Giardiasis, *Clostridium perfringens* Enterotoxicosis, *Trichomonas foetus*, and Cryptosporidiosis

Todd R. Tams, DVM, Dipl ACVIM
VCA West Los Angeles Animal Hospital
Chief Medical Officer
VCA Antech

**Introduction**
*Giardia*, *Clostridium perfringens* enterotoxin, and *Cryptosporidium* are important causes of diarrhea in dogs and cats. *Trichomonas foetus* is an important problem in cats. These disorders should be investigated early in the course of diarrhea, whether it is persistent or intermittent, along with evaluation for dietary causes of GI signs, nematode parasites, bacterial and viral causes, and acute idiopathic colitis. This group of disorders constitutes a thorough differential list for animals with acute and intermittent diarrhea (Table 1).

The challenge to veterinarians is in making an accurate diagnosis, so that the best therapy can be instituted as early as possible. This will then lead to the best opportunity for successful control of the medical disorder. It is also important to recognize that some animals may have several disorders at the same time, so a thorough diagnostic approach is recommended. This is why it is often best to run tests for these disorders at the same time, through use of a “fecal diagnostics panel” that is now available at many commercial laboratories. A single fecal sample is submitted to the lab, and tests for each of these disorders is done at the same time. This provides a prompt and thorough analysis for important clinical disorders of the GI tract. The clinician then has more clear direction on how to proceed with treatment, or other diagnostic tests in the event that none of these disorders is identified.

**Table 1:** Common Causes of Acute Diarrhea in Dogs and Cats

<table>
<thead>
<tr>
<th>Young Animals</th>
<th>Older Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary problems</td>
<td>Dietary problems</td>
</tr>
<tr>
<td><strong>Parasites</strong></td>
<td><strong>Parasites less common but always possible</strong></td>
</tr>
<tr>
<td>- nematodes</td>
<td>- nematodes</td>
</tr>
<tr>
<td>- protozoa (<em>Giardia, Trichomonads</em>)</td>
<td>- protozoa (<em>Giardia, Trichomonads</em>)</td>
</tr>
<tr>
<td>- coccidia (including <em>Cryptosporidium</em>)</td>
<td>- coccidia (including <em>Cryptosporidium</em>)</td>
</tr>
<tr>
<td><strong>Viral and bacterial</strong></td>
<td><strong>Viral causes uncommon in older animals</strong></td>
</tr>
<tr>
<td><strong>Clostridium perfringens enterotoxicosis (CPE)</strong></td>
<td><strong>CPE (common in older animals)</strong></td>
</tr>
<tr>
<td><strong>Acute colitis</strong> (fairly common cause of diarrhea in older animals)</td>
<td><strong>Acute colitis</strong> (fairly common cause of diarrhea in older animals)</td>
</tr>
</tbody>
</table>

*Giardia* is an important cause of diarrhea, and for some patients other GI signs as well. It is an important pathogen in dogs and cats, as well as humans and other species. Historically, accurate diagnosis of *Giardia* has posed a significant challenge to veterinary practitioners,
but there are now much more sensitive tests readily available for veterinarians to use on a routine basis. Because of the impact that this organism can have on animals, and also humans because of its zoonotic potential, it is important that veterinarians perform accurate diagnostic testing on animals to determine whether or not an animal is infected with *Giardia*. These notes will emphasize steps for accurate diagnosis, and also management of giardiasis.

*Clostridium perfringens* enterotoxidosis is a common cause of intermittent diarrhea in dogs and cats. Veterinary practitioners should test for the enterotoxin whenever faced with a patient that has unexplained diarrhea.

Cryptosporidiosis is now recognized to be a more common disorder in dogs and cats than was previously thought. It can cause significant abnormalities, and it has zoonotic potential. Cryptosporidiosis can be fatal in people that also are immunosuppressed (e.g., on chemotherapy or corticosteroids, carriers of HIV). Therefore, it is incumbent on veterinarians to test for this disorder, as there are important implications to both the patient as well as to humans who may come in contact with an infected animal.

### Early Diagnostic Screening in Animals with Diarrhea

<table>
<thead>
<tr>
<th>Diarrhea – Making the Correct Diagnosis(es)</th>
<th>Diarrhea – CATS (initial screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Diarrhea – DOGS (initial screening)</strong></td>
<td><strong>Acute Diarrhea – CATS (initial screening)</strong></td>
</tr>
<tr>
<td>□ Direct smear in house (fresh sample (perform by &lt;1hr)</td>
<td>□ Direct smear in house (fresh sample (perform by &lt;1hr)</td>
</tr>
<tr>
<td>□ ZnSO₄ w/centrifugation</td>
<td>□ ZnSO₄ w/centrifugation</td>
</tr>
<tr>
<td>□ Giardia antigen test</td>
<td>□ Giardia antigen test</td>
</tr>
<tr>
<td>□ Parvo test if indicated</td>
<td></td>
</tr>
</tbody>
</table>

**Later if Persistent:**
- □ Repeat all of the above
- □ Cryptosporidium IFA
- □ Clostridium perf enterotoxin assay

**Antech SA 350 Fecal Panel Includes:**
- Giardia Antigen and IFA
- Cryptosporidium IFA
- Clostridium perfingens enterotoxin assay

**Negative results do not make a rule-out. Be persistent, as retesting can be very important.**
Options for Therapy of Nonspecific Diarrhea (GI parasites already ruled out via appropriate testing)

- Change food (trial 2-3 weeks), may need to try several different foods
- Colitis signs?
  - Metronidazole or sulfasalazine (Azulfidine)
- Metronidazole (antibacterial/anti-inflammatory effect)
- Probiotics
- Tylosin
- Or, some combination if mono therapy doesn’t work (**but don’t wait too long on further diagnostics if the response is inadequate)

Diagnosis and Management of Giardia

**Diagnosis**
Standard diagnostic tests used in any practice setting should include fresh saline fecal smears and zinc sulfate flotation with centrifugation. Zinc sulfate flotation with centrifugation, rather than gravity flotation alone, is a somewhat more sensitive means of testing for Giardia and other parasites. Trophozoites are more likely to be found in loose stools, while cysts are more often found in semi-formed or formed stools. Performing both zinc sulfate concentration with centrifugation and a Giardia antigen test together constitutes the most accurate means of evaluating a patient for the presence of Giardia. This has been recognized as the “gold standard” in human medicine, and is true also in veterinary medicine.

**Direct Saline Smear**
Direct smears should be performed on fresh fecal samples as soon as possible after being passed, but definitely within 1 hour. A fresh saline smear is made by mixing a drop of feces with a drop of saline on a glass slide. A coverslip is applied and the preparation is examined immediately under 40x magnification. Trophozoites are pear-shaped and have a characteristic concave ventral disk. They demonstrate rolling/wobbling motion (e.g., like a falling leaf). Adding a drop of Lugol’s solution of iodine on the edge of the coverslip can be done as an optional procedure and this will enhance the morphologic features of the organisms and make them easier to find. The iodine kills the parasite, so motion will no longer be seen if this procedure is used. Differentiation of trichomonads from Giardia is based on a different motion pattern (more forward motion with trichomonads versus rolling motion with Giardia), the absence of a concave disk, a single nucleus, and the presence of an undulating membrane. Identification of Giardia trophozoites is diagnostic, while their absence in fecal samples does not rule out presence of infection.
**Zinc Sulfate Concentration with Centrifugation**

Many studies have now shown that zinc sulfate concentration with centrifugation is the most reliable test available for demonstration of *Giardia* cysts in fecal samples. The test can be done in any practice setting, and the technique is described below. Alternatively, because the best accuracy in detection of *Giardia* is achieved through well trained and experienced lab personnel consistently setting up the assay and studying the microscopic specimens on time, many practices now submit fecal samples for centrifugation assays to a commercial laboratory.

Zinc sulfate centrifugation is also a very effective method for identifying nematode eggs in feces. It is therefore now used as the standard test for screening for intestinal parasites in most academic and many private practices. Studies have shown that approximately 70-75 percent of *Giardia* positive dogs can be identified on a single zinc sulfate centrifugation test (as opposed to approximately 40 percent of dogs after 3 separate saline smear preparations). Slides should be examined within 10 minutes of preparation because the cysts may begin to shrink. **Since animals shed *Giardia* on an intermittent basis it is recommended that a series of zinc sulfate concentration tests be run over a 3 to 5 day period in order to maximize chances of accurately diagnosing or ruling out *Giardia* in animals with chronic diarrhea (or, alternatively, an antigen test can be run at the same time to help increase diagnostic efficiency and accuracy – this is what I recommend now as a standard practice).** Diagnostic efficiency increases to 95 percent when 3 zinc sulfate examinations are conducted over a 3 to 5 day period. A positive result on any of the tests warrants treatment for *Giardia*.

**Caution:** It is not uncommon for plant spores, yeast bodies, and other amorphous debris to be mistaken for *Giardia* cysts. In fact, *Giardia* is frequently misdiagnosed – either it is being diagnosed incorrectly, or the wrong tests are being run and animals with *Giardia* are being missed. Giardia cysts are 11-13 u in size, and the subtle characteristics of the nuclei, axostyles, and median bodies are often more easily observed under 100X oil immersion magnification. Sometimes there are crescent shaped indentations of the cyst wall. Yeast bodies are similar to *Giardia* in size, shape, and color. Yeast bodies appear to be far more common than *Giardia*.

**Zinc Sulfate Concentration - Summary**
- Zinc sulfate is the flotation solution of choice in small animal practices (excellent for detection of *Giardia* as well as nematodes)
- Zinc sulfate concentration with centrifugation is the best test for identification of *Giardia* cysts
- Causes less distortion of *Giardia* cysts than standard salt solution

**Zinc Sulfate Centrifugation Flotation Technique**
1. Thoroughly mix approximately 2 grams of feces with approximately 15 milliliters of 33% zinc sulfate solution (33 grams zinc sulfate made up to 100 milliliters with distilled water; specific gravity 1.18).
2. Strain the solution through cheesecloth or a tea strainer.
3. Pour the strained suspension into a 15-milliliter centrifuge tube; polypropylene tubes are preferable to polystyrene tubes.
4. Place the tube in a centrifuge (a standard bench-top centrifuge can be used). If the tubes hang vertically in the centrifuge, flotation solution can be added until a reverse meniscus forms. A coverslip is added and spun in place on top of the tube. If the
tubes are placed in the centrifuge at an angle, the surface layer is harvested after spinning.

5. Spin the tube at approximately 1500 rpm for three to five minutes.
6. Remove the coverslip and the adhering drop of fluid and place them on a microscope slide. When a coverslip is not used, collect the surface layer of fluid by touching a glass rod (a 3-milliliter blood collection tube makes a convenient substitute) or bacteriologic loop to the surface of the centrifuge tube. As previously described, however, use of a coverslip is preferred. Deposit the collected fluid on a slide, add a coverslip (if not already used) and examine. Lugol’s iodine may be added, if desired, to stain organisms.

Initially mixing the sample with water and centrifuging it can remove some of the debris in the fecal sample. Resultant supernatant is discarded, and zinc sulfate solution is added to the pellet and centrifuged as described above. This initial water wash is not necessary on a routine basis. When steatorrhea is present, large amounts of fat float with the *Giardia* cysts and may complicate reading of the slide. In these situations, an ethyl acetate sedimentation technique can be used: the sample is mixed with water, filtered, and placed in a centrifuge tube with two to three milliliters of ethyl acetate or ether. After centrifuging, the supernatant, including a distinct layer containing the organic solvent and fat, is discarded. The pellet is then resuspended, and a drop is stained with Lugol’s iodine and examined.


**Differentiation of Cyst Structures**

*Giardia*
1. Floats in 33% zinc sulfate solution under centrifugal flotation. Doesn’t float readily in other flotation solutions.
2. Size 12-15 microns in length, usually very consistent in size, usually egg-shaped, and refractile green in color.
3. Contains axoneme/nuclei/median bodies, however, these structures are not always visible. The use of oil immersion (100X) objective is helpful in seeing these structures when one is having difficulty at a lower magnification. Usually the median bodies are the most visible of the three structures.
4. Some cysts have a crescent-shaped indentation caused by high salt concentration.
5. Cysts appear to float in their own fecal plane just beneath the cover glass.
6. When scanning the slide, use 10X objective magnification with a moderate amount of light and a reduced diaphragm aperture for high light contrast.

**Yeast Bodies**
1. Float in all commonly used flotation solutions. Float in both simple and centrifugal flotation procedures.
2. Similar to *Giardia* in size, shape, and color. Yeast bodies appear to be far more common than *Giardia*.
3. Contains circular vacuoles, but no structures resembling axonemes, nuclei, or median bodies.
4. Cytoplasm doesn’t indent in flotation solutions.
5. If yeasts are actively growing, buds can form on the yeast bodies.
6. The yeast *Saccharomyces* is seen occasionally in dogs. The yeast is much larger than *Giardia* and has the shape of a gelatin capsule. Not a proven pathogen, but it is often found in dogs suffering from GI distress.

*Sarcocystis sp.* and *Cryptosporidium sp.*
1. *Sarcocystis sp.* sporocysts are about the same size as *Giardia* cysts. They float in all commonly used flotation solutions. Their internal structure consists of four banana-shaped sporozoites and a clump of material called a residium. Because of its relatively thicker cyst wall, *Sarcocystis* is more easily seen than *Giardia.*
2. *Cryptosporidium sp.* is spherical and measures 3 to 5 microns in diameter. They are so small that they are often missed during fecal examination.

**Giardia Antigen Testing**
Other diagnostic tests for *Giardia* include an enzyme-linked immunosorbent assay (ELISA) test for *Giardia* antigen in feces, a direct immunofluorescent assay, duodenal aspiration under endoscopic guidance, and the peroral string test. The latter two tests are impractical for routine use in small animal practice, especially when the effectiveness of today’s fecal tests is recognized.

The fecal ELISA test detects *Giardia* antigen that is produced by dividing trophozoites. The test is very sensitive in humans and reportedly detects 30 percent more cases of *Giardia* than does zinc sulfate. Studies have now confirmed that this is also an excellent test for use in animals. One advantage of the ELISA test is that, since it detects *Giardia* specific antigen in the feces, it avoids the problem of intermittent cyst excretion in the feces. This test can be a significant aid in accurate diagnosis of *Giardia* in any private practice setting, and I highly recommend that veterinarians utilize this test in order to more consistently make an accurate diagnosis of giardiasis in their small animal patients.

**Indications for Running Giardia Antigen Test:**
- Cases of acute or chronic diarrhea in which zinc sulfate centrifugation tests are negative for parasites
  *Including young dogs with suspected viral or bacterial enteritis – *Giardia* and other parasitic infections can significantly compromise animals with these conditions. **I recommend that all puppies with parvoviral enteritis be screened early for parasites with a combination of zinc sulfate with centrifugation and a *Giardia* antigen test (both tests day one or two on a single fecal sample)**
- Cases in which it is unclear whether *Giardia* cysts are being seen on flotation tests (e.g., vs. plant spores)
- For evaluation of animals with unexplained weight loss, unthriftiness, abdominal pain
- Acute or chronic vomiting **(some animals with disease related to *Giardia* have only vomiting as a clinical sign)**
- **Many hospitals are now using the ZnSO4 with centrifugation and *Giardia* antigen combination assay as a routine screening test for GI parasites and wellness testing.** This is because there are animals that have *Giardia* but that do not have any GI signs (loose stools, vomiting, etc) at the time of the exam. The addition of the antigen assay significantly improves the diagnostic sensitivity for *Giardia.* In
summary, this approach offers: Better more sensitive diagnostic testing, more convenience to the client (one sample only), and ultimately it is more economical.

**Treatment of Giardia**

For many years the primary treatment for *Giardia* in dogs and cats has involved metronidazole. For dogs in which metronidazole proved ineffective, quinacrine was often used in the past. However, although quinacrine has been shown to be more effective than metronidazole, it frequently causes side effects, including lethargy, anorexia, and vomiting. It was also used in cats. Quinacrine is no longer available, however. More recently it was shown that albendazole (Valbazen) is highly effective in controlling *Giardia*. I recommended albendazole as an effective treatment for *Giardia* from 1993-1997, but experience with albendazole in dogs and cats has shown that it can cause bothersome side effects; including leukopenia, lethargy, and inappetence. Therefore, I have not recommended albendazole for many years. I mention it here because some veterinarians still do use it.

**Fenbendazole (Panacur)**, well known for its effectiveness against a variety of intestinal parasites, also appears to be very effective against *Giardia*. In a controlled trial at Cornell University 6/6 dogs were effectively treated in an initial study. The same dose that is used to treat roundworms, hookworms, whipworms, and the tapeworm *Taenia pisiformis* (50 mg/kg orally once daily for 5 consecutive days [there have been treatment failures occasionally when therapy is given for only 3 days]) is used to treat *Giardia*. If the infection is not cleared on this regimen, a longer course of therapy is used (7 days). Fenbendazole has a proven track record for being very safe and is thought to not have any teratogenic effects. **Fenbendazole is therefore the drug of choice for treatment of Giardia in pregnant animals.** This is now also the preferred treatment for *Giardia* in cats.

**Drontal Plus (Bayer Animal Health)** is also an excellent choice for treatment of *Giardia*. This product includes febantel in addition to praziquantel and pyrantel pamoate. Febantel is the drug component that treats *Giardia*. Febantel is metabolized into fenbendazole and oxyfenbendazole after oral administration. Drontal Plus is administered once daily for 3 to 5 consecutive days for treatment of *Giardia*. Drontal Plus has been approved for use in dogs. Drontal Plus has been administered to cats empirically at a dosage of two small dog tablets per cat (about 50 mg/kg febantel) orally for 5 days with subsequent demonstration of decreased shedding of cysts (Scorza, Radecki, and Lappin).

**Metronidazole** is still a useful drug for treating *Giardia*, and it has the added advantage of having antibacterial as well as antiinflammatory properties. In situations in which it is unclear whether diarrhea is due to giardiasis, bacterial overgrowth, or mild inflammatory bowel disease, metronidazole is an excellent choice, especially when a client requests empirical therapy rather than definitive diagnostic testing. Metronidazole is only 67-74 percent effective in eliminating *Giardia* from dogs, however, and if a positive diagnosis is made fenbendazole or febantel would also be a reasonable choice. Potential side effects of metronidazole include anorexia, vomiting, and neurologic problems (ataxia, vestibular problems, seizures). In my experience these side effects are not common. They are more likely to occur when the anti-*Giardia* dose is used (25 to 30 mg/kg orally every 12 hours for 5 to 7 days). **The total dose of metronidazole should not exceed 65 mg/kg per day (30 mg/lb per day).** A lower dose (10 to 20 mg/kg every 12 hours) is used in treatment of intestinal bacterial overgrowth and inflammatory bowel disease. Side effects are infrequent at this dose. In the past, if a 5 to 7 day course of metronidazole failed to eliminate *Giardia*, a longer
follow-up course (10 to 14 days) was often used. With the availability of fenbendazole and Drontal Plus it is recommended that one of these drugs be used instead in this situation.

Metronidazole neuro toxicity can be resolved more quickly by administering diazepam for several days. This is likely related to modulation of the GABA receptor within the cerebellar and vestibular systems.

In addition to use of pharmacotherapy to eradicate *Giardia*, it is important to consider environmental control so as to minimize chances of reinfection, especially in kennel or cattery situations. Cysts present in a cool environment can remain infective for a long period of time. Cages and runs should be thoroughly cleaned of all solid fecal material. Steam cleaning, or treatment with a quaternary ammonium compound (e.g. A 33) are both very effective measures for killing cysts. Allowing time for thorough drying is important, to desiccate any remaining cysts.

**Bathing:** Steps to prevent reinfection play an important role in resolution of giardiasis in dogs. Dogs may be reinfected with cysts from the hair or the environment, and bathing at the time that drug therapy is concluded, thereby removing cysts that could be licked from the hair coat by the animal, may be a very helpful additional step in decreasing the chances of reinfection. Changing the environment, if possible, can also be beneficial.

**Dietary Therapy and Supplementation:**
In animals that are known to be chronic carriers of *Giardia*, it may be beneficial to supplement the diet with fiber. Increased dietary roughage may make it more difficult for *Giardia* trophozoites to attach to the small intestinal mucosa (use either commercial diets or simply add a fiber source such as Metamucil or pumpkin, for example, to the animal's standard diet

**Rx for Chronic Giardiasis: Will Probiotics Help?**
- *Lactobacillus johnsonii* has been shown to inhibit *Giardia* proliferation in vitro
  - Due to alterations in pH from production of lactic acid
  - In guinea pigs, *in vivo*, prophylactic feeding of Lj greatly reduced fecal shedding following experimental inoculation with *G. intestinalis*

- *Enterococcus faecium* SF68 fed to mice
  - Stimulated increase in anti-*Giardia* intestinal IgA and circulating IgG
  - Increased CD4+ immunocytes

- Reduced shedding and more rapid clearance of *Giardia*?
- **Studies are ongoing**

**Zoonotic Potential:** Current information indicates that zoonotic potential may exist with some *Giardia* genotypes, but certainly not all. When both animals and humans living in the same environment become infected, a common source of infection rather than direct transmission must also be considered.

**Are most *Giardia* spp. infections shared between animals and man?** The genus *Giardia* contains multiple species of flagellated protozoans that are indistinguishable morphologically. Host specificity was thought to be minimal for *Giardia* spp., but not all small animal isolates cause disease in human beings. There have been varying results concerning cross-infection potential of *Giardia* spp.. Human *Giardia* isolates usually grow in cell culture, animal isolates
often do not. Recent genetic analysis has revealed 2 major genotypes in people. Assemblage A (G. duodenalis) has been found in infected humans and many other mammals including dogs and cats. Assemblage B (G. enterica) has been found in infected humans and dogs, but not cats. It appears that there are specific genotypes of Giardia that infect dogs (G. canis; Assemblages C and D) and cats (G. felis; Assemblage F) but not people. Accordingly, healthy pets are not considered significant human health risks for HIV infected people by the Centers for Disease Control (www.cdc.gov/hiv/pubs/brochure/oi_pets.htm).

Should Giardia Positive But Asymptomatic Animals Be Treated?
The question whether animals that are asymptomatic carriers of Giardia should be treated is often asked. Giardia cysts have been found in many animals with well-formed feces. Giardia is clearly not pathogenic in some animals, while in others it causes significant enteritis. And there may be others that experience intermittent GI upsets that could potentially be related to chronic parasite carriage, and that may benefit in the long term from more effective parasite control. Because the public health considerations must still be considered, I do recommend that all animals with fecal samples that are positive for Giardia be treated, using these guidelines:

- Administer Fenbendazole (Panacur) 5 days
- Re-check fecal at 14-28 days, not later – use the zinc sulfate w/centrif assay, NOT the antigen test (we don’t know how long it takes to go negative)
- If positive on O&P, treat once more
  - Fenbendazole again, or febantel (in Drontal PLUS); could also combine with metronidazole for this second round of therapy
- If still not clinical, stop here, don’t re-check again
  - Pet is not clinical and likelihood of transmission of any infectious agent to a human is very low
  - Is the Giardia even a significant problem for the patient?

NOTE: We do not want to overtreat! The antigen test should not be used as a recheck test in the immediate post treatment phase. The idea is to use the best diagnostic approach up front and then to manage the patient judiciously.

Preventing Infection/Premises Control
In controlled environments, the following methods should be used to keep the area as decontaminated as possible:

1. Decontaminate the environment
2. Treat all animals in the environment
3. Bathe at the conclusion of drug therapy to remove cysts from haircoats
4. Prevent reintroduction of infection

In hospital and kennel/cattery situations (controlled environments) moving animals away from contaminated areas so they can be cleaned and decontaminated is very important. Steam cleaning after all fecal material has been removed is very effective. Chemical disinfection can be effectively accomplished using quaternary ammonium (QUAT) – containing disinfectants (e.g. Roccal, Totil), which will inactivate cysts in one minute at room temperature. The area should be allowed to dry completely and if possible left open for a
few days. Animals should be bathed with a general cleansing shampoo before being returned. In some situations, e.g., shelters, research facilities, it may also be advisable to bathe the animals a second time, especially around the perianal area, using a quaternary ammonium compound. These can be safely left on the coat for 3 to 5 minutes, before being thoroughly rinsed off (longer exposure can cause irritation). Allow the coat to dry thoroughly before returning the animal to the clean area, and then administer one more course of anti-Giardia therapy, preferably using a different drug than was used during the initial course. Subsequently, any new animals introduced to the kennel or cattery should be tested as a matter of routine, but also bathed and treated as well, regardless of whether the fecal tests are positive or negative for Giardia.

**Vaccination:** Giardia Vaccine (GiardiaVax)

In 1999 a new vaccine was released by Ft. Dodge for control of Giardia. The vaccine is a killed product containing chemically inactivated trophozoites. Efficacy studies showed that vaccinated dogs were less severely affected clinically and shed cysts for a shorter time following challenge with infective cysts, compared with nonvaccinated dogs. In addition, chronic giardiasis resolved after dogs were vaccinated with this product. In these studies clinical signs of infection were less severe by 21 to 35 days after vaccination, and cysts were no longer detected in the feces by 21 to 70 days. However, subsequent studies have not demonstrated significant reduction in incidence of giardiasis, so the effectiveness of the vaccine remains in question. This is not a “core” vaccine (i.e., recommended for annual vaccination of all dogs and cats), but there may still be a place for it in our armamentarium. The vaccine has been approved for use in both dogs and cats.

Which Dogs Should Be Considered Candidates for Vaccination?

Pets considered at higher risk of exposure to Giardia (and therefore candidates for vaccination) include dogs that frequently visit parks or play areas frequented by other dogs, dogs in multi-pet households, dogs living in endemic areas, hunting dogs, dogs that travel to pet shows, farm dogs, dogs that board at training kennels, dogs that board frequently at boarding kennels, and dogs that have chronic giardiasis with poor response to therapy.

One ml of vaccine is administered subcutaneously and repeated 2-4 weeks later. Annual vaccination is recommended at this time.


**Tritrichomonas foetus**

Tritrichomonas foetus is a recently identified enteric protozoan of cats. It causes chronic large bowel diarrhea (loose stools, presence of blood and mucus, straining to defecate), and is most commonly seen in young cats that have resided in densely populated housing such as catteries and shelters. The diarrhea may be intermittent or persistent. Loose stool may dribble out (lack of control) and the anal area may become edematous. The organism is present in the ileum, cecum, and colon as a trophozoite. The organism does not encyst, so trophozoites are the only recognized stage. Infection in feral cats and healthy cats appears to be uncommon.
Until 2005 no effective treatment had been identified. Unfortunately, some cats with chronic diarrhea and dyschezia were euthanized due to a lack of any therapy that could control the clinical signs. It was exciting news in 2005 when Dr. Jody Gookin and colleagues at North Carolina State University reported that the nitroimidazole drug ronidazole is effective in controlling *T. foetus*. Although the diarrhea eventually resolves over a period of time (months up to one to two years) in untreated cats, ronidazole is the recommended therapy once a diagnosis has been established. It is important that an accurate diagnosis be made so that clients can be counseled appropriately, i.e., they should expect that their cat(s) will continue to have abnormal stools for some period of time. Further, there can be side effects of significant concern related to ronidazole, so this is NOT a drug that should be used empirically in lieu of testing. Also, it is not uncommon for cats to be co-infected with *Giardia* or *Cryptosporidium* or even both, so a thorough evaluation for parasites is important (run a minimum of one zinc sulfate with centrifugation and a *Giardia* antigen test and consider IFA fecal assays to check for *Cryptosporidium*). Accurate and thorough testing is essential and once any causative agents are identified they can be treated appropriately for the benefit of the patient and its owner.

*Tritrichomonas foetus* is commonly mistaken for *Giardia* trophozoites on direct smear exam. All trichomonads possess three to five anterior flagella, an undulating membrane, and a recurrent flagellum attached to the edge of the undulating membrane. All flagella originate from an anterior basal body. An axostyle extends the length of the trichomonad and extends posteriorly. A cyst stage is not known for this genus. Video clips showing both *Giardia* and *Tritrichomonas* trophozoites are available on the North Carolina State University website cited in the reference list below.

Definitive diagnosis can be made in some cases by direct smear of fresh feces in saline and examined at 200 to 400x magnification. Sensitivity is low, however, for diagnosis by direct smear (only 14% in one study), so results can often be false negative. To increase the chance of finding *Tritrichomonas* trophozoites on direct smear, it is recommended that multiple direct smears be done on the same day. Whenever possible, a cat with suggestive signs should be hospitalized for part or all of a day so that each fecal sample that is passed can be examined quickly via direct saline smear.

*Tritrichomonas foetus* can also be grown from feces via incubation at 37 degrees C in Diamond’s medium. A commercially available culture system is also available and is recommended for use in clinical practice (InPouch TF, Biomed Diagnostics Inc., San Jose, CA). The medium in InPouch does not support the growth of *Giardia* species or *Pentatrichomonas hominis* so presence of organisms is consistent with *T. foetus*. PCR is the most sensitive means for confirming a diagnosis. In one study of 36 cats with *T. foetus* infection, 20/36 were positive on the InPouch TF test and 34/36 were positive on PCR. Details on the PCR assay can be reviewed on the North Carolina State website.

Studies at North Carolina State University in 2005 showed that ronidazole is effective for treatment of *T. foetus*. The original dosage guidance was to administer 30 mg/kg BID for 14 days. However, a study reported in 2008 provided new guidance: 30 kg/kg once daily is effective and safer, i.e., less likely to cause neurologic adverse events (RONIDAZOLE PHARMACOKINETICS IN CATS AFTER IV ADMINISTRATION AND ORAL ADMINISTRATION OF AN IMMEDIATE RELEASE CAPSULE AND A COLON-TARGETED DELAYED RELEASE TABLET; Levine, Papich, Gookin et al).
Ronidazole is a nitroimidazole antimicrobial that is not licensed for any use in the U.S. The medication has become more readily available in the United States through compounding pharmacies. The drug has mutagenic properties, so it must be compounded the same way as chemotherapy drugs. We have had some cats experience mild neurological side effects to ronidazole, similar to what can be seen with metronidazole. These resolved upon discontinuation of the drug. It is expected that there will be fewer instances of neurotoxicity with the new schedule of 30 mg/kg on a once daily dosing schedule. It is important that an accurate diagnosis be made so that clients can be counseled appropriately, i.e., they should expect that their cat(s) will continue to have abnormal stools for some period of time until definitive treatment can be administered.

Other recommended steps during therapy include isolating cats to decrease the risk of reinfection and to discard any litter boxes the cat has used, after treatment is completed.

Follow-up testing: Dr. Gookin recommends testing by PCR at 1 to 2 weeks and 20+ weeks after treatment is completed. Negative results should be interpreted with caution since PCR cannot prove the absence of infection and prolonged symptomatic carriage of the organism after antimicrobial therapy may be common.

An alternative drug which can be tried is tinidazole. This is also a nitroimidazole antimicrobial. A dose of 15-30 mg/kg SID can be tried. It should be safe and may or may not be effective. Studies have been ongoing, however, and results have not been very impressive.

References:


Website for periodic updates and video clips of motile trophozoites: www.cvm.ncsu.edu/mbs/gookin_jody.htm

**Clostridium Perfringens Enterotoxicosis**

Over the last 12 years Clostridium perfringens enterotoxicosis (CPE) has emerged as a frequently recognized cause of chronic intermittent diarrhea in dogs. Although it is likely a less common cause of diarrhea in cats it is still diagnosed frequently enough that it should be considered in the diagnosis of diarrhea in cats as well. This is not a new disease. Frequent use of the definitive test (enterotoxin assay performed on feces) for this disorder has revealed that CPE is seen relatively commonly in clinical practice and that CPE is a disorder that should be considered in any dog or cat with intermittent or chronic persistent diarrhea.
*C. perfringens* is a normal vegetative enteric organism. Simply identifying *C. perfringens* on a fecal culture is meaningless. The pathogenesis of CPE is through an enterotoxin that is produced after certain strains of *C. perfringens* sporulate. The toxin damages epithelial cells of the distal ileum and colon. Inciting factors that promote sporulation are not clearly understood but may include stress, diet changes, concurrent disease, or inherent immune status.

The most common clinical signs are chronic intermittent or persistent diarrhea. In some animals acute diarrhea is the primary sign. In fact, some of the cases of hemorrhagic gastroenteritis (HGE syndrome), characterized by acute bloody diarrhea and an increased packed cell volume that most practitioners have seen over the years, may have been due to CPE. Many animals exhibit signs of large bowel diarrhea, but small bowel signs may be seen as well. In some cases signs may be seen for only a day or two at a time, with persistent recurrences on a weekly, monthly, or on a less frequent basis. Stressful events or diet changes may incite flare-ups of clinical signs. In other cases *C. perfringens* enterotoxicosis is one of several problems that an animal may have concurrently and diarrhea may be persistent.

**Diagnosis**

CPE must be considered whenever more than one animal in the environment has diarrhea (e.g., household, kennel, cattery). Transmission from animal to animal can occur. A presumptive diagnosis may be suggested on fecal cytology in which more than 3-4 spores per high power oil immersion field are observed (the spores have a safety pin appearance and are larger than most bacteria). However, **definitive diagnosis** is by identification of enterotoxin which is currently done via a fecal assay. Clinicians should be aware that simply seeing spores on fecal cytology does not establish a definitive diagnosis (see JAVMA February 1, 1999). Stool is submitted to the lab for enterotoxin analysis. Fecal samples that will be shipped off from the hospital directly to a laboratory should be sent on ice via overnight express. If a courier service will be picking up samples for transport to the laboratory it is sufficient to keep the sample refrigerated until pick-up. The courier service will keep the sample properly chilled during transport. The minimum amount of stool that should be submitted is the size of a pea. Typically I submit samples in a red top tube, without serum separator. In animals with intermittent diarrhea the chances of a positive toxin finding are greater when abnormal rather than a normal stool is examined. **A negative result does not definitively rule-out CPE.**

**Treatment**

Several antibacterial drugs are effective in controlling CPE. Acute cases often respond well to amoxicillin (22 mg/kg BID) or metronidazole (10-20 mg/kg BID) for 7-28 days. Many clinicians have likely treated CPE with these medications empirically without knowing what they were treating. Chronic cases tend to respond best to tylosin powder. The recommended dose is: Animals greater than 23 kg ¼ tsp BID, 12 to 23 kg 1/8 tsp BID, 5 to 12 kg 1/12 tsp BID, and less than 4.5 kg 1/16 tsp BID (a “pinch”). Cats definitely do not accept the powder well at all, even when it is mixed in very tasty foods. It is best to have the powder reconstituted to capsule form for administration to cats. The medication is very safe. Some animals require treatment for several to many months (3 to12 months or more). Over time the dose may in some cases be successfully reduced to SID and then every other day dosage (after several months or more on a BID schedule).
Dietary fiber supplementation may also help control CPE. Probable mechanisms include decreased *C. perfringens* fecal concentration, lower colonic pH, which prevents sporulation, and increased concentrations of SCFA. Some patients may respond well to dietary fiber supplementation alone.

Follow-up testing at 3-6 months can be done to determine if toxin persists. Once daily to every other day tylosin in conjunction with dietary fiber supplementation are used in chronic cases.

**Cryptosporidiosis**

Infection with *Cryptosporidium* is much more common than most small animal practitioners recognize. Currently it is recommended that all dogs and cats with diarrhea, whether acute or chronic, be screened for *Cryptosporidium* in addition to testing for nematode and protozoan parasites. In 2004 the American Association of Feline Practitioners adopted a position statement recommending that all kittens and adult cats with diarrhea be screened for *Cryptosporidium*. It is recommended that the same policy be followed with dogs (given that the cause is not simple diarrhea related to an acute upset due to sudden change in diet or dietary sensitivity).

*Cryptosporidium* spp. are coccidians that reside in the gastrointestinal tract. Infection can be associated with diarrhea in both immunocompetent and immunodeficient hosts. In the past, most of the cases of mammalian cryptosporidiosis were attributed to *C. parvum*. However, molecular studies have demonstrated that cats are usually infected with the host-specific *C. felis*, dogs are infected with *C. canis*, and people are infected with *C. parvum* or *C. hominus* (Scorza and Lappin). In a recent study at Colorado State University, they documented the presence of *Cryptosporidium* spp. DNA in diarrhea from 24.3% of the 292 animals tested (180 cats, 112 dogs) (Scorza and Lappin). This highlights the importance of testing dogs and cats for cryptosporidiosis. PCR is much more sensitive than the tests that are used most commonly at this time (acid fast staining of fecal smears or IFA). In this same series with 24.3% positive on PCR, only 2.7% were positive on IFA.

All dogs and cats infected with *Giardia* or *Cryptosporidium* species should be considered potentially zoonotic, even though the number of cases in which humans are infected through contact with pets is probably not high. Infection in humans is sometimes fatal in the presence of severe immunosuppression. Acute symptoms may include diarrhea, abdominal pain, vomiting, fever, and listless behavior. Infection can also be subclinical in dogs and cats. Chronic unresponsive diarrhea has been associated with cryptosporidiosis in cats with serious underlying disease as well as in dogs.

Because *Cryptosporidia* oocysts are quite small (as little as one-tenth the size of common *Isospora* oocysts) and are usually present in the feces in small numbers, they are very difficult to detect on routine fecal flotation and microscopy. The best tests currently available for routine testing for *Cryptosporidium* are fecal IFA and acid fast staining of fecal smears; however, they lack sensitivity. These tests are readily available at commercial laboratories (acid fast staining can also be done in house). PCR is a much more sensitive test but is labor intensive, expensive and is only available at a limited number of laboratories. Antigen tests for detecting *C. parvum* in human species are not sensitive for use in dogs and cats. In time there will be more sensitive tests readily available.
**Treatment**

The following treatment regimens may be used for cryptosporidiosis:

<table>
<thead>
<tr>
<th>Canine</th>
<th>Feline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Azithromycin</strong> 5-10 mg/kg, BID orally, for 14-28 days</td>
<td><strong>Azithromycin</strong> 7-15 mg/kg, BID, orally, for 14-28 days</td>
</tr>
<tr>
<td><strong>Paromomycin</strong> 150 mg/kg, SID orally, for 5 days</td>
<td><strong>Paromomycin</strong> 150 mg/kg, SID orally, for 5 days</td>
</tr>
<tr>
<td><strong>Tylosin</strong> 15 mg/kg, BID orally, for 21-28 days</td>
<td><strong>Tylosin</strong> 15 mg/kg, BID orally, for 21-28 days</td>
</tr>
</tbody>
</table>

**References**


Blagburn BL and Butler JM. Optimize intestinal parasite detection with centrifugal fecal flotation. Veterinary Medicine 2006; 101: 455-464.


Scorza AV and Lappin MR. An update on three important protozoan parasitic infections of cats: cryptosporidiosis, giardiasis, and tritrichomoniasis. Supplement to Veterinary Medicine, March 2006; 18-32.

