Region (Texas, Oklahoma, Arkansas, and Louisiana) was 5.5 times (95% CI: 5.2–5.4) that of dogs seen in the Mountain Region. Among all four United States regions studied, this region had the highest prevalence. Puppies (<0.5 years) had a higher infection prevalence (10.9%) than dogs aged at least 5 years (1.0%), supporting a transplacental mode of infection.[8] Infection seems to be more prevalent in strays and older male dogs, whereas neutered males and spayed females, which typically receive better care, show lower prevalence.[8,9,13] Similarly, 15.2% of dogs in animal shelters nationwide shed ascarid eggs,[14] compared with 2.2% of pet dogs (2.2%).[15]

Very few surveys of feline-associated *T cati* infection have been published, which limits our ability to estimate the

prevalence and risk factors in the southern United States.[16] In a study conducted among 2000 cats seen in small animal hospitals in Pennsylvania between 1983 and 1991, the *T cati* infection prevalence was estimated as 16.0%.[16] A survey of pet cats and animal shelter cats in New York revealed that 27.2% and 36.9%, respectively, were shedding *T cati*.[17] In a collaborative project using data from a national diagnostic service laboratory, 5.5% of pet cats shed ascarid eggs; the prevalence was 7.6% in cats in the southern United States and 10.6% in cats in the Midwest (Johnson and Little, unpublished observations). Transmammary transmission is believed to be the primary mode of infection in kittens.[8] Cats may also acquire infection from ingestion of paratenic hosts, most often mice and rats.[2]

Epidemiology in Humans

The recent availability of enzyme-linked immunosorbent assay kits for the diagnosis of human toxocariasis has resulted in more accurate estimates of infection prevalence.[8–10] Several studies have estimated prevalence within select populations[4,7,10,18]; results of 1 large-scale survey are available.[19] The National Health and Nutritional Examination Survey sampled 33,994 people across the United States and found an overall age-adjusted seroprevalence among those aged older than 6 years of 13.9% (95% CI: 12.5–15.3).[19] Seroprevalences of 21.2% (95% CI: 19.7–22.8), 12.0% (95% CI: 10.2–13.8) and 10.7% (95% CI: 9.5–11.9) were found among non-Hispanic blacks, non-Hispanic whites and Mexican Americans, respectively.[19] The southern United States had the highest seroprevalence of 17.4% (95% CI: 14.4–20.5). Risk factors for positive serology included living in the southern United States (OR = 2.2, 95% CI: 1.5–3.2), living below the poverty line (OR = 1.5, 95% CI: 1.3–1.8), having a low education level (OR = 2.2; 95% CI: 1.8–2.8), dog ownership (OR = 1.2, 95% CI: 1.1–1.4), being male (OR = 1.5, 95% CI:1.3–1.7), non-U.S. birth (OR = 1.9, 95% CI: 1.4–2.6) and living in rural areas (OR = 1.3, 95% CI: 1.1–1.7).[19] Higher prevalence rates were not observed in children.[7,8]

Animal Infection

Infected adult dogs are usually asymptomatic but may present with increased liver enzymes and IgG levels.[8] Symptomatic disease is most commonly observed in puppies and includes perinatal pneumonia, diarrhea, constipation, vomiting, abdominal distention, cough, nasal secretions and eosinophilia.[8] Diagnosis relies on analysis of fecal samples. Treatment options for *T canis* infections include febantel, fenbendazole, moxidectin, milbemycin oxime and pyrantel pamoate.[8,9] Fenbendazole was found to reduce transmission of infection from bitches to puppies in a randomized clinical trial conducted among 23 Beagle bitches.[8,20]

Infection in kittens is often unapparent, and unlike puppies, kittens are more likely to thrive despite being infected.[8] Infected adult cats may present with potbelly, coarse coat and diarrhea.[8] Treatment of *T cati* infections includes emodepside, milbemycin oxime, moxidectin, pyrantel pamoate, and selamectin.

Human Infection

The human seroprevalence data above suggest that most human infections are asymptomatic, because most of those that are seropositive have no history of compatible illness.[11,21] Toxocariasis can manifest as ocular larva migrans, VLM, covert infection, common infection or neurotoxocariasis.[19] Ocular larva migrans occurs most often in older children and adolescents and most typically presents as a chorioretinitis that can progress to blindness.[21] Other ocular presentations including panuveitis may occur. Presumably a larva, trapped in the eye by chance, provokes an eosinophilic inflammatory response. Patients with ocular larva migrans usually do not have a history of or a present illness compatible with VLM. Eosinophilia is usually lacking. Serodiagnosis is not reliable. Effective therapy has not been established.

VLM occurs most frequently in children aged younger than 6 years. Although most infections are asymptomatic, fulminant infection and death may occur. VLM is the result of dissemination of the larvae to visceral organs, most commonly the liver and lungs.[7] Patients typically present with fever, generalized symptoms, cough and wheezing.[21] Hepatomegaly, leukocytosis with eosinophilia (>50% of total white blood cells in peripheral blood), hypergammaglobulinemia and elevated isohemagglutinin titers to A and B blood group antigens (presumably from cross-reacting parasite antigens) are common signs. The accuracy of the diagnosis may be improved by enzyme-linked immunosorbent assay using recombinant antigens, such as rTES-120 and RTES-30 (detecting antibody to *Toxocara* excretory secretory antigens with various molecular weight limits), which have provided sensitivities of 100% in laboratory settings and specificities of up to 96.2%.[22] Most patients recover without specific therapy. Treatment with glucocorticosteroids with and without albendazole, thiabendazole, mebendazole, diethylcarbamazine and other antihelminthics has been provided to those with severe and/or complicated disease.[21]

A disease entity called common infection in children and covert infection in adults is the most common clinical form of toxocariasis in humans.[11] Cough, abdominal pain, headache, sleep disturbance and behavioral disturbances are the major symptoms.[10] As the name implies, diagnosis is difficult and primarily based on serology. Treatment is generally not indicated.[19]

Neurotoxocariasis can result in impaired cognitive development and decreased intelligence.[18] Three recent case–control studies reported associations between seropositivity to *Toxocara* species and epilepsy with adjusted odds ratios of 2.70 (95% CI: 1.41–5.19), 2.13 (95% CI: 1.18–3.83) and 3.90 (95% CI: 1.91–7.98), in Bolivia, Burundi and Italy, respectively.[23–25]

Control Measures

Veterinarians play a key role in the prevention of toxocariasis and must emphasize deworming of pet animals, especially pregnant bitches and puppies.[8] Pet owners also have an important role to play in not letting their animals defecate in public places and roam and catch rodents or birds.[8,9] The Centers for Disease Control and Prevention parasite prevention program provides in-depth prevention guidelines.[26] Continued education for proper hand hygiene and food preparation is important, especially among those thought to be at high risk, including children and those living in poor, rural areas of the southern United States. Acknowledgment of the potentially higher prevalence of toxocariasis in the southern United States will hopefully enhance calls for epidemiologic and clinical research and implementation of direct control measures within high-risk populations.

BOVINE TUBERCULOSIS

Bovine tuberculosis (BT) is a zoonotic infection of animals and humans caused by *Mycobacterium bovis*. *M bovis* is part of the *Mycobacterium tuberculosis* complex, along with *M tuberculosis*, *Mycobacterium africanum*, *Mycobacterium microti*, *Mycobacterium canetti*, *Mycobacterium caprae* and