

Efficacy of *Giardia* vaccination in the treatment of giardiasis in cats

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Objective—To assess efficacy of *Giardia* vaccination as a treatment for giardiasis in experimentally infected cats.

Design—Original study.

Animals—16 young-adult cats.

Procedure—Cats were experimentally infected by orogastric administration of *Giardia* cysts. On weeks 4, 6, and 10, cats in the treatment group (n = 8) were given *Giardia* vaccine SC. For the first 28 weeks after infection, 3 fecal samples from each cat were examined weekly for *Giardia* cysts, and cyst numbers were counted. Fecal consistency was scored daily for the duration of the study. Results from vaccinated and unvaccinated cats were compared by logistic regression.

Results—All cats became infected and were shedding *Giardia* cysts by the end of week 2. Throughout the study, diarrhea was rare and was mild and transient when it did occur. By week 28, 5 of 8 vaccinated cats and 7 of 8 control cats had patent *Giardia* infections. Magnitude of infection, based on number of fecal samples with cysts and number of cysts per sample, decreased progressively in both groups over time.

Conclusions and Clinical Relevance—Administration of 3 doses of a *Giardia* vaccine did not completely eliminate the organism from experimentally infected cats in the study period. Since clinical signs were minimal in both groups of cats, it could not be determined whether vaccination lessened severity of clinical disease. Results may have been negatively influenced by the large inoculation dose. Whether *Giardia* vaccination is an effective treatment for giardiasis in naturally infected cats remains to be determined. (*J Am Vet Med Assoc* 2003;222:1548–1551)

The genus *Giardia* consists of flagellate organisms with worldwide distribution that can cause clinically important gastrointestinal tract disease in dogs, cats, and people.¹ The organism is thought to have a wide host range, and all mammalian isolates are currently classified as *Giardia lamblia*, although some nomenclature systems use the name *G duodenalis* or *G intestinalis*. However, recent evaluations of DNA sequences from a number of different genes suggest

that there are 2 or 3 *Giardia* genotypes that can be isolated from people,^{2,3} 2 distinct genetic groups that can be isolated exclusively from dogs,^{4,5} and a distinct genetic group that can be isolated from cats.⁵ Whether these genotypes vary in biologic activity, including zoonotic potential, is for the most part unknown.

Small intestinal diarrhea resulting from giardiasis can be severe and is persistent in some cats. Because the organism can survive in the environment outside the host, reexposure is likely to be common once an initial infection occurs, and infection of cats appears to be common. For instance, *Giardia* infection was detected in 5 of 206 (2.4%) adult cats in north-central Colorado⁶ and in 19 of 263 (7.2%) cats < 1 year old in central New York state.⁷

A number of drugs, including metronidazole, fenbendazole, albendazole, quinacrine, and furazolidone, have been used to treat cats with giardiasis.^{8–12} However, the number of cats treated with these drugs is small, and efficacy is essentially unknown. Additionally, some of these drugs are known to have toxic effects. In 1 report,⁸ metronidazole was effective for the treatment of 5 cats with *Giardia* infection; however, the drug can be difficult to administer to cats in the tablet formulation currently available in the United States, and CNS toxicoses can occur.¹³ Albendazole has been effective for the treatment of giardiasis in dogs¹² but was ineffective in cats⁹ and has been associated with bone marrow suppression.¹⁴ While fenbendazole is effective for the treatment of giardiasis in most dogs^{15,16} and is apparently safe in cats, administration of the drug eliminated cyst shedding in only 4 of 8 cats coinfecting with *Cryptosporidium parvum* in 1 study,¹⁷ so efficacy is questionable. Quinacrine is not available in the United States, and furazolidone is not tolerated by most cats. Thus, additional treatments for giardiasis in cats are needed.

A *Giardia* vaccine^b is now commercially available in the United States. When used as a preventative in kittens challenged with a heterogenous *Giardia* isolate, the vaccine lessened the severity of clinical signs of giardiasis and greatly lessened cyst shedding.¹⁸ In addition, the use of *Giardia* vaccination as an immunotherapy led to cessation of diarrhea and cyst shedding in 6 naturally infected dogs.¹⁹ However, in another study,²⁰ vaccination did not appear to be of benefit for the treatment of giardiasis in dogs. It is possible that vaccination or immunotherapy may not be effective for all genetically diverse strains of *Giardia* spp. However, in 1 study,²¹ antigenic characteristics of multiple isolates were similar, leading to the hypothesis that vaccination or immunotherapy with 1 strain of *Giardia* spp would be effective for other strains. The purpose of the study reported here was to determine whether *Giardia* vacci-

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nation would be efficacious in the treatment of cats with experimentally induced giardiasis.

Materials and Methods

Cats—Sixteen young-adult (7 to 9 months of age) cats of either sex purchased from a commercial source were used in the study. Prior to the study, results of tests for FeLV p27 antigen and FIV antibody^c were negative for all cats, and cats were housed individually to avoid cross-infection in facilities at the Veterinary Teaching Hospital at Colorado State University.

Experimental design—Prior to the study, each cat was shown to be free from *Giardia* infection on the basis of negative results for zinc sulfate centrifugation fecal flotation tests and a commercially available immunofluorescent antibody (IFA) assay^d performed on 3 fecal samples. On day 0, cats were sedated with ketamine hydrochloride (10 mg, IV), and 10⁶ (5 mL of a suspension containing 2 × 10⁵ cysts/mL) *Giardia* cysts of a strain initially isolated from a human^e were administered to all cats via an orogastric tube. Cats were monitored until recovery was complete, and no vomiting or other adverse effects were observed. On day 28, cats were each randomly assigned to a treatment (vaccination) or control group with 8 cats/group. On days 28, 42, and 60, cats in the treatment group were given the *Giardia* vaccine^b SC.

Clinical monitoring—For 28 weeks after infection, cats were observed daily, and attitude was assessed. Feces were collected daily, and fecal consistency was scored as 0 (normal consistency) or 1 (soft or watery consistency).

Fecal assay—During each of the 28 weeks after infection, 3 fecal samples were collected from each cat and examined for *Giardia* cysts. Each fecal sample was diluted 1:4 in 0.01M phosphate-buffered saline solution (pH, 7.2), and a thin smear was made on a microscope slide supplied in an in vitro direct IFA assay^d capable of simultaneous detection of *Giardia* cysts and *Cryptosporidium* oocysts. After slides were stained as instructed by the manufacturer, the number of cysts per slide was counted with a fluorescence microscope. A cyst score from 0 to 4 was then assigned as follows: 0, 0 cysts/slide; 1, 1 to 250 cysts/slide; 2, 251 to 500 cysts/slide; 3, > 501 cysts/slide; and 4, cysts too numerous to count (ie, > 100 cysts/10× objective field). A single individual (JES) who did not know which samples were from vaccinated versus control cats performed all fecal assays.

Data analysis—For samples collected on days 13 through 70 (ie, weeks 4 through 23 after infection), mean cyst scores and percentage of fecal samples positive for *Giardia* cysts were calculated for each group. Cyst scores, percentage of samples positive for *Giardia* cysts, and fecal consistency scores were compared between vaccinated and control cats by means of logistic regression for repeated measures. Commercial software^f was used for statistical analyses. Values of $P < 0.05$ were considered significant.

Results

There were no detectable acute or chronic reactions to vaccine administration. All cats were shedding *Giardia* cysts by the end of week 2, confirming infection. By week 28, 5 of 8 vaccinated cats and 7 of 8 unvaccinated cats maintained patent *Giardia* infections. No time by group interaction was detected ($P = 0.317$) for cyst scores. The magnitude of infection, based on cyst scores, decreased progressively in both groups over time (Fig 1; P for a time effect < 0.001), but there was no significant difference in cyst scores

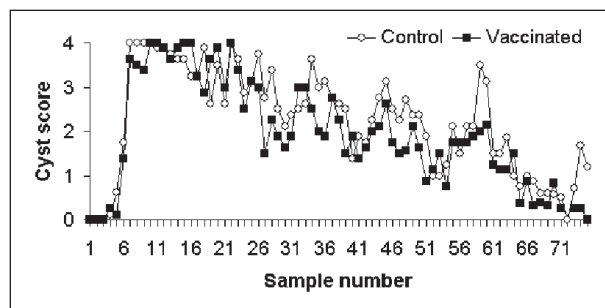


Figure 1—Mean *Giardia* cyst scores (0, 0 cysts/slide; 1, 1 to 250 cysts/slide; 2, 251 to 500 cysts/slide; 3, > 501 cysts/slide; and 4, cysts too numerous to count) in cats experimentally infected with *Giardia* spp and given 3 doses of a *Giardia* vaccine (28, 42, and 60 days after infection; $n = 8$) or not vaccinated (control; 8). For each cat, 3 fecal samples were collected per week for 28 weeks.

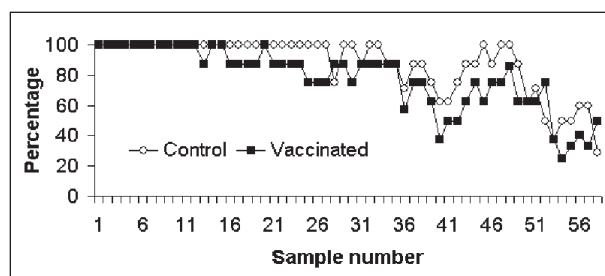


Figure 2—Percentage of fecal samples positive for *Giardia* cysts in cats experimentally infected with *Giardia* spp and given 3 doses of a *Giardia* vaccine (28, 42, and 60 days after infection; $n = 8$) or not vaccinated (control; 8). For each cat, 3 fecal samples were collected per week for 28 weeks.

between groups ($P = 0.874$). The percentage of fecal samples positive for *Giardia* cysts also decreased progressively ($P < 0.001$) over time (Fig 2), but no time by group interaction was detected ($P = 0.122$), and there was no significant difference between groups ($P = 0.127$).

Individual cat fecal consistency scores varied over time, but when abnormal feces were detected, they were usually just soft, and abnormal feces were typically present for only 1 or 2 days. No cat developed severe clinical illness, and all cats continued to eat throughout the study. Cumulative fecal consistency scores before, during, and after vaccination were compared between groups. Prior to vaccination, a significant group by time interaction was detected, with an increase in the percentage of control cats that had abnormal feces at the end of this period. During and after vaccination, however, there were no significant differences in fecal consistency scores between groups.

Discussion

To our knowledge, use of this *Giardia* vaccine for treatment of giardiasis in cats has not been reported previously. However, use of the canine vaccine for treatment of dogs with giardiasis has shown variable success. In a study¹⁹ of 6 dogs with chronic clinical giardiasis, fecal cyst shedding was eliminated, and persistent diarrhea resolved between 21 and 70 days after vaccination. In contrast, in another study²⁰ of dogs with giardiasis, vaccination combined with parasiticide administration was no better than administration of

the parasiticide alone at decreasing the number of cysts in feces within 24 days after treatment. The *Giardia* vaccine used in this study has been shown to be of benefit when used as a preventative in kittens.¹⁸ However, in this study, administration of 3 doses of the vaccine to cats currently infected with *Giardia* spp failed to change the course of infection, compared with unvaccinated control cats, suggesting that any immune responses that were induced were insufficient to eliminate established infection.

It has been hypothesized but not proven that because there are antigenic similarities between *Giardia* isolates, vaccination with antigens from a single isolate could be effective against challenge with multiple strains.²¹ Because *Giardia* vaccination was apparently effective for treatment of giardiasis in 6 dogs that presumably were infected with different strains, this cross-protection hypothesis may also be true for treatment of giardiasis in dogs. However, because of the genetic variation among *Giardia* isolates, vaccination may not be effective as a preventative or treatment for all strains. Thus, while vaccination was not effective for treatment of giardiasis in the cats in the present report, it may still prove effective for treatment of cats infected with other strains.

Because use of the feline *Giardia* vaccine prior to challenge with the isolate used in the present study lessened clinical signs of giardiasis and attenuated cyst shedding in vaccinates, compared with unvaccinated controls,¹⁸ we predicted that vaccination would be effective for treatment of established infection as well. It is possible that whatever immune responses were induced by vaccination were overwhelmed by the inoculation dose of *Giardia* cysts we used. It is impossible to know how many *Giardia* cysts a naturally infected cat ingests to become infected, but it is unlikely to be 10⁶ cysts. However, inoculation dose may not have been an important factor in this study, because *Giardia* spp replicates in the host and can result in massive infections within days after ingestion of a small number of cysts. Since this study evaluated a small number of cats experimentally inoculated with a large number of cysts of a single strain of *Giardia* spp, further work is needed to assess the potential benefits of vaccination for treatment of clinical cases of giardiasis in cats.

Because diarrhea was mild, intermittent, and transient in both groups of cats in this study, it cannot be stated conclusively whether vaccination lessened the severity of clinical signs of giardiasis. The strain of *Giardia* spp used has previously been shown to consistently cause diarrhea in adult cats in vaccine challenge studies.⁵ The difference between results of the present study and results of these previous studies has several potential explanations. Clinical signs of *Giardia* infection are often different between individuals, and it is possible that the cats used in the present study were naturally resistant to the disease. The organism used in the present study was grown in culture in another laboratory and shipped by overnight express to the study site. Thus, it is possible that sample handling attenuated the organism. However, this seems unlikely, since all cats became infected, and most maintained patent infection for 28 weeks. It is also possible that the

Giardia strain used in this study has been attenuated by maintenance in the laboratory over time.

Because *Giardia* organisms have a direct life cycle, initial infection may occur via horizontal transmission or through contact with contaminated fomites. Therefore, reinfection is common. In cats, infection may occur following ingestion of cysts in a contaminated environment or while grooming a contaminated haircoat.²² Environmental decontamination, including frequent disinfection of bowls and litter boxes along with bathing and treatment of all exposed cats, is therefore critical to successful management and prevention of feline giardiasis.

There have been differing results concerning the cross-infection potential of *Giardia* isolates. In 1 study,²³ *Giardia* spp from humans were inoculated into cats, and the cats were found to be relatively resistant to infection. In contrast, evaluation of human and feline *Giardia* isolates by isoenzyme electrophoresis suggests that cats could serve as a reservoir for human infections.²⁴ Since it is impossible to determine which strains of *Giardia* spp are zoonotic by microscopic examination, it seems prudent to assume feces from all dogs and cats infected with *Giardia* spp are a potential human health risk. Given the potential zoonotic risk of *Giardia* spp and the possibility that dogs and cats could serve as reservoir hosts for human infection, the need to develop effective treatments for giardiasis is clear. Owing to the difficulty of effectively eliminating the organism with traditional drug treatment, particularly in chronically infected animals, the use of immunotherapy remains an intriguing alternative. Although administration of 3 doses of a *Giardia* vaccine proved ineffective for elimination of this strain of *Giardia* spp from cats, whether vaccination may be an effective treatment for giardiasis in naturally infected cats remains to be determined.

^aBarr SC, Bowman DD, Heller RL, et al. Efficacy of albendazole against *Giardia* sp in dogs and cats, in *Proceedings*. Am Assoc Vet Parasitol 1993;83:56.

^bFel-O-Vax *Giardia*, Fort Dodge Laboratories, Fort Dodge, Iowa.

^cFeline Leukemia Virus Antigen-Feline Immunodeficiency Virus Antibody Test Kit, IDEXX Laboratories, Westbrook, Me.

^dMerifluor Crypto/*Giardia* IFA kit, Meridian Diagnostic Corp, Cincinnati, Ohio.

^eMaintained in cell culture and supplied by Fort Dodge Laboratories, Fort Dodge, Iowa.

^fGENMOD, SAS Institute Inc, Cary, NC.

^gInformation on file, Fort Dodge Laboratories, Fort Dodge, Iowa.

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