PARASITIC ZOONOSES AND THE ROLE FOR VETERINARIANS IN PREVENTION OF HUMAN DISEASE

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INTRODUCTION

Practicing veterinarians are on the "front lines" of prevention of transmission of zoonotic disease agents from pets to people. The veterinarian is usually aware of the characteristics of the pets owned by his/her clients and is looked to by the client as the best source of information about those pets. I think that this also includes information about the potential disease risks of pet ownership and how to prevent them. The client's physicians are unlikely to be informed about their patients' pet ownership, at least until it is too late for prevention! Given our potentially effective role in preventing human disease, it is necessary to continually upgrade our knowledge about these diseasess, the risks for infection, and how to prevent them. This role is especially highlighted today with the increase ibn frequency of conditions causing immune deficiency, most notably HIV/AIDS.

In this report I am going to discuss the current status of several parasitic agents of zoonotic disease: *Toxocara* species, *Echinococcus multilocularis*, and *Cryptosporidium parvum*. Each of these three infections is currently recognized as causing human disease in the United States, but at very different rates. *Toxocara* species are very well known and understood by parasitologists and public health workers; but, as I will emphasize, this zoonotic disease continues to be transmitted

frequently to humans despite our knowledge and understanding. *Echinococcus multilocularis* is much less well known, yet. Recent surveys indicate that it has spread rapidly in a large area of Central North America. We don't know yet what our response should be to this parasite. I want to emphasize what the issues are and what is needed to resolve them. Cryptosporidiosis has emerged, in the last 15 years, from virtual obscurity, to being recognized as themost common cause of waterborne disease in the United States. It's prevalence in domestic livestock and pet animals raises important issues that must be addressed by veterinarians.

TOXOCARIASIS

Toxocaral larva migrans, or infection by the common ascarid worms of dogs and cats, is arguably the most common zoonotic infection associated with pet animals in the United States and other industrialized countries (Stehr-Green and Schantz, 1987). We have estimated that, every year in the United States, this infection causes hundreds of cases of unilateral blindness and uncountable numbers of less permanent forms of illness in children (Glickman and Schantz 1981; Schantz, 1989). About 40 years ago when *Toxocara* worms were first discovered to be a cause of human disease, most of the information for preventing it became apparent (Beaver et al., 1952; Beaver, 1956). Its continuing importance as a cause of zoonotic infection is a cause for some embarrassment, especially given the current availability

of many safe and effective drugs to eliminate these infections from pets. Veterinarians are ideally placed to limit transmission of toxocariasis and one of our greatest opportunities as public health veterinarians is to try harder to promote the involvement of our colleagues in practice to prevent this zoonosis.

Some recent surveys suggest that the prevalence of intestinal helminth infections in dogs has declined in the last 20 years (Greve, 1989; Jordan, et al., 1993); however, such a conclusion is misleading. Those studies are from University veterinary clinics in which most of the dogs are referrals and were likely to have been previously treated with anthelminthic drugs. In fact, intestinal helminths remain quite prevalent in dogs and cats that have not been treated, as seen in the results of a study we did last summer in pound dogs in Atlanta. Ascarids, hookworms, whipworms, and flea tapeworms remain very prevalent in these dogs, the majority of which had spent sometime in or around human households (Unpublished data, 1993). In dogs aged 7 weeks to 3 months, *Toxocara* infection was nearly 100%. Although about 80% of dogs 6 weeks or less of age had worms in their intestine, only 20% were positive for *Toxocara* eggs on stool examination, thus illustrating why preventive treatments have to be given to young pups. Stool examinations are not helpful with young pups because they often give false negative results (Lillis, 1967).

The reason for the high prevalence of *Toxocara* infection in pups is that their major source of infection is their dams from which larvae are transferred prenatally or via her milk (Parsons, 1987). Most pups are infected this way and unless anthelminthic treatments are administered before 4 weeks of age, the pups will contaminate the environment because female worms become gravid and produce eggs when the pups are 3 weeks of age (Barriga, 1988). Furthermore, these eggs remain infective in most environments for months or even years. A recent AVMA survey determined that more than half of American households currently own dogs or cats, or both (Wise and Yang, 1992a); this, combined with high rates of *Toxocara* infection in these pets, produce widespread environmental contamination with *Toxocara* eggs, thus serving as a source of infection for humans, particularly children whose play habits put them most at risk (Glickman and Schantz, 1981; Schantz, 1989).

The disease produced by *Toxocara* infection depends on how many larvae are ingested, the frequency of reinfection, and other factors still poorly understood (Glickman, 1984). We know that the great majority of human infections with *Toxocara* larvae are very well tolerated, even asymptomatic; however, a proportion of infected persons develop larval migrans syndromes which may be systemic or which may be confined to the eye. When a larvae invades the eye it almost always leaves the patient partially or totally blind in that eye. Based on data obtained from the CDC

serologic diagnostic reference service, we estimate that a minimum of 750 cases of ocular larva migrans occurs every year in the United States. The numbers of the visceral larval migrans syndrome are much greater; however, our estimates of these are quite imprecise (Schantz, 1989).

Beginning in the late 1970s and throughout the 1980s we collaborated with groups outside of CDC, particularly Larry Glickman's group, then at Cornell University and, later, at the University of Pennsylvania, in performing clinical and epidemiologic studies on human toxocariasis (Glickman and Schantz, 1981). A major scientific breakthrough that allowed these studies was the development of a reliable serodiagnostic test based on the use of excretory-secretory antigens of cultured *Toxocara* larvae (de Savigny, 1975; Cypess et al., 1977; Glickman et al., 1986). We were able to validate the sensitivity and specificity of this test and use it in a national seroprevalence survey and as a tool for a variety of case-control and other studies aimed at defining the risk factors for infection (Glickman et al., 1978, 1985; Glickman and Schantz, 1985; Schantz et al., 1979, 1980; Pollard et al., 1979; Hermann et al., 1985; Thompson et al., 1986).

It became apparent that *Toxocara* was a much more common infectious disease than most persons were previously aware (Glickman and Schantz, 1981). The principal risk factors for

infection were the presence of a household dog, particularly a pup, in the patients' household within 6 months of onset of illness (Schantz et al., 1979, 1980). When this is combined with pica behavior, especially dirt eating, the statistical association becomes very strong. Another consistent finding was that pet owners do not know that their pets might carry illnesses transmissible to people (Schantz et al., 1979, 1980). Pet owners are well informed about rabies and the need to vaccinate their animals; however, their knowledge of other zoonotic risks is usually absent or incorrect (Fontaine et al., 1989). Without such information, pet owners are neither informed nor motivated to take the simple precautions necessary to protect themselves and their families.

We carried out surveys of practicing veterinarians, in 1979 and again in 1989, to assess practices that would lead to prevention of zoonotic toxocariasis and we found that current veterinary practices and recommendations to pet owners are generally insufficient to prevent transmission (Kornblatt and Schantz, 1980; Harvey, 1991). We found that less than half of surveyed veterinarians take the preventive, or prophylactic, approach to treatment of roundworms.

When asked at what age they recommend first examination or treatment for intestinal worms, only about a third of veterinarians responded "at 4 weeks of age or less," which is the

timing necessary to most efficiently prevent excretion of *Toxocara* eggs. Approximately another third of surveyed veterinarians recommended examinations or treatments beginning at 7 or more weeks of age, in which cases environmental contamination might have occurred for at least a month prior to the time the pup was examined. The results of our surveys indicated that veterinarians are ambivalent about discussing the questions of the potential zoonotic hazards of roundworms and hookworms with clients. Somewhat less than a third indicated that they either "never" discussed this subject or did "only when asked." Thirty-eight percent discussed it "when worms are diagnosed in the practice" and the remaining third reported they discuss this with "new clients" or with "all clients."

I can think of several reasons why practitioners are not "doing the right thing": first, the information about the life cycle of roundworms and hookworms in dogs and the need for early preventive treatments (that we all learned in our parasitology courses) are not being reinforced in our subsequent training, especially in the clinical and postgraduate years. With time out of school, this information becomes vague and it is understandable that veterinarians are uncomfortable talking about it. Moreover, practicing veterinarians do not want to alarm their clients, particularly if this might lead them to give up their pets. This latter concern has been raised on a number of occasions. There may be some basis for that concern, although I

have never seen any data documenting that fear of disease transmission is a factor associating with keeping, or not keeping, pets.

To help correct this situation, the American Association of Veterinary Parasitologists and CDC prepared recommendations for veterinarians on treatment of roundworms and hookworms in dogs and cats. The guidelines recommend strategically-timed preventive anthelmintic treatments and provide details on advising pet-owners how to avoid the potential zoonotic disease risks. These were printed by CDC as a pamphlet form and have been reviewed and endorsed by the National Association of State Public Health Veterinarians and the Conference of Public Health Veterinarians (now the American Association of Public Health Veterinarians). Through the membership of these organizations, through pharmaceutical companies and by direct request of individual veterinarians, we have distributed more than 50,000 copies of these guidelines veterinary students and practitioners. With our present knowledge of this situation, and with the availability of safe and effective anthelmintic drugs there is no excuse for not preventing the spread of infection. I believe that veterinarians could be playing a direct and much more effective role in preventing transmission of *Toxocara*, and other zoonotic helminths, to people, and that this service could be used to strenghten their practices and bolster their public images. The preventive approach to intestinal helminth control

can also generate practice income. Recent surveys confirm that more than 80% of all dog-owners, and about 62% of cat-owners visit their veterinarians at least once per year, and that they look to their veterinarians as the major source of information on matters related to their pets (Wise and Yang, 1992b). This is one of many opportunities for veterinarians to increase their relationships with clients (Pritchard, 1993). What better way for the practitioner than to show concern for the family and to demonstrate that he or she has the knowledge and services to help protect the family's health.

ECHINOCOCCOSIS

Echinococcus multilocularis, the cause of the alveolar form of human hydatid disease, is an emerging zoonotic infection about which practicing veterinarians must be concerned. This tapeworm occurs extensively in the northern hemisphere in life cycles normally involving foxes and coyotes and the rodents upon which those carnivores prey (Rausch, 1986). Dogs and cats are also susceptible and can become infected if they eat an infected rodent. Eggs passed in stools of any of these final hosts can expose human beings to infection. The well-known regions with important public health problems include the tundra zone of North America and Eurasia and extensive areas in Siberia and Central Asia. Recent investigations in China are revealing what appears to be one of the most important endemic areas (Craig et al.,

1991). Situations of most intense transmission to humans appear to be those with commensal cycles involving dogs, from which transmission to humans commonly occurs.

Echinococcus multilocularis was not known to be present in the Central North American region until the 1960s when it was described in red foxes and deer mice in North Dakota (Leiby and Olsen, 1964; Leiby et al., 1970). How long it has been here and how it got here may never be known but much evidence points to its continuing spread and increasing prevalence; it is now known to exist in foxes, coyotes, and several species of rodents in all or part of 10 contiguous states and three Canadian provinces. The most recent surveys extended its known occurrence to as far east as east-central Illinois, Indiana, and Ohio (Storandt and Kazacos, 1993) and as far south as Missouri (Green, T.J., Storandt, S., Bates K.M., Kazacos, K., unpublished). To date the cestode has been documented in foxes, coyotes and several species of rodents in all or part of 12 contiguous states and 3 Canadian provinces (Fig. 3). Where surveys have been carried out repeatedly, the prevalence has tended to increase (Leiby et al., 1970; Rausch and Richards, 1971; Ballard, 1984; Hildreth and Schneider, 1989; Storandt and Kazacos, 1993); recent rates of infections in samples of red foxes and coyotes have ranged from 69%-90% in North Dakota and South Dakota to 19%-35% in Illinois, Indiana and Ohio (Fig. 3).

E. multilocularis life cycles in central North America involve the red fox (*Vulpes vulpes*) and the coyote (*Canis latrans*) as final hosts. Where foxes and coyotes occur together, prevalence of infection in coyotes was higher or equal to that in foxes and worm burdens are higher, suggesting that the coyote may be the more important host epidemiologically (Samuel et al., 1978; Storandt and Kazacos, 1993). The gray fox, *Urocyon cineroargeneus*, has been found infected rarely. The deer mouse (*Peromyscus maniculatus*) and the meadow vole (*Microtus pennsylvanicus*) serve as the most important intermediate hosts. Other animals occasionally reported with larval *E. multilocularis* infection in this region include the muskrat (*Ondatra zibethicus*), the woodrat (*Neotoma cinerea*) and the house mouse (*Mus musculus*). Most of the records of *E. multilocularis* in central North America are from the prairie (steppe, or grassland) biome. This region has been extensively modified for agriculture in ways that favor the increase in populations of foxes and rodents.Given the abundance of suitable definitive and intermediate hosts throughout the United States, it may be assumed that the cestode will continue to spread and become established in contiguous states. In 1989 a shipment of foxes and coyotes was confiscated in South Carolina by federal and state wildlife authorities ; *Echinococcus multilocularis* was identified in 3 of 44 red foxes that had been translocated illegally from eastern Indiana and western Ohio and were to be released into fox hunting enclosures in southeastern states

(Davidson et al., 1992). Subsequent investigation revealed that the practice of translocating foxes from areas where *E. multilocularis* is currently enzootic into southeastern states is apparently common. There is no evidence that the tapeworm has become established yet in southeastern states (Lee et al., 1993); however, if the practice of translocation continues it almost certainly will be.

Alveolar hydatid disease is a serious disease in humans (Wilson and Rausch, 1980). The parasitic lesion resides in the liver and grows slowly and insidiously, so that by the time symptoms are produced, the lesion has often advanced so far that it cannot be completely resected. Such patients then ultimately die, and the case-fatality rate in the disease often exceeds 50%, although recent success with benzimidazole chemotherapy has improved survival. Although numerous cases are diagnosed every year in the endemic areas of Siberia, Central Asia, Europe, and the tundra zone of North America, only two cases acquired in this growing area of central North America where *E. multilocularis* is enzootic have yet been diagnosed (Gamble et al., 1979). The apparently few human cases from this region seems quite remarkable given the size of the human population living within the range of the tapeworm. Humans can become exposed by direct handling of foxes or coyotes, or by food or fomites contaminated by these hosts, and, perhaps more importantly, from dogs or cats. Such pets can become infected if they ingest infected rodents.

Domestic cats have been found infected (2%) in Sakatchewan (Wobeser, 1971) and in North Dakota (1%-5%) (Kritsky and Leiby, 1978, cited by Gamble et al., 1979). Surveys of dogs have not been carried out in the U.S. The only way to absolutely prevent the possibility of pets becoming infected would be to completely control these pets' diets, something not usually carefully monitored in rural areas. The fact that we have not recognized many more cases suggests that the human risk is currently low. The incubation period of this disease is usually prolonged 10 or more years, however, and there could be considerable human infection before we even become aware of it. There are many gaps in our knowledge of this problem and we need more information to formulate an adequate response and prevent this from becoming an important public health problem.

To that end, we must continue parasite surveys of foxes and coyotes, and of potential rodent intermediate hosts, especially at the limits of the known distribution to monitor the spread of the tapeworm. More extensive ecologic studies are needed to define the dynamics of transmission between the hosts. Surveys of dogs and cats must be done in areas where the infection is enzootic to determine their involvement in the parasitic cycle. Excellent serodiagnostic tests are now available and they can be used for screening of fox trappers and other persons believed to be at high risk of acquiring the disease. We must also formulate appropriate recommendations for protecting ourselves from this

infection according to the local situation. In areas where *Echinococcus multilocularis* is endemic, persons who have contact with wild canids or free-ranging cats and dogs should take appropriate precautions to avoid infection from these animals. Veterinarians must know about the prevalence of *Echinococcus multilocularis* in their practice area to protect themselves as well as their employees, clients, and patients. Recommendations for preventing infection and counseling pet owners should be based on the degree of danger in their practice area. In areas where *Echinococcus multilocularis* is present, pet owners should be instructed to control the diets of their pets and should wash their hands after handling them. If pets are known to have ingested wild rodents, infection can be prevented or eliminated by medication with praziquantel (Rausch, 1990).

Practicing veterinarians are key potential players in this public health issue as they are to prevention practice for roundworms and hookworms. CDC and the American Association of Veterinary Parasitologists are working together to develop and communicate a balanced information and prevention message to veterinarians.

CRYPTOSPORIDIOSIS

The coccidial protozoan, *Cryptosporidium parvum*, that infects many species of wild and domestic animals, is an excellent

example of the phenomena of "emerging infections". It was first recognized as a human pathogen only 20 years ago, then rapidly emerged as one of the most frequent causes of opportunistic infections in persons with HIV/AIDS, and is now recognized as one of the most common causes of waterborne outbreaks of human diseases in the United States (Anon, 1995a; Juranek, 1995).

Cryptosporidium parvum was recognized as a human pathogen in 1976. From 1976 to 1982, the disease was rarely reported; the number of cases began to increase dramatically in 1982 along with the AIDS epidemic. Initially, the increase was limited to immunocompromised persons; however, with the aid of newly developed laboratory diagnostic techniques, outbreaks in immunocompetent persons began to be recognized. In immunocompetent persons, cryptosporidiosis is manifested as an acute, self-limiting diarrheal illness lasting 7-14 days, and it is often accompanied by nausea, abdominal cramps, and low-grade fever. In patients with AIDS, cryptosporidiosis is generally chronic and more severe than that in immunocompetent persons; the voluminous watery diarrhea is often debilitating and may be accompanied by severe abdominal cramps, weight loss, anorexia, malaise, and low-grade fever.

No safe and effective form of treatment for cryptosporidiosis has been identified to date. On the basis of initial human treatment trials, several drugs have been reported to decrease the

frequency or volume of stool production in some patients. However, to date none of these initially "promising" drugs have lived up to expectations when subjected to larger, controlled studies or to widespread use by physicians in clinical practice.

Cryptosporidiosis is among the most common causes of diarrhea in patients with AIDS in the United States. About 2.2% of all patients whose cases of AIDS are reported to the Centers for Disease Control and Prevention (CDC) have cryptosporidiosis as their AIDS-defining illness; 3.5% of children whose cases of AIDS are reported to the CDC have cryptosporidiosis. Hospital-based studies indicate that cryptosporidiosis is diagnosed in 10%-20% of patients with AIDS who have diarrhea. Because diarrhea occurs in about one-half of all patients with AIDS each year, it is estimated that the annual rate of cryptosporidial infection among all patients with AIDS may approach 5%-10% (reviewed by Juranek, 1995).

Cryptosporidium species are transmitted by ingestion of oocysts excreted in the feces of infected humans or animals. Cryptosporidial infection can therefore be transmitted from person to person, through ingestion of fecally contaminated water or food, from animal to person, or by contact with fecally contaminated environmental surfaces.

Approximately ten well-documented outbreaks of cryptosporidiosis

attributed to drinking water have been recognized in the United States, including an outbreak in Milwaukee in 1993 that affected over 400,000 person. The source of drinking water used by utility companies in these outbreaks included surface water (lakes, rivers, and streams), well water, and spring water. Several outbreaks have also been associated with exposure to lakes, swimming pools and amusement park wave pools or water slides.

There is considerable circumstantial evidence that low-level (nonepidemic) transmission of *Cryptosporidium* species through drinking water may be occurring throughout the United States. Recent studies indicate that *Cryptosporidium* oocysts are present in 65%–97% of surface waters (rivers, lakes, etc.) tested throughout the country (reviewed in Juranek, 1995). Moreover, recent surveys for the occurrence of *Cryptosporidium* oocysts in fully treated (disinfected and filtered) municipal water demonstrate that small numbers of oocysts were able to breach filters and were present in tap water in 27%–54% of communities evaluated. Most recently, an outbreak of waterborne cryptosporidiosis was identified in a city with an apparently perfectly functioning filtration system (Goldstein et al., 1996).

Animals are important reservoirs of *C. parvum* which is apparently capable of infecting all species of mammals, including humans (Juranek, 1995). In animals, patent cryptosporidiosis occurs

almost exclusively in newborns. There are no data on the national prevalence of cryptosporidial infection in puppies or kittens in the United States, but in a study in Atlanta, 10% of puppies examined at an animal shelter were found to infected with the organism and shedding oocysts. To date, there have been no confirmed instances of *C.parvum* transmission from infected household pets to humans. Two suspicious episodes have been reported in which an infected cat was found in the house of an immunodeficient person with cryptosporidiosis; in neither instance could the direction of spread be clearly elucidated (Bennett et al., 1985; Koch et al., 1983).

Other species of *Cryptosporidium* that infect birds (*C.meleagridis* and *C. baileyi*), rodents (*C. muris*), reptiles (*C. serpentis*), and fish (*C. nasorum*) are not generally considered to be infectious for humans (Dubey et al., 1990). To date, only one case of human infection with any of these species has been reported (Ditrich et al., 1991); this case occurred in an HIV-infected patient from whom a parasite resembling *C. baileyi* was isolated but who did not have a pet bird or any other specific exposure to birds.

In strong contrast to the weak epidemiologic data implicating household pets as sources of cryptosporidiosis in humans, the evidence for C. parvum transmission from calves to humans is unequivocal (Anderson et al., 1982; Current et al., 1983; Pohjola et al., 1986; Lengerich et al., 1993; Levin et al., 1988; Miron

et al., 1991). It is estimated that 50% of dairy calves shed oocysts and that the parasite is present on >90% of dairy farms (Anderson et al., 1982; Aurich et al ., 1990; Ongerth & Stibbs, 1989). While relatively few patients with AIDS are directly exposed to calves or to premises where calves are raised, the high prevalence of infected calves, especially on dairy farms, raises additional questions about the prudence of drinking unpasteurized milk (Juranek, 1995).

The proportion of cases of cryptosporidiosis in HIV-infected persons that can be attributed to each mode of transmission is unknown. Identification of the most common route(s) of transmission and a better understanding of the specific risk factors for exposure that lead to infection would greatly facilitate development of a more targeted prevention strategy. Until such data become available, doing what one can to avoid each of the commonly recognized modes of transmission should reduce the risk of infection. As with many other opportunistic infections for which effective treatment is not available, prevention of infection is the most effective approach to disease control.

The increasing prevalence in our society, of persons with compromised immune systems, most notably HIV/AIDS, creates added responsibilities and challenges for veterinarians in prevention of zoonoses. Nearly half of patients with AIDS live with pets,

most commonly dogs and cats (Conti et al. 1995) and health care providers are increasingly recognizing pets as important part of thesupport system for these patients. These animals may be host to numerous infectious agents, however, and some of them, like *Cryptosporidium*, are potentially life-threatening. Nevertheless, pet owners with AIDS were remarkably ignorant of the potential risks to their health (Conti et al. 1995). Veterinarians must be well-informed and prepared to provide them clients with information about zoonoses prevention (Angulo, et al, 1994; Glaser et al., 1994). Current recommendations for prevention of exposure to cryptosporidiosis in patients with AIDS are complex and reflect the multiple modes of transmission (CDC, 1995): those specifically related to transmission from animals include:

(1) HIV-infected persons should be educated and counseled about the many ways that *Cryptosporidium* can be transmitted including contact with infected animals.

(2) HIV-infected persons should avoid contact with animals feces. They should be advised to wash their hands after handling of pets, and after gardening or other contact with soil. (In situations where it is not possible to avoid such contact, e.g., cleaning a cat litter box or removing feces from shoes or other items that may have been contaminated, patients should be instructed to wear disposable gloves.)

(3) HIV-infected persons should be advised that very young pets may pose a small risk of cryptosporidial infection, but they should not be advised to destroy or give away healthy pets. Persons contemplating the acquisition of a new pet should avoid bringing any animal with diarrhea into their households, should avoid purchasing a dog or cat >6 months of age, and should not adopt stray pets. HIV-infected persons who wish to assume the small risk of acquiring a puppy or kitten >6 months of age should request that their veterinarian examine the animal's stool for *Cryptosporidium* before they have contact with the animal.

(4) HIV-infected persons should avoid exposure to calves and lambs and to premises where these animals are raised.

Assumption of this responsibility for prevention of transmission of zoonoses from pets to people is on of the social responsibilities of veterinarians and establishes our profession as an important part of the public health team.

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