

UPDATE ON FELINE INFECTIOUS GI DISEASES

Michael R. Lappin, DVM, PhD, DACVIM
The Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine
College of Veterinary Medicine and Biomedical Sciences
Colorado State University, Fort Collins Colorado

Clinical problem and differentials. Vomiting is the forceful ejection of stomach and proximal duodenal contents through the mouth. Vomiting can be induced by vestibular, vagal, chemoreceptor trigger zone, or direct input to the emetic center. Diarrhea is characterized by increased frequency of defecation, increased fluid content of the stool, or increased volume of stool. Markedly increased frequency of defecation, small volume stools, tenesmus, urgency, hematochezia, and mucus are consistent with large bowel diarrhea. Slight increase in frequency of defecation, large volume, melena, steatorrhea, and polysystemic clinical signs are more consistent with small bowel diarrhea. Mixed bowel diarrhea is a combination of characteristics or clinical signs.

Gastrointestinal (GI) signs can be the result of primary diseases of the GI system or secondary GI diseases. The secondary GI diseases are generally those of the kidneys, liver, pancreas (pancreatitis or exocrine pancreatic insufficiency), endocrine system (hypoadrenocorticism; diabetic ketoacidosis; hyperthyroidism), or central nervous system. Differential diagnoses for primary GI diseases are often grouped into obstruction (masses, foreign body, and intussusception), dietary intolerance, drugs/toxins (garbage gut), inflammatory gastric and bowel diseases, neoplasia, infectious diseases, and parasites. The primary bacteria associated with gastrointestinal tract disease in cats include *Salmonella* spp., *Campylobacter jejuni*, *Clostridium perfringens*, *Helicobacter* spp., bacterial overgrowth syndrome, bacterial peritonitis, and bacterial cholangiohepatitis. The primary viral agents include feline coronaviruses, feline leukemia virus, feline immunodeficiency virus, and feline panleukopenia virus. The primary nematodes are *Ancylostoma/Uncinaria*, *Strongyloides cati*, *Dirofilaria immitis* (vomiting), *Toxocara cati*, *Toxascaris leonina*, *Ollulanus tricuspis*, and *Physaloptera* spp. Enteric protozoans include *Giardia* spp., *Cystoisospora* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, and *Tritrichomonas foetus*. The cestodes *Taenia*, *Dipylidium*, and *Echinococcus* generally cause subclinical infection.

DIAGNOSTIC PROCEDURES FOR INFECTIOUS DISEASES

Direct smear. Liquid feces or feces that contains large quantities of mucus should be microscopically examined immediately for the presence of protozoal trophozoites, including those of *Giardia* spp. and *Tritrichomonas foetus*. A direct saline smear can be made to potentiate observation of these motile organisms. The amount of feces required to cover the head of a match is mixed thoroughly with one drop of 0.9% NaCl. Following application of a coverslip, the smear is evaluated for motile organisms by examining it under 100X magnification. The sample should be fresh. The material for evaluation should be collected from the surface of the fecal material, preferably mucous if present. Alternately, a rectal scraping can be used.

Stained smear. A thin smear of feces should be made from all cats with large or small bowel diarrhea. Material should be collected by rectal swab if possible to increase chances of finding white blood cells. A cotton swab is gently introduced 3-4 cm through the anus into the terminal rectum, directed to the wall of the rectum, and gently rotated several times. Placing a drop of 0.9% NaCl on the cotton swab will facilitate passage through the anus, but not adversely affect cell morphology. The cotton swab is rolled on a microscope slide gently multiple times to give areas with varying smear thickness. Following air drying, the slide can be stained. White blood cells and bacteria morphologically consistent with *Campylobacter jejuni* or *Clostridium perfringens* can be observed after staining with Diff-Quick or Wright's-Giemsa stains. *Histoplasma capsulatum* or *Prototheca* may be observed in the cytoplasm of mononuclear cells. Methylene blue in acetate buffer (pH 3.6) stains trophozoites of the enteric protozoans. Iodine stains and acid methyl green are also used for the demonstration of protozoans. Acid-fast or monoclonal antibody staining of a fecal smear should be performed in cats with diarrhea to aid in the diagnosis of cryptosporidiosis. *Cryptosporidium parvum* is the only enteric organism of approximately 4 to 6 μ in diameter that will stain pink to red with acid-fast stain. Presence of neutrophils on rectal cytology can suggest inflammation induced by *Salmonella* spp., *Campylobacter* spp., or *Clostridium perfringens*; fecal culture is indicated in these cases. Fecal enterotoxin measurement should be considered for cats with spore-forming rods morphologically consistent with *C. perfringens*.

Fecal flotation. Cysts, oocysts, and eggs in feces can be concentrated to increase sensitivity of detection. Most eggs, oocysts, and cysts are easily identified after sugar or zinc sulfate centrifugal flotation. These procedures are considered by many to be optimal for the demonstration of protozoan cysts, in particular, *Giardia* spp. and so is a good choice for a routine flotation technique in practice. Sugar centrifugation can be used for routine parasite evaluation and may be superior to many techniques for the demonstration of oocysts of *Toxoplasma gondii* and *Cryptosporidium* spp.. *Giardia* cysts are distorted by sugar centrifugation but can still be easily identified. Fecal sedimentation will recover most cysts and ova, but will also contain debris. This technique may be superior to flotation procedures for the documentation of *Eurytrema procyonis*, the pancreatic fluke. *Strongyloides cati* larva may be easier to identify after concentration using the Baerman funnel technique.

Culture. Culture of feces for *Salmonella* spp., *Campylobacter* spp., and *Clostridium perfringens* is occasionally indicated in small animal practice. Approximately 2-3 grams of fresh feces should be submitted to the laboratory immediately for optimal results, however, *Salmonella* and *Campylobacter* are often viable in refrigerated fecal specimens for 3-7 days. Appropriate transport media should be available through your laboratory. The laboratory should be notified of the suspected pathogen so appropriate culture media can be used. More than 1 culture may be needed to prove infection. *Tritrichomonas foetus* can be cultured from feces of cats in general practice using a commercially available kit (InpouchTM, Biomed Diagnostics). Some *Giardia* spp. isolated from cats will grow on culture media, but this technique is not generally performed in small animal practice.

Immunologic techniques. Parvovirus, *Cryptosporidium parvum*, and *Giardia* spp. antigen detection procedures are available for use with feces. Canine parvovirus antigen assays appear to detect feline parvovirus antigen but some can have weak positive results after administration

of modified live vaccines. A fluorescein-labeled monoclonal antibody system is available that contains monoclonal antibodies that react with *Cryptosporidium* spp. oocysts and *Giardia* spp. cysts. It appears that this assay also detects *Cryptosporidium* spp. oocysts and *Giardia* spp. of cats and is used as the gold standard diagnostic test in many studies. A fluorescence microscope is required and so the assay can only be performed in diagnostic laboratories. Antigens of *Giardia* spp. or *Cryptosporidium* spp. can be detected in feces by enzyme-linked immunosorbent assays. Most fecal antigen studies in cats have evaluated with kits developed for use with human feces and so it is possible that cat isolates may not always be detected. This appears to be true for *Cryptosporidium* spp. assays and they should not be used with cat feces. Recently, an in clinic *Giardia* spp. antigen test for use with dog and cat feces was released that detects feline isolates. *Giardia* antigen assays can be added to fecal flotation and wet mount examination to increase *Giardia* diagnostic sensitivity in cats with small bowel diarrhea. Whether or not to screen healthy cats for *Giardia* antigens is controversial and is not recommended by many parasitologists. Serum antibodies against *D. immitis* can be measured in cat serum but positive test results do not prove current infection or disease induced by *D. immitis*. If a vomiting cat is suspected to have *D. immitis* infection, it should be screened with both antigen and antibody assays. FeLV can cause lymphoma and induces the panleukopenia-like syndrome. FIV has been associated with lymphoma and can cause enteritis. Detection of FIV antibodies or FeLV antigen in serum documents exposure, but does not prove that clinical disease is due to the virus. The only way to document that gastrointestinal signs are due to FeLV or FIV is to exclude other known causes.

Endoscopy or exploratory laparotomy. *Ollulanus* and *Physaloptera* rarely pass ova in feces and so frequently are diagnosed only by endoscopy. Diagnosis of diffuse inflammatory diseases can be made by evaluation of endoscopy or surgically obtained tissue samples. Endoscopically obtained biopsies are small; I generally take at least 8-10 biopsies from stomach, duodenum, colon, and ileum if possible. Even if a lesion is present, endoscopically obtained biopsies can be falsely negative requiring full thickness biopsies. Gastric biopsies should be placed on urea slants to assess for urease which is found in the cell wall of *Helicobacter* spp.. The combination of inflammation, exclusion of other causes of inflammation, presence of gastric spiral bacteria, and positive urease testing can be used as a presumptive diagnosis of gastric helicobacteriosis. There is no benefit to performing duodenal aspirates for quantitative bacterial cultures or *Giardia* trophozoite evaluations in cats; the normal bacterial count range is very broad in cats and *Giardia* is found in the distal small intestine. Regional enteritis due to feline infectious peritonitis can be confirmed by documenting the organism in tissue after immunohistochemical staining.

Polymerase chain reaction. Polymerase chain reaction (PCR) is currently available to detect *Giardia* spp., *Cryptosporidium* spp., and *T. foetus* in feline feces. For *Cryptosporidium* spp., PCR is 10 to 1,000 fold more sensitive than IFA. Because of PCR inhibitors in feces, some *Giardia* PCR assays are less sensitive than IFA or antigen tests. I personally only recommend PCR for these two organisms if genotyping is desired. Most kittens with clinical illness from *T. foetus* infection will have trophozoites seen on wet mount examination and so PCR is usually not needed. PCR for *Giardia* spp., *Cryptosporidium* spp., and *T. foetus* can also detect subclinical carrier cats and so the assays have low positive predictive value. Some larger diagnostic laboratories also test for *Salmonella* spp. by PCR but if bacterial GI disease is suspected

(*Salmonella* spp. and *Campylobacter* spp.) the feces should be cultured instead of being assessed by PCR to provide antibiotic susceptibility testing. Testing for genes of *Clostridium* spp. in feces has minimal predictive value unless combined with enterotoxin assays. Parvovirus can be detected by antigen testing and so fecal PCR for this agent is not needed. In a recent study in our laboratory, we showed that this PCR assay could be positive from administration of modified live vaccines. Reverse-transcriptase PCR can be used to detect coronavirus RNA in feces of cats but is not specific for feline infectious peritonitis and results do not correlate with the presence or absence of diarrhea. In a recent study in our laboratory, the results of this PCR did not correlate with the presence of diarrhea in shelter cats.

INFECTIOUS DISEASE TREATMENT OPTIONS

There are multiple drugs used in the treatment of gastrointestinal parasitic infections. For all kittens, the strategic deworming recommendations for the control of hookworm and roundworm infections from the Centers for Disease Control and the American Association of Veterinary Parasitologists should be followed by veterinary practitioners.

<http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm>

Kittens should be administered an anthelmintic at 3, 5, 7, and 9 weeks of age and then periodically monitored or treated. If the kitten is not presented to the clinic until 6-8 weeks of age, administer the anthelmintic at least 2-3 times, 2-3 weeks apart. Pyrantel pamoate and fenbendazole are usually effective drugs for use in strategic deworming programs and for the treatment of nematodes causing gastrointestinal tract disease. Albendazole is more likely to cause hematologic side-effects than fenbendazole and so should not be used in cats. Even if anthelmintics for hookworms and roundworms are administered, a fecal flotation should be performed to evaluate for other parasites.

Monthly *D. immitis* preventatives can help control or eliminate some nematode infections as well as prevent heartworm infection. Ivermectin at heartworm preventative doses is effective for control of hookworms but not roundworms. Thus, selamectin, milbemycin, or moxidectin should be used in regions where roundworm infections are common. Selamectin and imidocarb-moxidectin have the advantage of controlling fleas as well and so may lessen the potential for *Bartonella* spp., *Rickettsia felis*, and *Haemobartonella* (*Mycoplasma*) spp. infections. In a recent study in our laboratory, administration of imidacloprid-moxidectin monthly blocked flea transmission of *B. henselae* amongst cats. *Dipylidium* and *T. taeniaformis* infestations usually are eliminated by praziquantel or espiprantel; fenbendazole is effective for *Taenia taeniaformis*. Since *Echinococcus multilocularis* can be a significant zoonosis transmitted to cats by carnivorous hunting cats in endemic areas should be treated up to monthly. Administration of a pyrantel/praziquantel combination may be effective in these cats since praziquantel is approved for the treatment of *Echinococcus* and roundworms are also transmitted by carnivorous hunting cats.

Withholding food for 24 to 48 hours is indicated in cats with acute vomiting or diarrhea. Highly digestible, bland diets are used most frequently if vomiting and small bowel diarrhea are the primary manifestations of disease. High fiber diets are generally indicated if large bowel diarrhea is occurring. Diarrhea associated with *Giardia* spp. generally resolves during or after

administration of metronidazole. In a recent study, cyst shedding resolved in 26 cats after the administration of metronidazole benzoate at 25 mg/kg, PO, q12hr for 7 days. Metronidazole also helps correct the anaerobic bacterial overgrowth that commonly accompanies giardiasis. If inflammatory changes exist, metronidazole may also be beneficial due to inhibition of lymphocyte function. Central nervous system toxicity occasionally occurs with this drug; it is unlikely if no more than 50 mg/kg, PO, total daily dose is given. Fenbendazole has not been studied extensively for treatment of giardiasis in cats. In one experiment study of cats coinfecting with *Giardia* spp. and *Cryptosporidium* spp., four of eight cats treated with fenbendazole at 50 mg/kg, PO, daily for 5 days stopped shedding *Giardia* cysts. The combination product of febantel, pyrantel, and praziquantel has been shown to have anti-*Giardia* activity in dogs. When given at the febantel dose of approximately 56 mg/kg, PO, daily for 5 days, *Giardia* cyst shedding was eliminated in some cats. Metronidazole and fenbendazole can be given concurrently in resistant cases. A single dose of secnidazole was evaluated in one trial but additional data is needed before the use of this drug can be recommended routinely. Albendazole has been evaluated for treatment of giardiasis in a limited number of dogs, but has been associated with neutropenia. Furazolidone (4 mg/kg, PO, q12hr, for 7 days) and paromomycin (appropriate dosing interval for cats is unknown) are other drugs with anti-*Giardia* effects but have not been evaluated extensively in cats. There are no known advantages of using tinidazole or ronidazole compared to metronidazole in cats and ronidazole has a greater risk of CNS toxicity. Previously, the feline *Giardia* spp. vaccine could be attempted as an immunotherapy but the vaccine has been discontinued. In some cats with *Giardia* and diarrhea, administration of a probiotics or addition of fiber to the food and retreating can result in resolution of diarrhea. The primary goal of *Giardia* therapy is to resolve diarrhea. It is unlikely the infection can be eliminated in most cats and reinfection is common. If treatment is to be monitored, a fecal flotation (not antigen assay) could be performed within 14 days of ending therapy.

Multiple drugs have been evaluated for the treatment of cats with *T. foetus* infections; until recently no drug eliminated infection and diarrhea rarely resolves during the treatment period. Recently ronidazole at 30 mg/kg, PO, q24hr, for 14 days eliminated clinical signs of disease and trophozoites from cats infected with one strain of the organism. Ronidazole is more neurotoxic than metronidazole and so should be used carefully. In another one small study, administration of metronidazole and enrofloxacin lessened diarrhea in kittens but it is unknown if the organisms infecting those cats was *T. foetus*. It is possible that some cats with *T. foetus* have other enteric coinfections and so antihelmintics or drugs with activity against *Giardia* spp., *Cryptosporidium* spp., and enteric bacteria like *Campylobacter* spp. are often prescribed. Paromomycin should be avoided cats with bloody stools because of the potential for being absorbed and inducing renal disease or deafness. In one study, 23 of 26 cats with diarrhea and *T. foetus* infection had complete resolution of diarrhea a median of 9 months after initial diagnosis.

Cryptosporidium spp. associated diarrhea sometimes resolves after administration of tylosin (10-15 mg/kg, PO, BID for at least 14 days) or azithromycin (10 mg/kg, PO, daily for at least 14 days). If the cat is responding to therapy, continue treatment for 1 week past clinical resolution. Some cats may require several weeks of treatment. Nitazoxanide at 10 mg/kg, PO, twice daily for at least 14 days has been effective for controlling *Cryptosporidium* spp. diarrhea, but is a gastric irritant that commonly induces vomiting.

The *Toxoplasma gondii* oocyst shedding period can be shortened by administration of clindamycin, sulfadimethoxine, or ponazuril. *Cystoisospora* spp. generally responds to the administration of sulfadimethoxine or other sulfa-containing drugs. Clindamycin, trimethoprim-sulfa, or ponazuril are also options. Ponazuril and toltrazuril are very safe for kittens and ponazuril can be administered once (50 mg/kg, PO) or twice, two days consecutively (20 mg/kg, PO).

Since many of the gastrointestinal parasites that infect cats are transmitted by carnivorous cats, cats should not be allowed to hunt or be fed raw meats. Additionally, infection of cats by many feline parasites results from ingestion of contaminated water. Clinical disease in some parasitized cats can be lessened by eliminating stress and providing a quality diet and clean environment.

Clostridium perfringens and bacterial overgrowth generally respond to treatment with tylosin, metronidazole, ampicillin, amoxicillin, or tetracyclines. The drug of choice for campylobacteriosis is erythromycin; however, oral administration of quinolones is often less likely to potentiate vomiting. Salmonellosis should only be treated parenterally due to rapid resistance that occurs following oral administration of antibiotics. Appropriate antibiotics for the empirical treatment of salmonellosis while awaiting susceptibility testing results include chloramphenicol, trimethoprim-sulfa, amoxicillin; quinolones are also effective. *Helicobacter* spp. infections are usually treated with the combination of metronidazole and tetracycline or amoxicillin and metronidazole in dogs. Clarithromycin or azithromycin may be logical choices in cats since the species is often difficult to treat with multiple drugs. Whether to concurrently administer an antacid like famotidine is controversial but seems to lessen vomiting in some cats.

Cats with apparent bacteremia due to enteric bacteria should be treated with parenteral antibiotics with a spectrum against anaerobic and gram negative organisms. The combination of enrofloxacin with a penicillin or first generation cephalosporin is generally effective. Second generation cephalosporins or imipenem are also appropriate choices.

Cats that have hepatic infections and signs of bacteremia should be treated with antibiotics that kill gram positive, gram negative and anaerobic bacteria as discussed before. Non septic hepatic infections generally respond to amoxicillin, amoxicillin-clavulanate, first-generation cephalosporins, or chloramphenicol. Decreasing numbers of enteric flora by oral administration of penicillins, metronidazole, or neomycin can lessen the clinical signs of hepatic encephalopathy.

Panleukopenia virus, feline leukemia virus, feline immunodeficiency virus, and coronaviruses are the most common viral causes of gastrointestinal tract disease in cats. Viral diseases are managed by supportive treatment. Make sure to maintain hydration, correct hypoglycemia, and maintain normal potassium concentrations. Use of jugular catheters is superior to leg veins since blood samples can be drawn and CVP can be measured. Based on results in dogs with parvovirus infection, administration of plasma or serum (1 ml/kg) from your hyperimmune blood donor cat may lessen morbidity in cats with panleukopenia due to passive transfer of immunity. This is effective because parvoviruses induce a viremic state; virus particles are complexed by the antibodies transferred passively. Administration of interferon alpha at 10,000 U/kg, SQ, once

daily may have anti-viral effects. Antibiotics effective against gram negative and anaerobic bacteria are commonly indicated. Vaccines are available for the prevention of parvovirus, coronaviruses, and feline leukemia virus infection.

Histoplasma capsulatum infection is the most common fungal infection of the gastrointestinal tract of cats in the United States. Treatment with itraconazole can be effective.

Zoonotic considerations. Infection of people by feline enteric agents is usually from contact with feces in the environment, by ingestion of contaminated food or water, or by ingestion of undercooked meat (*T. gondii*). Contact with infected cats is an unlikely way for humans to acquire infection. The following guidelines may lessen the risk of transfer of feline enteric zoonotic agents to people.

- Perform a thorough physical examination and zoonoses risk assessment on all new cats.
- Perform a physical examination and fecal examination at least once or twice yearly.
- Take all cats with vomiting or diarrhea to a veterinarian for evaluation.
- Fecal material produced in the home environment should be removed daily, preferably by someone other than an immunocompromised individual. Use litterbox liners and periodically clean the litterbox with scalding water and detergent.
- Do not allow cats to drink from the toilet.
- Follow the CDC strategic deworming guidelines.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling cats.
- Maintain cats within the home environment to lessen exposure to other animals and their feces.
- Feed cats only commercially processed food.
- Do not share food utensils with cats.
- Avoid being licked by cats.
- Control potential transport hosts like flies, rodents, and cockroaches.
- Cook meat for human consumption to 80 C for 15 minutes minimum (medium-well).
- Wear gloves when handling meat and wash hands thoroughly with soap and water when finished.

Suggested readings

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Management of *Giardia* spp. in Cats: Frequently Asked Questions

Are most *Giardia* spp. infections shared between cats 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 but rarely dogs and cats. Assemblage B (*G. enterica*) has been found in infected humans but rarely dogs and not cats. It appears that there are specific genotypes of *Giardia* that commonly 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). Genotyping of feline *Giardia* cases is routinely available in the USA (www.dlab.colostate.edu) if the owner would like to know if the cat is carrying a zoonotic genotype.

What are the optimal diagnostic tests? The primary diagnostic tests that are available include direct smear of feces, direct saline preparation, passive fecal flotation, centrifugal fecal flotation (zinc sulfate and sugar are used most frequently), fecal immunofluorescence assay (IFA), fecal antigen ELISA, and fecal PCR assay. These tests can be used alone or in combination.

How should I evaluate fresh feces from cats with diarrhea? Fresh, liquid feces or feces that contains large quantities of mucus should be microscopically examined immediately in the clinic for the presence of protozoal trophozoites of *Giardia* spp. (small bowel diarrhea), *Tritrichomonas foetus* (large bowel diarrhea), and *Pentatrichomonas hominus* (large bowel diarrhea). A direct saline smear can be made to potentiate observation of these motile organisms. A 2mm X 2mm X 2mm quantity of fresh feces is mixed thoroughly with one drop of 0.9% NaCl or water. The surface of the feces or mucus coating the feces should be used as the trophozoites are most common in these areas. After application of a coverslip, the smear is evaluated for motile organisms by examining it under 100X magnification. Culture (*T. foetus*), antigen testing (*Giardia*) or PCR (*T. foetus* or *Giardia*) can be used to distinguish between specific organisms. Results of *T. foetus* culture may take over a week to return and a negative culture for *T. foetus* (InPouch TF assay; Biomed, San Jose, CA) does not always rule-out presence of a *T. foetus* infection. Thus, the fecal PCR assay, a much more rapid and sensitive test, may be required to identify this organism.

What are my options for fecal flotation? Fecal flotation with the zinc sulfate centrifugal flotation technique (specific gravity 1.18-1.20) is one of the optimal techniques for the demonstration of cysts (www.capcvet.org) and is more sensitive for detection of *Giardia* spp. cysts than passive flotation. Sugar and other salt solutions lead to distortion of cysts but are also sensitive tests. Cysts are shed intermittently and their presence does not correlate to clinical signs of disease. Evaluation of a single fecal flotation has a sensitivity of approximately 70%. Therefore, an animal with a *Giardia* infection may go undetected if screening testing is limited to a single zinc sulfate centrifugal flotation test. Sensitivity increases to > 90% if at least 3 stool specimens are examined within 5 days (both humans and animals).

Do currently available antigen ELISA detect dog and cat strains of *Giardia*? Multiple ELISAs for detection of *Giardia* antigens in stool are available. In experiments performed in our laboratory, all human and veterinary assays assessed to date have detected *G. canis* and *G. felis*.

What is the sensitivity and specificity of currently available *Giardia* spp. antigen assays?

There is approximately a 2-5% false positive and 2-5% false negative rate for the assays. While it is unknown why false positive rates occur, it is likely that other antigens are non-specifically binding to the reagents. False negative results likely relate to the sensitivity cutoffs of the individual assays. It is currently unknown how long *Giardia* antigens will persist in feces after successful treatment (resolution of diarrhea). In one study in our laboratory (ML), 62.5% of *Giardia* cyst or antigen positive dogs administered fenbendazole or nitazoxanide previously were again positive for cysts or antigen on day 34. It is unknown whether these infections were not eliminated or if the dogs were re-infected.

Does the IFA produced for human feces detect *Cryptosporidium* spp. and *Giardia* spp. in cat feces. The IFA for simultaneous detection of *Giardia* spp. cysts and *Cryptosporidium* oocysts is currently available in most commercial veterinary laboratories and has been shown in our laboratory to identify *C. felis*, *C. canis*, *G. felis*, and *G. canis*.

When should I use PCR for amplification of *Giardia* spp. DNA from feces? Currently available PCR assays appear to be less sensitive than other tests with some fecal samples and should not be used in lieu of fecal centrifugal flotation or other tests. False negative PCR assay results likely relate to the presence of PCR inhibitors in feces. These assays should only be used if genotyping of the previously detected *Giardia* spp. is desired.

Which cats should be screened for *Giardia* spp. infections and what tests should I use? In all healthy cats, a fecal centrifugal flotation should be performed at least once or twice yearly. In cats with vomiting or diarrhea (GI parasites can cause either of these symptoms), the combination of a direct saline preparation (for cats with diarrhea) with fecal centrifugal flotation and a *Giardia* antigen assay is often used as the minimum initial screening tests for *Giardia* infection as well as other parasites. As discussed, concurrent use of a *Giardia* antigen assay is used to increase sensitivity but should not be used in lieu of the other assays. In cases with severe small bowel diarrhea, the *Giardia/Cryptosporidium* IFA should be considered as *Cryptosporidium* spp. are usually not detected on fecal flotation.

What are the best drugs for *Giardia* spp. infection in cats? *Giardia* spp. have specific antimicrobial sensitivity patterns like bacteria and so it is currently impossible to predict which anti-*Giardia* drug will be effective. Because *G. felis* can be difficult to cultivate, there is little *in vitro* susceptibility test result information available. While there have been multiple drugs used for the treatment of giardiasis in cats, there are few studies that utilized dose titrations and evaluation of drugs in experimentally infected animals. In most studies, fecal samples were only assessed for short periods of time after treatment and immune suppression was not induced to evaluate whether infection was eliminated or merely suppressed. Infection with *Giardia* does not appear to cause permanent immunity and so reinfection can occur, a finding that also hampers assessment of treatment studies. Treatment options currently available or used historically in cats with giardiasis

include metronidazole, ronidazole, fenbendazole, albendazole, pyrantel/praziquantel/febantel, quinacrine, furazolidone, secnidazole, and nitazoxanide.

How do I choose which of these drugs to use? If spore-forming rods, morphologically consistent with *Clostridium perfringens* are concurrently detected with *Giardia*, use of metronidazole is indicated as this drug is an antibiotic. If there is clinical evidence to suggest concurrent infection with a nematode, fenbendazole or febantel are indicated. Many clinicians currently utilize fenbendazole once daily for 5 days as initial therapy. Some clinicians currently recommend the combination of metronidazole and fenbendazole. Others only resort to combination therapy if there is evidence of a persistent infection not cleared by monotherapy.

What are the goals of *Giardia* spp. treatment? The primary goal of treatment is to stop diarrhea. Because healthy cats are not considered human health risks, elimination of infection (which is difficult) is a secondary goal.

What do I do if diarrhea continues and *Giardia* infection is still detected? *Giardia* spp. can have resistant patterns and so if the first drug fails to clear the infection (cysts or antigen) or resolve the diarrhea, a second drug from an alternate class is indicated. The addition of fiber to the diet may help control clinical signs of giardiasis in some animals by helping with bacterial overgrowth or by inhibiting organism attachment to microvilli. Probiotic administration may also be beneficial in some animals, but was ineffective in one recent dog study. In one study, bathing the dog on the last day of treatment was a beneficial adjunct therapy. In cats with persistent diarrhea and *Giardia* spp. infection, a more extensive workup to attempt to diagnose other underlying diseases is indicated if several therapeutic trials fail. Common underlying disorders include cryptosporidiosis, *T. foetus* in cats, inflammatory bowel disease, bacterial overgrowth, and immunodeficiencies.

Should healthy cats with *Giardia* infection be treated? Healthy pets are not considered significant human health risks by the Centers for Disease Control (www.cdc.gov/hiv/pubs/brochure/oi_pets.htm). However, because clinical signs induced by *Giardia* spp. can be intermittent and since some *Giardia* spp. may be zoonotic, treatment of healthy infected cats should be considered with each owner. Treatment of healthy cats is controversial because all of the drugs can potentially cause side-effects, animals with normal stools are not considered human health risks, treatment is unlikely to eliminate infection, and re-infection can occur within days. For example, in a recent study of naturally infected dogs, > 15% of treated dogs were still *Giardia* infected when rechecked 9 or 16 days after treatment. If treatment deemed indicated by the clinician and owner, many clinicians currently recommend that a 5 day course of fenbendazole be administered for apparently healthy cats that test positive for *Giardia*.

Should healthy housemates of *Giardia* infected cats be tested? Whether to test all housemates of infected cats is controversial because all parasite diagnostic tests can give false negative results. Ideally however, it is always a good idea to periodically screen all cats for parasites. The information gained from testing all cats could be valuable particularly if recurrent GI signs of disease occur. Occasionally, the cats in a household will be found to have varying parasite infections. If the client can not afford to test each cat, then it may be more viable to at least treat all animals in lieu of testing but this increased the chance of drug toxicity and drug resistance.

Should healthy housemates of *Giardia* infected cats be treated? Whether to treat all healthy housemates of infected cats is controversial because all of the drugs have potential side-effects, cats with normal stools are not considered human health risks, treatment is unlikely to eliminate infection, and re-infection can occur within days. However, the safety margin of fenbendazole is very wide and so if treatment chosen, this drug seems to be a reasonable choice, administered for a 5 day course.

Should I follow *Giardia* test results after treatment? The AAFP Advisory Panel on Zoonoses recommends attempting to remove the source of infection during the treatment period and performing a fecal centrifugal flotation after *Giardia* treatment one time, within 2-4 weeks after the end of the treatment period (www.aafponline.org), even if centrifugal flotation was negative while the antigen test was positive when used to establish the initial diagnosis. If the animal is healthy and negative for cysts, retesting is not indicated again until the next scheduled fecal flotation. Currently it is not recommended for any of the *Giardia* antigen tests to be used as a recheck test in the early post treatment phase. As discussed, it is currently unknown how long *Giardia* antigens will persist in feces after successful treatment.

What should I do with cats that have normal stool and are *Giardia* antigen positive, *Giardia* cyst negative? This issue continues to be a dilemma and a source of ongoing discussion among parasitologists and clinicians alike. These animals have either a low grade infection or a low percentage of animals (approximately 2-5%) have false positive antigen test results. To further evaluate for cyst shedding, the veterinarian can perform an IFA test or 2 additional fecal flotations (3 negative centrifugal flotation assays run within 5 days is considered adequate to rule-out a *Giardia* infection in both animals and humans); if these other test results are negative, the antigen test was likely falsely positive.

What should I do if *Giardia* spp. infection persists in a healthy cat? If cysts are still identified after fecal centrifugal flotation performed 2-4 weeks after appropriate administration of a drug with anti-*Giardia* activity, then a second course of therapy may be indicated using a drug from an alternate class. Some clinicians and parasitologists recommend the combination of metronidazole and fenbendazole for 5 days and then further treatment and testing are suspended. It is not recommended that apparently well animals be treated beyond two courses of therapy. No further diagnostics are indicated until GI signs occur or the animal is again due for routine fecal screening.

What can I do to prevent re-infection with *Giardia* spp.? Prevention involves boiling or filtering of water collected from the environment prior to drinking and disinfection of premises contaminated with infected feces with steam cleaning or quaternary ammonium compounds (1 minute contact time). Transport hosts should be controlled and treatment and bathing of all animals in the environment could be considered. Feces from infected animals should be removed from the environment promptly. To date, no study has shown the *Giardia* spp. vaccines licensed for dogs and cats to have lessened *Giardia* spp. infections in the field and so both vaccines have been classified by AAHA and AAFP as generally not recommended as preventatives. As discussed, the feline vaccine product has been discontinued.

Suggested readings

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