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Chapter 15

Diarrhea in Kittens

Stanley L. Marks and Michael D. Willard

Diarrhea in kittens is one of the most common maladies facing the small animal clinician and managers of feline shelters and catteries.[1] A recent survey of the Association of Shelter Veterinarians identified kitten diarrhea as one of the top two concerns of veterinarians who treat shelter cats, second only to upper respiratory infections.[2] Clinical signs can range in severity from a mild, self-limiting diarrhea to a potentially fatal acute hemorrhagic diarrheal syndrome. Despite the significant clinical importance of diarrhea in kittens, veterinary literature does not provide much specific information on the causes and diagnosis of this malady. Antibiotics often are administered injudiciously to diarrheic kittens, and subsequent resolution of clinical signs often is equated wrongly with eradication of a "putative" infectious pathogen. Indiscriminate antibiotic therapy may even alter the commensal intestinal microflora, which leads to an exacerbation of the animal's diarrhea or development of antibiotic resistance.[3] Knowledge of the most common causes of diarrhea in kittens is integral to formulation of appropriate diagnostic and therapeutic plans and guidance for the veterinarian when standard therapeutic recommendations fail. Although diarrhea in kittens can be associated with a number of different etiologies, infectious causes are believed to play an important role in many of these cases.

PARASITIC CAUSES OF DIARRHEA

Trichomonosis

Tritrichomonas foetus, the primary causative agent of bovine trichomoniasis, recently has been recognized as a protozoal pathogen in cats (Figure 15-1).[4,5] In cattle, the obligate symbiotic protozoan is found primarily on the mucosal surface of urogenital cavities. It causes early embryonic death, abortion, and pyometra in infected cows.[6] Interestingly, *T. foetus* is found primarily on the large intestinal mucosal lining in cats.[4] Infected cats generally are young but have ranged in age from 3 months to 13 years of age (median 9 months). The pathogenicity of *T. foetus* for cats was demonstrated in a recent study in which eight cats were infected experimentally with a *T. foetus* strain isolated from a diarrheic kitten.[7] Trophozoites were cultured from the feces of all eight cats within 1 week after oral inoculation; infection persisted throughout the entire 203 days of the study, even when stools became normal.

Prevalence of T. foetus

The prevalence of *T. foetus* infection at an international cat show was found to be 31 per cent (36 out of 117 cats), with 28 out of 89 catteries affected.[5] Co-infection by *T. foetus* and *Giardia* spp. was common and was documented in 12 per cent of cats.

Misdiagnosis of *Giardia* spp. is common in cats with *T. foetus* infection. It may explain why cats diagnosed with apparent *Giardia spp.* infection do not respond to appropriate therapy. Risk factors for protozoal shedding and exacerbation of diarrhea included concurrent infection with *Cryptosporidium* spp., and cats living in close proximity with one another.[5] The predominance of infection in young cats from dense housing conditions may reflect an increased opportunity for exposure, or enhanced susceptibility to infection because of environmental stress or immunological immaturity.

Clinical Signs

T. foetus infection in cats can be associated with a chronic or recurrent large intestinal diarrhea characterized by increased mucus, tenesmus, occasional hematochezia, and increased frequency. The anus frequently is red, swollen, and painful, and fecal incontinence is not uncommon. Most cats usually are bright, alert, and responsive, and in good body condition with a normal appetite. *T. foetus* also can be cultured from the feces of asymptomatic cats, many of whom will not develop diarrhea.

Diagnosis

The following four methods of diagnosis should be considered in the order presented here.

MULTIPLE DIRECT FECAL SMEARS ON DIARRHEIC FECAL SPECIMENS. Direct fecal smears are indicated for the recovery of motile trophozoites of *Giardia* spp. and trichomonads such

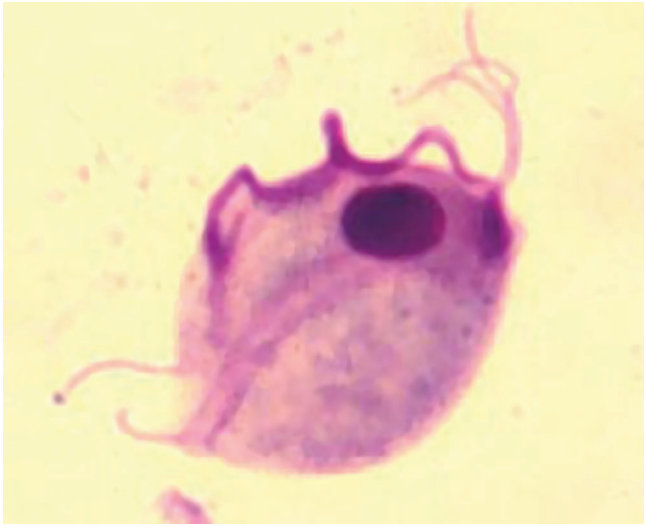

Figure 15-1. Giemsa-stained fecal smear showing characteristic appearance of *T. foetus* with its three anterior flagellae and long, undulating membrane.

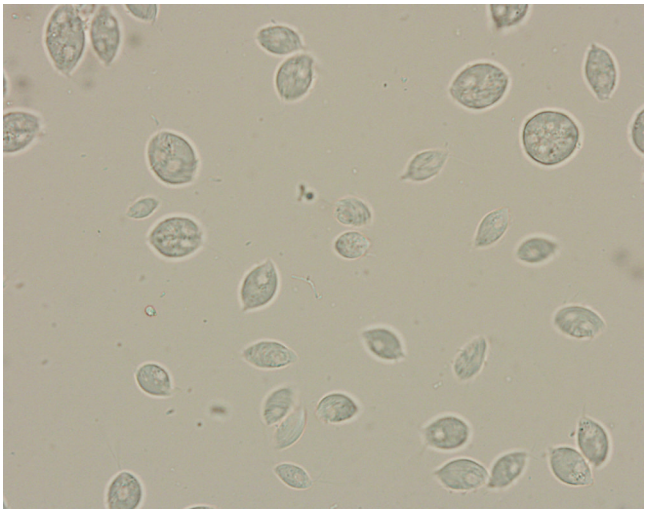

Figure 15-2. *T. foetus* trophozoites in culture medium (InPouch TF) isolated from a diarrheic cat (magnification ×400).

as *T. foetus*. The procedure should be performed with saline (0.9 per cent) and with use of fresh feces (body temperature, <2 hours old). Trophozoites in older specimens lose their motility and degenerate and become unrecognizable. The survival of trichomonads can be prolonged by adding 3 ml of 0.9 per cent saline to 2 g of feces. A small amount of feces is placed on a warm slide and a drop of 0.9 per cent saline is mixed with the feces. Alternatively, a miniscule amount of fresh feces can be collected by insertion of a cotton-tipped swab into the rectum. The smear must not be too thick, because trophozoites will be missed easily. A simple rule of thumb is that the observer should be able to read the fine newsprint of a newspaper through the smear.

After application of a coverslip, the smear is evaluated for motile organisms by examining at 10× magnification, with confirmation at 40× magnification. After the wet preparation has been checked thoroughly for motile trophozoites, a drop of D'Antoni's iodine can be placed at the edge of the coverslip, or a new wet mount can be prepared with iodine alone for morphological identification of the organism. A weak iodine solution that resembles "strong tea" is recommended.

The main limitation of direct fecal smears is sample size, with the result that negative smears are not uncommon with low parasite burdens. The sensitivity of direct fecal smear examination for diagnosis of *T. foetus* is relatively low in cats with spontaneous disease (14 per cent).[8] In addition, *T. foetus* can be difficult to distinguish from nonpathogenic intestinal trichomonads such as *Pentatrichomonas hominis* using light microscopy. *T. foetus* should be distinguished from *Giardia* spp. *Giardia* trophozoites have a concave ventral disc, and motility that mimics a falling leaf. In contrast, trichomonads are spindle-shaped, have an undulating membrane that courses the entire length of the body, and move in a more irregular and jerky fashion. In contrast to *Giardia* spp., trichomonads do not have a cyst stage, which underscores the limitations of fecal flotation technique for diagnosis of trichomoniasis. *Trichomonads will not survive refrigeration and are found rarely in formed fecal specimens*.

FECAL CULTURES PERFORMED WITH AN INPOUCH TF KIT. A commercially available system marketed for diagnosis of *T. foetus* infection in cattle (InPouch TF, Biomed Diagnostics, White City, OR) should be considered if multiple direct fecal smears are negative for trophozoites.[8] Approximately 0.05 g (less than a peppercorn) of freshly voided feces can be placed in the InPouch for culture, or alternatively, a saline-moistened cotton-tipped swab can be placed in the rectum and then gently agitated in the InPouch for culture. The InPouch should be incubated at room temperature in an upright position in the dark and examined every 48 hours for up to 12 days for motile trophozoites with use of a 20× or 40× objective (Figure 15-2). Before microscopic evaluation, it is easiest to place the pouch in a plastic clamp provided by the manufacturer that facilitates mounting of the pouch onto the stage of a light microscope. The media in the pouch does not support the growth of *Giardia* spp. or *Pentatrichomonas hominis*, although further studies to evaluate the specificity of the InPouch are warranted.

SINGLE TUBE-NESTED PCR OF DNA EXTRACTED FROM FECES. A sensitive and specific single-tube nested PCR based on amplification of a conserved portion of the *T. foetus* internal transcribed spacer region (ITS1 and ITS2) and 5.8 rRNA gene from feline feces has been described.[9] The PCR test is more sensitive than fecal culture and tested positive in 55 per cent of cultures that were negative for *T. foetus*, even when feces were normal.

COLONIC MUCOSAL BIOPSY. Colonic mucosal biopsies are advocated once the above mentioned diagnostics have been completed. Histopathological changes in colonic mucosal biopsies from infected cats have consisted predominantly of a lymphocytic and plasmacytic infiltrate with a significant neutrophilic component. The intestinal epithelium frequently is attenuated, and immunohistochemistry has been used to detect the trichomonads on the surface epithelium and within crypts.

Therapy

No therapy currently exists for elimination of *T. foetus*, and cats infected with *T. foetus* have failed treatment with recommended

and higher dosages of numerous antimicrobial drugs, including metronidazole, fenbendazole, sulfadimethoxine, furazolidone, tylosin, amoxicillin, and paromomycin.[4] Despite their failure to eradicate infection, some cats do show a mild improvement in fecal consistency while receiving antimicrobial drugs. This may reflect an alteration of the endogenous intestinal microflora that supports the trichomonads, or effective resolution of cofactors (*Giardia* spp., *Cryptosporidia* spp., other coccidia), that could exacerbate the cats' diarrhea. Prolonged use of antimicrobials has not been successful for long-term control of diarrhea and may delay the onset of clinical remission or exacerbate the diarrhea in some animals. In addition, higher doses of certain antibiotics such as metronidazole and paramomycin may cause adverse effects in cats, including neurotoxicity and nephrotoxicity,[10] respectively. A recent report showed that more than 50 per cent of cats diagnosed with *T. foetus*–associated diarrhea were still shedding the organism up to 5 years after diagnosis based on PCR confirmation, and diarrhea persisted for up to 3 years in many cats, despite aggressive antimicrobial administration.[11] Relapses of diarrhea were common and associated with dietary change, medical treatments unassociated with *T. foetus* infection, and travel.[11] Currently, it is unknown whether long-term infection of cats with *T. foetus* is a predisposing factor for development of inflammatory bowel disease. In light of the poor host specificity of *T. foetus* and the intimate association between infected cats and their human companions, the potential for zoonotic transmission should be considered. A single case of human infection with *T. foetus* has been documented in the literature to date. In that case, the infection presented as epididymitis and meningoencephalitis after immunosuppression and peripheral blood stem cell transplantation.[12]

Cryptosporidium Species

Coccidia of the genus *Cryptosporidium* spp. are small, ubiquitous protozoan parasites that replicate in the microvillous borders of intestinal and respiratory epithelium of many vertebrates, including birds, mammals, reptiles, and fish.[13]

Clinical Signs

Infection with *Cryptosporidium parvum* in kittens and immunosuppressed cats causes a spectrum of disease ranging from asymptomatic carrier state to mild, transient diarrhea, cholera-like illness, or prolonged, life-threatening malabsorption syndrome.[14] The organism also has been associated with diarrhea in adult cats without obvious evidence of immunosuppression.[15] In addition, *C. parvum* infection has been diagnosed in association with intestinal cellular infiltrates indistinguishable from those seen with inflammatory bowel disease in cats.[15] Caution should be heeded in overinterpretation of the presence of the organism with these infiltrates, because other co-factors, including diet, may have been associated with these cellular infiltrates.

Diagnosis

Despite the relatively high seroprevalence rates of *C. parvum*–specific IgG in cats (8.3 to 87 per cent),[16-18] the laboratory detection of this ubiquitous protozoan parasite in spontaneously infected diarrheic cats is difficult, predominantly because the organism is so small (average 4.6 × 4.0 μm) and difficult to find in fecal specimens via light microscopy[19] and because fecal shedding may be intermittent. Current laboratory protocols for detection of *Cryptosporidium* oocysts in fecal specimens include microscopic examination of smears stained with Giemsa, the modified Ziehl-Neelsen technique (Figure 15-3), the modified Kinyoun acid-fast technique, or use of an immunofluorescent detection procedure (Figure 15-4).[20,21] Immunofluorescent detection procedures are more sensitive and specific than acid-fast stains and generally are the method of choice for morphological diagnosis in human beings.[22] Microscopic techniques work well when clinical signs are present and oocyst numbers are relatively high; however, once clinical signs abate and oocyst numbers are greatly decreased, the sensitivity of tests relying on morphological identification is reduced and diagnosis often requires examination of multiple fecal specimens. In these cases, the newer enzyme immunoassays designed to detect *Cryptosporidium* spp. antigens in feces have proven more sensitive.[23] Difficulties in detection and enumeration of oocysts in fecal specimens are compounded by variation in consistency between individual fecal specimens, the amount of specimen used, and oocyst losses incurred during recovery processes. Although several diagnostic tests have come into widespread general use, the veterinary literature lacks published data that compare different diagnostic methods in cats. No single procedure has become adopted universally.

A recent study compared the performance characteristics of a Ziehl-Neelsen stain, direct fluorescent antibody technique, and three ELISA tests* (Table 15-1).[21] It revealed that the ProSpecT Microplate ELISA was the most sensitive diagnostic test for *Cryptosporidium* spp. on a single day, whereas the ProSpecT Rapid ELISA was highly insensitive and should not be used by veterinary diagnostic laboratories.

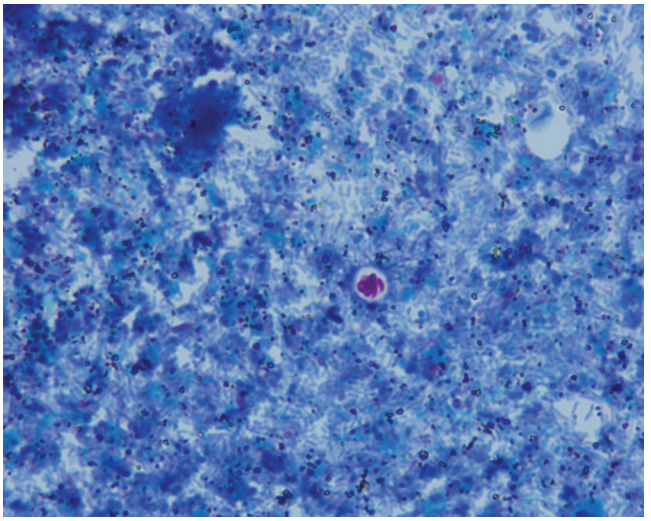

Figure 15-3. Fecal smear showing a single acid-fast (modified Ziehl-Neelsen) staining *Cryptosporidium* oocyst from a diarrheic cat (magnification ×1000).

*Premier Cryptosporidium ELISA, Meridian Biosciences Inc., Cincinnati, OH; Remel ProSpecT Microplate ELISA, Lenexa, KS; and Remel ProSpecT Cryptosporidium Rapid ELISA.

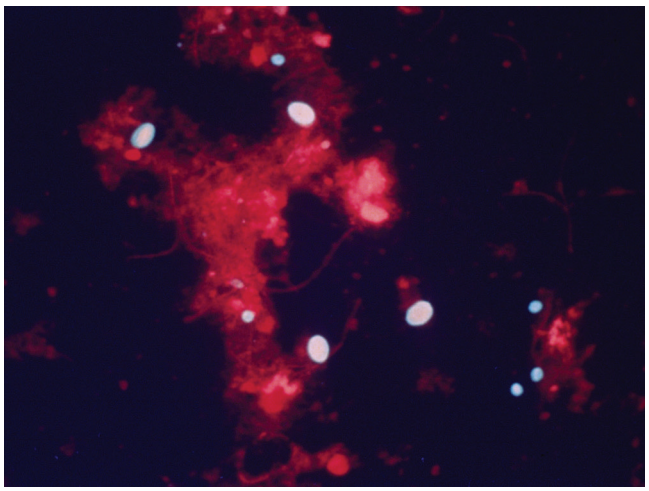

Figure 15-4. Direct immunofluorescent assay (Merifluor *Cryptosporidium/Giardia* direct immunofluorescent kit, Meridian Diagnostics Inc, Cincinnati, OH) showing fluorescent *Giardia* cysts (larger, oval) and *Cryptosporidium* oocysts (smaller, round).

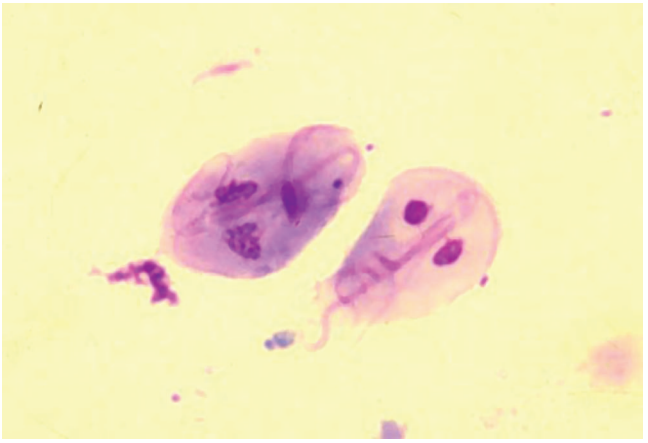

Figure 15-5. Giemsa-stained fecal smear showing two *Giardia* trophozoites exhibiting the characteristic pear, or teardrop, shape with bilateral symmetry when viewed from the top, two nuclei, and fibrils running the length of the parasite.

Table 15-1 | **Cumulative Sensitivities of Five Methods of Detection of *Cryptosporidium* Species in Fecal Specimens Collected Once Daily over 4 Consecutive Days from 104 Naturally Exposed Kittens**

DETECTION METHOD	DAY 1	DAY 3	DAY 4
Ziehl-Neelsen technique	72%	91%	94%
Direct immunofluorescence detection	50%	83%	84%
Meridian Premier ELISA	80%	93%	93%
Remel ProSpecT Microplate ELISA	89%	94%	95%
Remel ProSpecT Rapid ELISA	15%	43%	49%

Treatment

Eradication of this parasite has proven difficult, and many putatively effective drugs are either toxic or ineffective in cats. The aminoglycoside, paromomycin, is potentially nephrotoxic[10] and ototoxic in cats and preferably should not be used. Although the benzamide antimicrobial, nitazoxanide, has been shown to eradicate *Cryptosporidium* spp. in human beings and cats, its administration to cats was associated with unacceptable adverse effects (i.e., vomiting and anorexia). One report stated that tylosin was effective in eradicating *Cryptosporidium* infection in a cat[15]; however, I* recently completed a prospective double-blind study that failed to show any benefit for tylosin in naturally infected cats. Azithromycin is used in human beings for management of cryptosporidiosis and appears safe in cats when administered at a dosage of 7 to 10 mg/kg PO q12h for 7 days; however, the efficacy of this treatment in cats is unknown.

Giardia Species

Giardia spp. are an important cause of outbreaks of waterborne infection resulting from contamination of raw municipal water, back-country streams, and lakes with human effluent or infected animal feces.[24] The overall prevalence of *Giardia* spp. infection in cats in North America has been reported at about 4 per cent, with much higher levels in kittens and in cats housed in shelters.[25]

Clinical Signs

Giardia infections in adult cats often are subclinical or associated with a transient softening of the stool early in the infection; however, acute diarrhea tends to occur in kittens shortly after infection. Feces are often malodorous, pale, and may contain mucus.

Diagnosis

The diagnosis of *Giardia* infection traditionally has depended on microscopic identification of trophozoites (Figure 15-5) or cysts (Figure 15-6) in feces from affected animals. However, microscopic diagnosis of *Giardia* infection can be difficult, because (1) cysts may be shed intermittently and (2) they are so delicate. Many artifacts (e.g., grass pollen, yeast) mimic the morphology of *Giardia* cysts to varying degrees, and care must be exercised in differentiating these from *Giardia* spp. A recent survey evaluated the sensitivity of fecal flotation for detection of *Giardia* spp. in dogs and confirmed the poor performance of current in-house microscopy testing for *Giardia* spp. compared with microplate ELISA. In that study, microscopy following fecal flotation identified only half of the infected dogs and falsely diagnosed up to 25 per cent of uninfected animals.[26]

Accurate identification of these parasites in diarrheic cats is important because the organism could be a zoonosis[27] and failure to detect these parasites in diarrheic cats often leads to injudicious antibiotic therapy, which can exacerbate the diarrhea. Many veterinarians and reference laboratories have resorted to using ELISA tests that rely upon detection of *Giardia* cyst wall protein I (GCWP 1).[28] The ELISA tests are advantageous because they are generally easy to perform and results are easy to interpret. In addition, the test does not rely upon morphological identification of cysts or oocysts via

*One of the chapter co-authors, Stanley L. Marks.

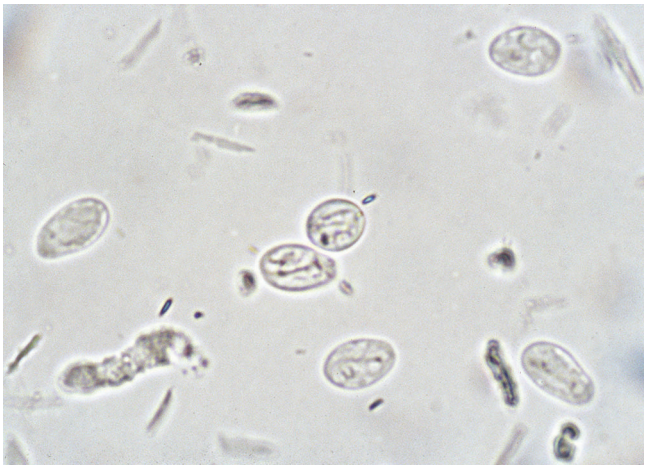

Figure 15-6. Zinc sulfate fecal flotation showing *Giardia* cysts with distinctive fibrils (axonemes) coursing the length of the cyst (magnification ×400).

microscopy, which saves technician time and potentially avoids false-negative interpretations. The ELISA tests also can detect GCWP 1 in the absence of detectable cysts.[28] However, virtually every commercially available ELISA is marketed for human use, and studies are few that appraise their performance characteristics in diarrheic cats and dogs.

Recently, a novel SNAP *Giardia* Test Kit (IDEXX Laboratories, Inc., Westbrook, Maine) for detection of GCWP 1 in canine and feline feces was released. The SNAP *Giardia* Test is a rapid in-house enzyme immunoassay that can be performed on fresh feces, previously frozen feces, or feces stored at 2 to 7° C for up to 7 days. This test represents the first commercially available ELISA designed specifically for dogs and cats and has the added advantages of simplicity, rapid availability of results (8 minutes after mixing of the conjugate solution with feces), and low cost. The performance characteristics of this test have not been well characterized; the test must be scrutinized against the performance characteristics of other ELISAs, fecal flotation, and the immunofluorescence assay. Preliminary studies in our laboratory found a relatively high sensitivity (86 per cent) for the Remel ProSpecT Microplate ELISA in cats naturally infected with Giardia spp., whereas the Remel ProSpecT Rapid ELISA had an unacceptably low sensitivity of 56 per cent.[29] Immunofluorescence detection procedures (see Figure 15-4) are more sensitive and specific than acid-fast stains and generally are the method of choice for morphological diagnosis of cryptosporidiosis in human beings.[22]

Treatment

Metronidazole was shown to be highly effective and safe when given at 25 mg/kg PO q12h for 7 days to cats with experimental infections.[30] Albendazole also is relatively effective when dosed at 25 mg/kg PO q12h for 5 days; however, the drug has been associated with pancytopenia and is teratogenic. A recent trial evaluating the efficacy of fenbendazole in cats co-infected with *C. parvum* revealed that the drug was safe; however, it was relatively ineffective (50 per cent).[31] Additional studies with this drug are warranted in cats with *Giardia* spp. and lack of co-infection. Drontal Plus was shown to be relatively safe and effective in experimentally infected kittens when given at twice the recommended dose. The dose of febantel used was 56.5 mg/kg PO.[32]

Control of Giardia *Infection*

The following four fundamental steps should be taken to control *Giardia* infection and minimize reinfection of treated animals:

1. The environment is decontaminated. Simultaneous treatment of animals with the medications and decontamination of the environment with a quaternary ammonium-based (QUAT) disinfectant (Roccal D, Totil, Quatsyl 256, or Aqua Quat 400) should improve effectiveness of treatment and maximize the possibility of eliminating *Giardia* spp. from the cattery or shelter. Specifically, gross fecal contamination should be removed as much as possible on a daily basis. Runs should be rinsed with water, after which a layer of disinfectant foam (Roccal D) should be applied. After 10 to 20 minutes, the foam should be rinsed away with fresh water. Cages should be sponged clean on a daily basis with a dilute disinfectant or mix of Clorox diluted at 1:32 and Quatsyl 256 at 1:256.[33]
2. The animal is treated with effective drugs.
3. The animal is bathed to clean cysts from the coat.
4. Reintroduction of infection is prevented.

Giardia *Vaccine*

A commercial *Giardia* vaccine (GiardiaVax, Fort Dodge Animal Health, Overland Park, KS) with chemically inactivated trophozoites has been prepared and licensed for use in cats in the United States. Efficacy studies conducted in kittens revealed that fewer vaccinated animals developed diarrhea after oral challenge, and diarrhea in vaccinated animals was of short duration compared with controls. Vaccination also reduced the duration of cyst shedding and the number of cysts shed in the feces when compared with control animals.[34] The administration of three doses of GiardiaVax as an immunotherapy to experimentally infected kittens was ineffective in eradicating cysts.[35] We do not advocate the routine vaccination for *Giardia* spp. in household cats.

Coccidia Species

Cats are infected with two species of coccidia, *Isospora rivolta* and *Isospora felis* (Figure 15-7). Immunity to *I. rivolta* is not complete, and some oocysts are shed after challenge.[36] Kittens that are 4 weeks old are most susceptible to infection with *I. felis*. Enteritis, emaciation, and death can occur after inoculation of 10^5 oocysts.[37] Studies indicate that cats infected naturally with *I. felis* develop lower antibody titers than do those inoculated experimentally with *I. felis*.[38]

Diagnosis

Fecal flotation with zinc sulfate is the recommended method. Examination of stools for bacterial and viral agents that cause disease in these animals is important because coccidiosis usually is asymptomatic. Cats can have oocysts in their fecal

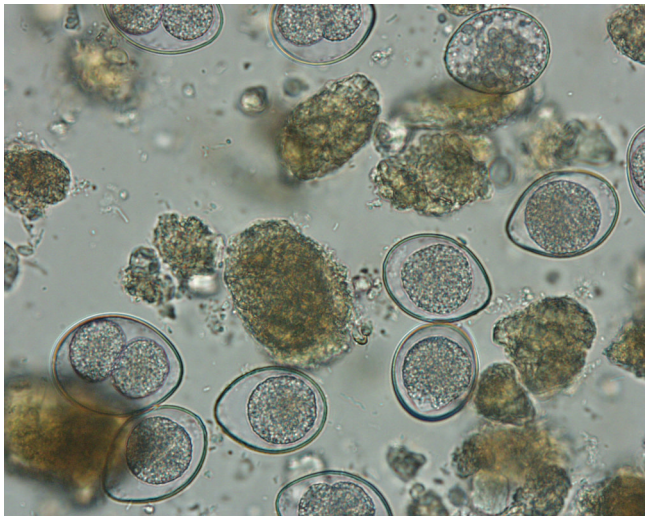

Figure 15-7. Zinc sulfate fecal flotation showing *Isospora* spp. oocysts recovered from a diarrheic kitten (magnification ×400).

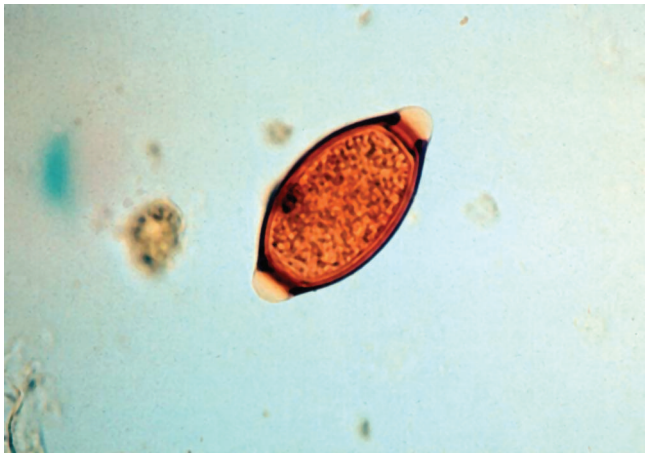

Figure 15-8. Fecal flotation showing biperculate *T. vulpis* ovum (magnification ×400).

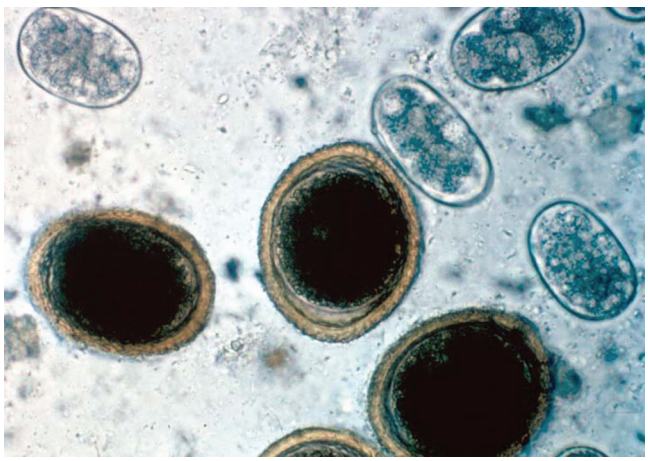

Figure 15-9. Fecal flotation showing large, thick-walled ova of *T. cati* and *Ancylostoma caninum* ova (magnification ×400).

specimens from ingestion of prey. These should be recognized as pseudoparasites. The most common of these are *Eimeria* species from ruminants, rabbits, or rodents. These oocysts will not be in the two-celled stage as is common for *Isospora* species. They often have ornamentations such as micropyle caps or dark thick walls that are not found on *Isospora* oocysts.

Treatment

Sulfadimethoxine given at 50 mg/kg PO q24h for 10 to 14 days eliminates oocyst excretion in most cats.[39] The combination of ormetoprim (11 mg/kg) and sulfadimethoxine (55 mg/kg) given orally for up to 23 days has been used effectively in dogs. Amprolium given at 300 to 400 mg/kg PO q24h for 5 days, or 110 to 220 mg/kg PO q24h for 7 to 12 days, is effective in treatment of coccidiosis in dogs. Other agents such as furazolidone, quinacrine, and metronidazole probably are of little clinical value.

Whipworms

Cats rarely acquire whipworm infections, although they are a possibility in animals with clinical signs of colitis. The adult worms burrow into the colonic and cecal mucosa and may cause inflammation, hematochezia, and intestinal protein loss.

Diagnosis

T. vulpis should be considered in animals with evidence of colonic disease. A fecal centrifugation flotation should allow recognition of the biperculate ova (Figure 15-8). However, intermittent shedding has been well documented in dogs; therefore cats with a negative fecal flotation should be dewormed empirically.

Treatment

Fenbendazole is a safe broad-spectrum anthelminthic. The drug is administered orally at 50 mg/kg q24h for 5 consecutive days, and the regimen is repeated at 3 weeks and 3 months after initiation of therapy.

Roundworms

Roundworms are common in cats (*Toxocara cati* and *Toxascaris leonina*) and can cause diarrhea, failure to thrive, a poor haircoat, and a "potbellied" appearance. Vomiting is observed occasionally when the roundworms gain access to the stomach.

Diagnosis

The large ova (approximately 80 µm) with a characteristic thick wall are easy to recognize on fecal flotation (Figure 15-9).

Treatment

Pyrantel at 20 mg/kg PO is safe in kittens. The treatment should be repeated at approximately 3 weeks. Fenbendazole also is an effective anthelminthic and can be administered to newborn kittens at 50 mg/kg PO for 3 days to kill more than 90 per cent of prenatal larvae. Kittens should be dewormed routinely every 2 weeks, starting at 2 weeks of age, until 8 weeks.

Hookworms

Cats are infected with *Ancylostoma tubaeforme*, *Ancylostoma braziliense*, *Uncinaria stenocephala*, and less commonly, the canine hookworm, *Ancylostoma caninum*. The worms are voracious blood suckers and attach to the mucosa of the small intestine. Hookworm infections in cats are relatively uncommon with reported prevalences of 0.9 and 1.1 per cent.[40] Kittens are infected by ova ingestion or through transcolostral transmission. Kittens occasionally can have life-threatening blood loss or iron-deficiency anemia, melena, hematochezia, and failure to thrive.

Diagnosis

Fecal flotation should be positive because the worms produce a large amount of eggs (see Figure 15-9).

Treatment

Fenbendazole and pyrantel are effective in cats.

MAXIMIZING THE DIAGNOSTIC YIELD OF A FECAL EXAMINATION

A fecal examination is integral to the diagnostic work-up of kittens with diarrhea, vomiting, and weight loss. The techniques used most commonly include direct fecal smear (wet prep), stained smear, and a fecal flotation. A Baermann technique is indicated when parasitic larval stages are being evaluated.

Stained Smear

Traditionally, stained smears have been examined to evaluate for the presence of endospores associated with *Clostridium perfringens*; for the presence of spiral-shaped, gram-negative bacteria consistent with *Campylobacter* spp.; or, for the presence of increased white blood cells. The diagnostic value of finding increased fecal endospores (Figure 15-10) is virtually zero, because healthy, nondiarrheic cats and dogs also can have increased fecal endospores. In addition, no correlation exists between increased fecal endospores and the presence of fecal enterotoxin. Finding spiral-shaped bacterial organisms should be interpreted with caution because many *Campylobacter* spp. are found in cats, and many are nonpathogenic. Perhaps the best use of stained fecal smears is to make a diagnosis of intestinal lymphoma, and intestinal *Histoplasma* or *Prototheca* infections, the latter two of which are rare in cats. The diagnostic yield of stained fecal smears can be increased by use of a cotton swab introduced into the rectum and rotated gently several times. The cotton swab is rolled onto a glass slide, which is then stained after air drying.

Fecal Flotation

Fecal flotations are indicated to find cysts, oocysts, and ova in feces. Fresh feces should be examined whenever possible, or a fresh specimen can be refrigerated for up to 72 hours for detection of cysts, oocysts, or eggs via a concentration technique. Fresh feces also can be placed in 10 per cent buffered formalin if evaluation will be delayed more than 72 hours. Specimens

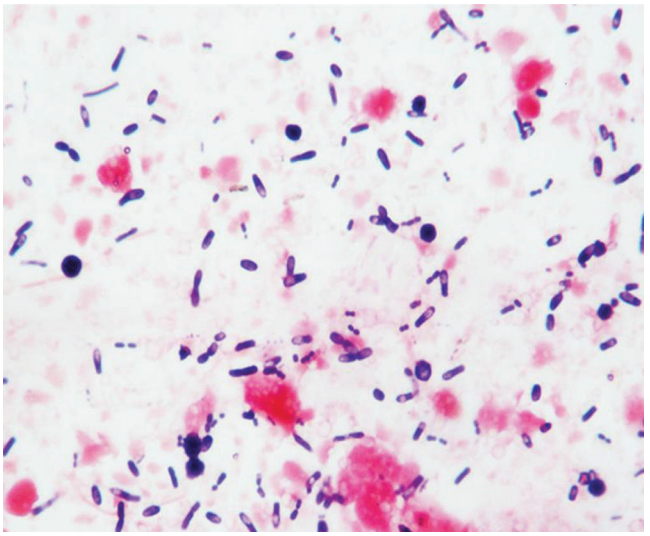

Figure 15-10. Stained fecal smear (modified Wright's stain) from a healthy, non-diarrheic cat showing numerous endospores of *C. perfringens* (magnification ×1000)

Figure 15-11. Centrifuge with free swinging buckets showing a coverslip in place before centrifugation.

fixed in formalin are suitable for concentration techniques, acid-fast stains, and immunoassays. Although standing (gravitational) flotation methods are easier and quicker to perform than centrifugation flotation (Figure 15-11), the latter clearly has superior sensitivity (up to eight times).[41] Animals with low parasite burdens could have a false-negative result if the gravitational method is used. Fecal flotations have limitations and should not be used to detect heavy ova that do not float (*Paragonimus* spp.) or larvae (*Aelurostronglyus* spp.).

The type of flotation medium used and specific gravity of flotation medium are important considerations. We recommend zinc sulfate with a specific gravity of 1.18 or 1.2 for flotations. This solution and specific gravity are optimal for flotation of ova and *Giardia* cysts, while the structural detail of the *Giardia* cyst is maintained.

Procedure for Centrifugal Flotation

1. A fecal emulsion is prepared with use of 2 to 5 g of feces and 5 to 10 ml of flotation solution.

2. The emulsion is strained through a tea strainer or cheesecloth with 10- to 15-ml flotation solution into a 15- to 20-ml conical centrifuge tube.
3. The tube is filled with flotation medium to create a positive meniscus.
4. A coverslip is placed on top of the tube.
5. The tube is balanced in the centrifuge.
6. The tubes are centrifuged for 10 minutes at 1500 to 2000 rpm.
7. The coverslips are removed carefully from the tubes by lifting straight up; they are placed on a clean slide.
8. The slide is examined within 10 minutes. The entire coverslip is examined at 10×. A magnification of 40× is used to confirm identification by visualizing internal structures and measuring the organism.

Modification

With a centrifuge that is fixed-angle and does not have free swinging buckets, the above procedure should be followed but the centrifuge tube is filled to within an inch or so from the top, and a coverslip is not added for the final spin. When the final centrifugation step is complete, the tube is set upright carefully in a test tube rack. A pipette is used to gently run additional flotation solution down the side of the tube while disturbing the contents as little possible. A positive meniscus is created and a coverslip set on top. This preparation should be allowed to stand for 5 minutes only. The coverslip is removed to a slide and examined as described in step 8.

BACTERIAL CAUSES OF DIARRHEA

Diagnosis of bacterial-associated diarrhea in kittens is difficult for two reasons: (1) the isolation rates for putative bacterial enteropathogens often are similar in diarrheic and nondiarrheic animals and (2) the incidence of bacterial-associated diarrhea is extremely variable. Caution should be heeded in interpretation of the results of fecal ELISAs for *C. perfringens* enterotoxin (CPE) and *C. difficile* toxin A and/or B in neonatal kittens because of the high incidence of positive ELISAs (up to 50 per cent) I* documented in apparently healthy kittens. The effects of *C. difficile* toxin A and B have been shown to be dependent on age in human beings and dogs, in whom high levels of toxins are detected in the feces of neonates in the absence of clinical signs of disease.[42,43] The reader is referred to Chapter 5 for a more detailed description of specific bacterial enteropathogens associated with diarrhea.

The indications for performance of fecal enteric panels on diarrheic kittens are poorly defined, which results in indiscriminate testing and misinterpretation of results. Fecal cultures and toxin analysis for specific bacteria should be reserved for (1) kittens that develop diarrhea after kenneling or show attendance once parasitic causes for diarrhea have been ruled out, (2) kittens with an acute onset of bloody diarrhea in association with evidence of sepsis, (3) outbreaks of diarrhea occurring in more than one household pet, and (4) screening for enteropathogens (*C. difficile*, *Campylobacter* spp., or *Salmonella* spp.) when zoonotic concerns are present. A recently published study documented the prevalence of five groups of potentially zoonotic enteric infections (*Salmonella* spp., *Campylobacter* spp., *Cryptosporidium* spp., *Giardia* spp., and *Toxocara cati*) in fecal samples from cats under 1 year of age that were either housed in humane shelters or presented to primary-care veterinarians in central New York State[44] (see Chapter 75). Possible associations of these organisms with the cat's source or with the presence of diarrhea were evaluated. The proportion of fecal samples with one or more zoonotic organisms was 35.1 per cent among client-owned cats and 44.2 per cent among shelter cats. The prevalence of *Salmonella* spp. was 0.8 per cent, which is similar to the reported prevalence of *Salmonella* spp. in cats in Colorado[27] and in kittens from shelters in Japan (1.1 per cent).[45] I* also have documented a relatively high incidence of *Campylobacter* spp. in fecal specimens from nondiarrheic cats and kittens (approximately 20 per cent).

Miscellaneous Bacterial Causes of Diarrhea

Anaerobiospirillum *Species*

Anaerobiospirillum spp. are motile, spiral-shaped, anaerobic gram-negative rods that were first identified by Malnick and coworkers (1983) in two human patients with diarrhea.[46] Since then, *Anaerobiospirillum succiniciproducens* and *Anaerobiospirillum thomasii* have been recognized as causes of septicemia, particularly in immunocompromised human beings, and have been isolated from the throat and feces of healthy cats and dogs.[47,48] We have identified three cats with clinical signs of acute onset of vomiting, diarrhea, and abdominal pain that progressed rapidly to systemic disease characterized by lethargy and collapse. On necropsy, an acute to subacute ileocolitis was found in association with abundant spiral-shaped organisms confirmed as *Anaerobiospirillum* spp.[49] (Figure 15-12).

Anaerobiospirillum spp. and *Campylobacter* spp. are similar morphologically and can be confused. *Anaerobiospirillum* spp. are oxidase and catalase negative, whereas *Campylobacter* spp. usually are oxidase and catalase positive. *Anaerobiospirillum* spp. demonstrate corkscrew motility, whereas *Campylobacter* spp. display darting motility. *Anaerobiospirillum* spp. have bipolar tufts of flagella, whereas *Campylobacter* spp. have a single flagellum on one or both poles. Although the organisms have been isolated from the rectal swabs of asymptomatic dogs and cats, they have not been isolated from the feces of asymptomatic human beings. Most human patients infected with *Anaerobiospirillum* spp. are immunocompromised, and the organism is a rare cause of bacteremia in people. According to the NCCLS breakpoints for anaerobes, the isolates are susceptible to amoxicillin-clavulanic acid, cefoxitin, imipenem, and penicillin, intermediately susceptible to metronidazole, and resistant to clindamycin.

Helicobacter *Species*

Helicobacter spp. are gram-negative, microaerophilic spiral-shaped, motile bacteria that colonize the gastrointestinal tract of several mammalian and avian hosts. Because inflammatory bowel disease (IBD) is a common clinical finding in domestic cats, and because *Helicobacter* spp. are associated with IBD in mice and rats, the possible relationship between helicobacters

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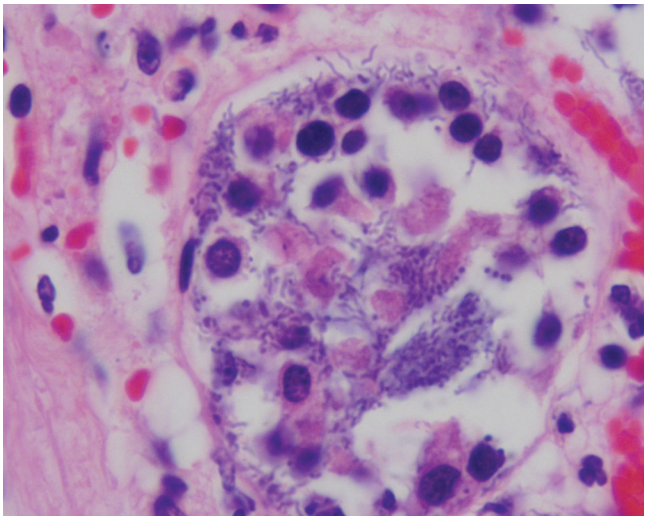

Figure 15-12. Light photomicrograph of colon obtained from a cat, showing spiral-shaped *Anaerobiospirillum* bacteria inside the lumen of a dilated crypt (Steiner stain) (magnification ×1200).

and IBD in cats should be explored. *Helicobacter canis* was isolated from four Bengal cats with and without chronic diarrhea.[50] Because the cats were coinfected with other potential pathogens, including *Campylobacter helveticus*, and because *H. canis* was isolated from nondiarrheic cats, the causal role of *H. canis* in production of the diarrhea could not be proven.[50] Histologically, the colons of the four affected cats were characterized by mild to moderate neutrophilic, plasmacytic, and histiocytic infiltrates in the lamina propria, with crypt abscesses.

A 4-month-old male British blue cat with catarrhal to hemorrhagic enteritis showed massive colonization of the stomach, small intestine, and cecum with spiral-shaped bacilli that strongly resembled *Flexispira rappini*, a spiral-shaped *Helicobacter* species known as a normal intestinal colonizer in dogs and mice.[51] Inflammatory infiltration was moderate and T-cell dominated. In the intestine, bacilli were found in the gut lumen, between villi, in crypt lumina, and within epithelial cells. Degeneration of crypt epithelial cells was observed, in addition to crypt dilation and moderate to massive macrophage-dominated infiltration of the mucosa and submucosa.

VIRAL CAUSES OF DIARRHEA

Feline viral enteritis usually is diagnosed in younger unvaccinated animals. The animal's signalment, history, clinical signs, and hematological findings are important in ranking a viral etiology as a likely cause of the animal's diarrhea.

Feline Panleukopenia

Feline panleukopenia (FP) is a viral disease characterized by fever, depression, anorexia, vomiting, and diarrhea. Historically, feline panleukopenia was caused exclusively by feline panleukopenia virus (FPV); however, it has now been confirmed that FP can be caused by canine parvoviruses CPV-2a and CPV-2b.[52] Feline panleukopenia has become an uncommon disease because of routine vaccination; however, outbreaks are seen occasionally in unvaccinated animals, particularly feral populations and catteries. The clinical signs are similar to those described for dogs with parvoviral enteritis.

Diagnosis

Diagnosis is based on the history, physical examination findings, results of a hemogram (neutropenia), and fecal ELISA. The ELISA test used to detect canine parvovirus has been reported to cross-react with feline parvovirus.

Treatment

Treatment is supportive and virtually identical to that described for dogs with parvovirus enteritis. Intravenous (IV) fluid and electrolyte therapy is indicated, with particular attention given to potassium repletion. The intramedullary route can be used in kittens, because the subcutaneous route is likely to be inadequate. Dextrose solution (2.5% to 5%) is added to the IV fluids if the kitten is hypoglycemic. Plasma or colloids (dextran 70 or hetastarch) are indicated if the serum albumin concentration drops below 2.0 g/dl. Antibiotics are administered to febrile or severely neutropenic cats. If the animal is neutropenic but afebrile, prophylactic administration of a first-generation cephalosporin is reasonable. Cats in septic shock should be treated with a broad-spectrum aerobic and anaerobic antibiotic (e.g., ampicillin plus amikacin). Human granulocyte colony-stimulating factor (G-CSF) at 5 µg/kg q24h SC will increase neutrophil numbers but may not influence outcome. Antiemetics such as prochlorperazine, metoclopramide, or ondansetron are indicated if vomiting is intractable. Metoclopramide is most effective when administered as a constant rate infusion at a dose of 1 mg/kg q24h. Gastric protectants including H_2-receptor antagonists and sucralfate are indicated when there is evidence of secondary esophagitis. Broad-spectrum anthelminthics to treat concurrent intestinal parasites should be administered when the cat is no longer vomiting. Most cats can be weaned gradually onto a digestible commercial enteral diet; however, intractable vomiting may warrant the administration of total or partial parenteral nutrition (see Chapter 16).

Feline Enteric Coronavirus

Feline enteric coronavirus is related to FIP-producing strains of coronavirus and invades the enterocytes at the tips of the villi. Infected cats may be asymptomatic or develop mild, transient diarrhea and fever. Infected cats can seroconvert and test positive on FIP serological testing. In addition, feline enteric coronavirus may mutate to FIP virus.

EMPIRICAL THERAPY FOR KITTENS WITH DIARRHEA OF UNKNOWN CAUSE

Unlike acute diarrhea, which often is self-limiting and may be managed with symptomatic or supportive therapy, chronic diarrhea usually requires specific diagnosis and therapy. Finding intestinal parasites in the feces of a kitten with diarrhea does not establish parasitism as the cause of the intestinal disease, although many kittens show a partial or complete resolution of clinical signs after administration of a broad-spectrum anthelminthic. We deworm diarrheic kittens routinely even in the face of a negative fecal flotation or negative *Giardia* ELISA. Serological screening for feline leukemia virus is

recommended for kittens with chronic diarrhea that have not responded to antiparasitic and dietary therapy. Metronidazole administration often is associated with some amelioration of diarrhea, possibly because of altering the intestinal microflora, dampening cell-mediated immunity, or killing a specific pathogen such as *Clostridium difficile*. Dietary modification should be considered in cats that fail to respond to empirical antiparasitic therapy and metronidazole administration. We frequently use commercial feline intestinal diets and have had success using a diet that is highly digestible and contains relatively large amounts of fermentable fiber. Kittens that fail to improve on a commercial diet can be fed a cooked turkey or chicken diet (without carbohydrates) for 5 to 10 days to provide a highly digestible meal containing moderate amounts of fat. Dietary fat restriction does not appear to be as important in cats with intestinal disease as it is in dogs. Home-cooked diets are not complete and balanced and should not be fed to kittens for more than 10 days.

Inflammatory bowel disease primarily is a disease of middle-aged to older cats, and kittens are more likely to have diarrhea resulting from an infectious cause. We discourage the administration of prednisone to diarrheic kittens unless a comprehensive work-up, including intestinal biopsies, warrants this therapy. Kittens with chronic ileitis could have secondary deficiencies of vitamin B_{12} (cobalamin), an important micronutrient for DNA replication in the intestinal crypts (see Chapter 13). Vitamin B_{12} can be administered empirically to kittens at 100 µg per kitten, given subcutaneously once weekly for 4 to 6 weeks. Repeat injections should be based on determination of serum cobalamin concentrations. Cobalamin is safe, easy to administer, and cheap. Use of prebiotics and probiotics for diarrheic animals has received tremendous attention recently; however, most studies completed have not been performed in animals with clinical disease. Furthermore, caution should be heeded when purchasing over-the-counter commercial probiotics because little federal regulation and quality control exist over many products, and label descriptions do not always match the ingredients.

CONCLUSION

Comprehensive fecal exams are pivotal in the diagnostic evaluation of kittens with diarrhea. The diagnostic yield will be increased markedly with the examination of fresh fecal specimens, the use of a centrifugation technique with zinc sulfate solution, and the timely incorporation of immunoassays for diagnosing *Giardia* and *Cryptosporidium* spp. Diagnosis of *T. foetus* is enhanced greatly with the utilization of InPouch culture kits that facilitate the growth and direct visualization of motile trophozoites. The clinical documentation of enteropathogenic bacteria that cause diarrhea in cats is clouded by the presence of many of these organisms existing as normal constituents of the indigenous intestinal flora. Attributing disease to a putative bacterial enteropathogen(s) in kittens should be made only after considering the animals' signalment, predisposing factors, clinical signs, serological assays for toxins, fecal culture, and/or PCR. Relying on results of fecal culture alone is wrong, because *C. perfringens*, *C. difficile*, *Campylobacter* spp., and pathogenic and nonpathogenic *E. coli* are isolated commonly from apparently healthy cats. Fecal cultures may be useful in procuring isolates for the application of molecular techniques such as PCR for detection of specific toxin genes, or for molecular typing of isolated strains to establish clonality in suspected outbreaks. Accurate diagnosis of infections may require diagnostic laboratories to incorporate PCR-based assays using genus- and species-specific primers to facilitate detection of toxin genes and differentiation of species that appear similar phenotypically and biochemically.

In assessment of a diarrheic kitten not responding to therapy and for which a diagnosis has not been made, repeating previously negative diagnostic tests frequently is more helpful than performing endoscopy and biopsy. The intestinal tract is a lymphoid organ (in addition to its absorptive and endocrine functions) and is expected to respond to antigenic stimulation with some degree of lymphoid hyperplasia. Simply finding intestinal lymphocytic or plasmacytic infiltrates does not mean that the kitten has inflammatory bowel disease, nor does it guarantee that steroid therapy will not be harmful.

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