The use of a *Giardia* vaccine as an immunotherapeutic agent in dogs

Merle E. Olson, Carl J. Hannigan, Patricia F. Gaviller, Libby A. Fulton

Abstract — Dogs (n = 13), which had failed to be cured of giardiosis following chemotherapeutic measures, were treated with a *Giardia* vaccine (2–3 injections). Clinical signs resolved between 16 and 42 days postvaccination and cessation of fecal cyst shedding was between 21 and 70 days. Vaccination is a potential method of treating giardiosis in dogs.

Résumé — Utilisation d'un vaccin anti *Giardia* comme agent immunothérapeutique chez le chien. Des chiens (n = 13) n'ayant pas été guéris de la giardiose suite à une chimiothérapie ont été traités avec un vaccin anti *Giardia* (2–3 injections). Les signes cliniques sont disparus entre 16 et 42 jours après la vaccination et l'arrêt de l'excrétion fécale des kystes s'est produit entre les 21^{e} et 70^{e} jours. La vaccination est une méthode potentielle de traitement de la giardiose chez le chien.

(Traduit par Docteur André Blouin)

Can Vet J 2001;42:865–868

Giardiosis is caused by a protozoan parasite *Giardia duodenalis* (synonymous with *Giardia lamblia*) that inhabits the small intestine. Dogs and cats with giardiosis can be asymptomatic or have clinical signs, such as small bowel diarrhea, vomiting, lethargy, and allergic dermatitis (1). Metronidazole and fenbendazole are the recommended treatments and are very effective in elimination of the parasite from the host, although resistant strains of *Giardia* have been reported (2). Treatment failures may also be associated with reinfection, as it may be difficult to remove the infective cysts from the animal's environment (1,3). *Giardia* cysts can survive for months in water or cool, moist environments (3).

The host immune system can eliminate the parasite from the intestines in some animals, while other animals remain infected with the parasite or without clinical signs of disease for several months (4–6). It is believed that in some cases of chronic giardiosis, the host develops immune tolerance to the *Giardia* antigens in the gut, similar to the beneficial tolerance that develops to dietary antigens (6,7). Recently, a *Giardia* vaccine (GiardiaVax; Ayerst/Fort Dodge Laboratories, Guelph, Ontario) has been released for prevention of clinical signs associated with giardiosis and reduction of shedding of *Giardia* cysts. This report describes the clinical and parasitological response to this vaccine, used as an immunotherapeutic agent in dogs with chronic giardiosis in which traditional treatments have been unsuccessful. Cases were selected by the attending veterinarian, based on the prior treatment failure. In all cases, the diagnosis of giardiosis was confirmed by a veterinary parasitologist or a veterinary clinical laboratory. *Giardia* cysts were concentrated and identified by using either sucrose gradient centrifugation (specific gravity 1.18), followed by immunofluorecent staining, or zinc sulfate centrifugation (specific gravity 1.18) and direct microscopic observation (1,8).

Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1 (Olson); Forest Lawn Veterinary Hospital, 2002–36 Street SE, Calgary, Alberta T2B 0X8 (Hannigan); Country Hills Veterinary Clinic, 5149 Country Hill Boulevard NW, Calgary, Alberta T2E 7A2 (Gaviller); Big Hills Veterinary Services, Box 1330, Cochrane, Alberta T0L 0W0 (Fulton).

Address correspondence and requests to Dr. Merle E. Olson.

This research was supported in part from a research grant provided by the Natural Sciences and Engineering Research Council of Canada.

Case #1

An 8-month-old, male blue heeler x keeshond was presented with diarrhea and large numbers of *Giardia* cysts in the feces. He was treated with metronidazole (15 mg/kg/body weight (BW), q12h, for 10 d) and the diarrhea resolved. Diarrhea reoccurred 10 d after the last treatment and became progressively more severe with large numbers of *Giardia* cysts in the feces. The dog was treated with yogurt and fenbendazole (50 mg/kg BW, q24h, for 10 d), but fecal cysts and diarrhea were still observed 12 d after the final treatment. He was retreated with fenbendazole (50 mg/kg BW, q24h, for 5 d). At this time, the dog was vaccinated with the *Giardia* vaccine and given a booster dose 20 d later. Intermittent diarrhea with shedding of *Giardia* cysts continued for 16 d after the first vaccination. At the time of the booster vaccination, the diarrhea had resolved and fecal cysts could not be demonstrated. This dog has continued to be free of clinical signs of giardiosis and detectable fecal *Giardia* cysts for over 12 mo.

Table 1. Summary of the clinical records of animals given immunotherapy

Breed, age, sex	Duration of giardiosis	Clinical signs	Treatments	Duration to normal stool	Duration to cyst elimination
Heeler x keeshond, 8 mo, M	42 d	moderate to severe diarrhea	metronidazole, fenbendazole, yogurt	16 d	21 d
Malamute, 3 y, F	1 y	diarrhea, gas, lethargy	metronidazole, albendazole, fenbendazole	32 d	32 d
Malamute (7 pups), 26 d, M and F	3 wk	diarrhea, vomiting	metronidazole	21 d	42 d
Labrador retriever, 14 wk, F	3 wk	diarrhea	fenbendazole	35 d	35 d
Shih tzu, 4 y, F	5 mo (possibly 2 y)	recurrent diarrhea, vomiting, pruritus	metronidazole, fenbendazole	42 d	70 d
Basset hound, 15 mo, M	2 mo (potentially 6 mo)	recurrent vomiting, pruritus	metronidazole	35 d (vomiting), 42 d (pruritus)	35 d
Labrador retriever, 12 mo, M	28 d	diarrhea, vomiting, pyoderma, otitis externa	topical antibiotics, cephalexin, fenbendazole	21 d	21 d

d — day; wk — week; mo — month; y — year; M — male; F — female

Case #2

A number of animals in a kennel with Alaskan malamutes had a history of intermittent diarrhea and gas over the past year. Giardiosis had been diagnosed in the kennel previously in a 5-month-old pup, which was treated with metronidazole (60 mg/kg BW, q24 h, for 1 d) and sold (status of this animal was unknown). A 3-year-old, pregnant female developed severe diarrhea with gas and lethargy 6 mo after the index case. A fecal examination demonstrated large numbers of *Giardia* cysts. The dog was treated with fenbendazole (50 mg/kg BW, q24h, for 5d) and the clinical signs subsided. During this time, the dog whelped, delivering 7 healthy pups. Diarrhea reoccurred 10 d after the last day of treatment and again there were large numbers of cysts in the feces. The diarrhea responded to retreatment with fenbendazole for 5 d but reoccurred less than a week later. The dog was then treated with metronidazole (60 mg/kg BW, q24h, for 5 d) but did not respond to treatment, so was treated with fenbendazole (50 mg/kg BW, q24h, for 2 d) and albendazole (50 mg/kg BW, q12h, for 2 d). Three days into this last treatment, she was vaccinated with the *Giardia* vaccine. Diarrhea reoccurred 5 d after the last attempt with chemotherapy. The dog was revaccinated at 4 and 7 wk after the first vaccination. Thirty-two days after the first vaccination, the stools became normal and cysts were not observed in the feces. The dog has not demonstrated clinical signs of giardiosis and fecal cysts have not been observed for over 1.5 y.

At 26 d of age, her pups presented with diarrhea and were treated with metronidazole (60 mg/kg BW, q24h, for 1 d). They vomited when treated with metronidazole, so therapy was withdrawn. Those pups still having diarrhea received their first vaccination against *Giardia* at 6 wk of age and were also treated with albendazole (25 mg/kg BW, q12h, for 4 d). They received booster doses of vaccine 3 and 6 wk after the first vaccination. Four weeks after the first vaccination, *Giardia* cysts were observed in the stools of only one pup. The pups remained asymptomatic and free of cysts at the time of the last immunization.

Case #3

A 14-week-old, female Labrador retriever had diarrhea with large numbers of *Giardia* cysts in the feces when she was first vaccinated against distemper virus, parvovirus, adenovirus, and parainfluenza virus. She was treated with fenbendazole (50 mg/kg BW, q24h, for 7 d), but 1 wk later the diarrhea reoccurred and she continued to shed *Giardia* cysts in the feces. She was vaccinated with the *Giardia* vaccine at this time and again at 21 wk of age, when she was also given the remaining booster vaccinations. The puppy continued to shed cysts and had recurrent diarrhea for another week before the diarrhea resolved, at which time cysts could not be demonstrated in the feces. *Giardia* cysts and diarrhea have not been observed for over a year.

Case #4

A 4-year-old, female Shih-Tzu that had moved recently from another city had a history of recurrent diarrhea and vomiting lasting 2 y. She had been treated repeatedly with metronidazole and metoclopramide to control diarrhea. She was brought to the veterinary clinic with a complaint of diarrhea and generalized pruritus. At the time of examination, large numbers of *Giardia* cysts were identified in the feces. The dog was treated with fenbendazole (50 mg/kg BW, q24h, for 7 d) and the diet was changed to duck, fish, and potatoes. The diarrhea and dermatitis resolved initially, but upon re-examination 3 wk later, fecal cysts and the clinical signs were noted. The dog was treated with metronidazole and fenbendazole for the next 5 mo for recurrent diarrhea and dermatitis. *Giardia* cysts were still observed in the feces over this time. Six months after the initial examination, the dog was vaccinated against *Giardia* and given a booster dose 5 wk later. *Giardia* cysts were demonstrated in the feces 6 wk after the first vaccination, but the diarrhea had resolved. *Giardia* cysts were absent in the feces 10 wk after the initial vaccination against *Giardia*. Six months after the dog received the *Giardia* vaccination, there was no diarrhea or dermatitis, and *Giardia* cysts could not be demonstrated in the feces.

Case #5

A 13-month-old, male basset hound, with a history of pruritus of the feet, ears, and ventral abdomen, and of recurrent vomiting, was diagnosed with giardiosis. He was treated with metronidazole (50 mg/kg BW, q12h, for 7 d). One month later, clinical signs returned and large numbers of *Giardia* cysts could be demonstrated in the feces. The dog was vaccinated against *Giardia* at 15 mo of age and received a booster vaccination 5 wk later. The vomiting resolved 5 wk after the first vaccination and the pruritus improved 3 wk later. *Giardia* cysts were absent in the feces at the time of the booster vaccination.

Case #6

A 1-year-old, yellow male labrador retriever had focal pyoderma on the chin and otitis externa at the time of initial examination. The pyoderma was treated with chlorhexadine, topical antibiotics, and oral cephalexin. The otitis externa was treated with a topical antipruritic. Three weeks later, the otitis externa had not resolved, and the dog was vomiting and passing soft, foul-smelling stools. *Giardia* cysts were observed in the feces, and the dog was treated with fenbendazole (50 mg/kg BW, q24h, for 7 d). The diarrhea resolved while the dog was on treatment, but the dermatitis persisted. Two weeks after the treatment ended, the dog vomited repeatedly and the otitis externa was becoming more severe. *Giardia* cysts were still identified in the feces. At this time, the dog was vaccinated against *Giardia* and received a booster dose 3 wk later. The dog had no gastrointestinal or dermal clinical signs 3 wk after being vaccinated.

The major features of the case histories are summarized in Table 1. In this study, the clinical signs of giardiosis were diarrhea, gas, vomiting, and pruritis; the same signs have commonly been reported in dogs and humans (1,3,4). The duration of the clinical signs had varied from 3 wk to 1 y before the dogs received the *Giardia* vaccine. Giardiosis in humans has been reported to produce recurrent diarrhea, gas, abdominal pain, and dermatitis that has lasted for years (3,4). It appears that a similar clinical picture exists in some dogs. It was observed that the clinical signs temporally resolved in some animals following benzimidazole (albendazole, fenbendazole) therapy, which suggests that the clinical signs observed were associated with giardiosis, as the activity of benzimidazoles is directed toward gastrointestinal parasites, such as *Giardia*, and intestinal nematodes (fecal nematode eggs were not identified in the dogs). Treatment failures can be attributed to *Giardia* resistance to drugs, which has been reported for metronidazole and albendazole (2) but may not be responsible for failures in some animals, as clinical improvement was observed following medication. Treatment failure can also be associated with client compliance and failure of the animal to adequately ingest the drug. In these cases, reinfection is the most likely cause of treatment failure, but failure of the therapy to completely eliminate the parasite cannot be ruled out. The source of reinfection may arise from the environment (fecal contaminated water and soil) and from the animal itself (contaminated hair and coprophagia) (1). *Giardia* cysts have been shown to be environmentally resistant and the infective dose is 10 cysts (3,4).

In these reported cases, immunotherapy using a *Giardia* vaccine has been shown to be effective in treating giardiosis in dogs. The *Giardia* vaccine appears particularly effective in dogs that have chronic clinical signs associated with giardiosis and have not responded to treatment. Vaccination relieved clinical signs in most animals in between 16 and 56 d. This period may be significantly less, as most animals did not visit the clinics between the vaccinations and, therefore, there was no accurate record of the day when clinical signs resolved. It required between 21 and 70 d following the vaccination for cyst shedding to be eliminated. Again, the time to cyst elimination may have been be overestimated, as fecal samples were only checked every 3 wk at the most, and animals may have stopped shedding for several weeks before the test. Adverse side effects to the vaccine were not observed in any animal.

Immunotherapy may act by stimulation of the host immune system to specific protective antigens that have been previously suppressed within the host. Many parasitic infections, including *Giardia*, induce a suppressor T lymphocyte response, thereby making the animal "tolerant" to the *Giardia* infection (6,7). Vaccination may break this tolerance by permitting the host to develop protective immunity through production of antibodies that are cytotoxic to the *Giardia* trophozoites and inactivate toxins (7). It has been shown that the vaccine can stimulate a strong humoral immune response within 3 wk (7,8,9). In some cases of chronic *Giardia* infections, the host response appears to resolve the clinical signs of the infection first, while the elimination of detectable cysts and trophozoites from the gut may require more time.

The clinical signs of giardiosis are associated with impairment of intestinal microvillus morphology and enterocyte physiology (10,11). This leads to malabsorptive and maldigestive diarrhea. *Giardia* infections induce macromolecular transport of food antigens from the gut into the circulation, which results in dermal and mucosal hypersensitivity reactions and pruritis (12,13). The *Giardia* parasites are eliminated by complement dependent and independent killing by immunoglobulin (Ig) G and by trophozoite coating with IgA, which prevents mucosal adherence (6,7). Cysts in immunized animals are frequently nonviable, as antibodies interfere in the encystation process (7).

This appears to be a promising and safe application of the *Giardia* vaccine, as it avoids the costly and inconvenient use of chemotherapeutic agents. Also, agents like metronidazole and albendazole can cause serious adverse reactions in dogs (1,2). Metronidazole has been associated with cases of neurotoxicity and is mutagenic (1). Albendazole has been reported to cause serious blood dyscrasias and is teratogenic (1,2). As this was not a controlled study and does not definitively prove that vaccination therapy cured these dogs, further research into the use of immunotherapy in the treatment of giardiosis is warranted. CVJ

References

1. Leib MS, Zajac AM. Giardiasis in dogs and cats. Vet Med 1999; 94:703–802.

2. Upcroft J, Upcroft P. My favorite cell: *Giardia*. Bioessays 1998; 20:256–263.
3. Marshall MM, Naumovitz D, Ortega Y, Sterling CR. Waterborne protozoan pathogens. Clin Microbiol Rev 1997;10:67–85.
4. Olson ME, Buret AG. *Giardia* and giardiasis. In: Samuel WM, Pybus MJ, Kocan AA, eds. Parasitic Diseases of Wild Mammals. 2nd ed. Ames: Iowa State Univ Pr, 2001:399–416.
5. Istre RE, Dunlop TS, Gaspard GB, Hopkins RS. Waterborne giardiasis at a mountain resort: evidence for acquired immunity. Am J Public Health 1984;74:602–604.
6. Faubert GM. The immune response to *Giardia*. Parasitol Today 1996;12:140–145.
7. Olson ME, Ceri H, Morck DW. *Giardia* vaccination. Parasitol Today 2000;16:213–217.
8. Olson ME, Morck DW, Ceri H. The efficacy of a *Giardia lamblia* vaccine in kittens. Can J Vet Res 1996;60:249–256.
9. Olson ME, Morck DW, Ceri H. Preliminary data on the efficacy of a *Giardia* vaccine in puppies. Can Vet J 1998;38:777–779.
10. O'Handley RM, Buret AG, McAllister TA, Jelinski M, Olson ME. Giardiasis in dairy calves: effects of fenbendazole treatment on intestinal structure and function. Int J Parasitol 2001;31:73–79.
11. Buret A, Gall DG, Nation PN, Olson ME. Intestinal protozoa and epithelial kinetics, structure and function. Parasitol Today 1990;6:375–380.
12. Hardin JA, Buret AG, Olson ME, Gall DG. Mast cell hyperplasia and increased macromolecular uptake in an animal model of giardiasis. J Parasitol 1997;83:908–912.
13. Di Priso MC, Hagel I, Lynch HR, Alverez N, Lopez R. Association between giardiasis and allergy. Ann Allergy Asthma Immunol 1998;81:261–265.

Books Received

Through the generosity of several book publishers, the ***Canadian Veterinary Journal*** *is able to inform readers of new publications that are now available to veterinary practitioners. Readers are invited to contact their local library, the publishers listed here, or the bookstores of Canadian veterinary colleges should they wish to obtain their own copies.*

- Mohr U, Carlton WW, Dungworth DL, Benjamin SA, Capen CC, Hahn FF, eds. ***Pathobiology of the Aging Dog.*** Iowa State University Press, Ames, IA, 2001, 700 pp, ISBN 0-8138-2808-2, US$59.95.
- Gonder JC, Smeby RR, Wolfle TL, eds. ***Performance Standards and Animal Welfare: Definition, Application and Assessment Parts I & II.*** Scientists Center for Animal Welfare, Greenbelt, MD, 2001, 81 pp, US$25.00.
- Gilbert FF, Dodds DG. ***The Philosophy and Practice of Wildlife Management.*** Krieger Publishing Company, Melbourne, FL, 2001, 370 pp, ISBN 1-57524-051-3, US$34.50.
- Klaas P. ***Tarantulas in the Vivarium.*** Krieger Publishing Company, Melbourne, FL, 2001, 152 pp, ISBN 1-57524-018-1, US$29.50.

Livres reçus

Grâce à la générosité d'un grand nombre d'éditeurs, la ***Revue vétérinaire canadienne*** est en mesure de tenir ses lecteurs au courant des nouvelles publications rendues disponibles aux médecins vétérinaires. On encourage les lecteurs qui désirent obtenir une de ces publications à entrer en contact avec leur bibliothèque, avec les éditeurs listés ci-bas ou avec les librairies aux facultés de médecine vétérinaire.

- ***International Animal Health Code: Mammals, Birds and Bees, 10th ed.*** World Organisation for Animal Health, Paris, 2001, 473 pp, ISBN 92-9044-526-2, 45 Euros.
- Cowart RP, Casteel SW. ***An Outline of Swine Diseases: A Handbook, 2nd ed.*** Iowa State University Press, Ames, 2001, 205 pp, ISBN 0-8138-2898-8, US$34.95.
- Speakman JR, ed. ***Body Composition Analysis of Animals: A Handbook of Non-Destructive Methods.*** Cambridge University Press, New York, 2001, 255 pp, ISBN 0-521-66338-5, US$74.95.
- Wall R, Shearer D. ***Veterinary Ectoparasites: Biology, Pathology and Control, 2nd ed.*** Iowa State University Press, Ames, 2001, 264 pp, ISBN 0-632-05618-5, US$56.95.