Diarrhea is one of the most common concerns of veterinarians evaluating kittens with a health problem. Often times, diarrhea in kittens can be attributed to dietary changes, parasites or infectious diseases, and these should be the focus of any investigation in these young cats. Adult cats often have different and more chronic causes of diarrhea than kittens, but the condition remains a common reason for cats to be presented to veterinarians for care. The purpose of this talk is to review some of the more common causes of diarrhea in kittens and cats, and to discuss the best approaches for diagnosis and treatment of diarrhea in kittens and cats. Where appropriate, the role of diet in both diagnosis and therapy of diarrhea will also be considered.

Infectious/Parasitic Causes of Diarrhea

Trichomonosis

Trichomonosis, caused by *Trichomonas foetus*, has been recently recognized as a pathogen in kittens and adult cats. This is the same protozoal organism that infects cattle, causing early embryonic death, abortion, and pyometra. However, in cats, the organism infects the large intestinal mucosa and causes chronic large bowel diarrhea characterized by increased mucus, tenesmus, hematochezia and increased frequency of defecation. Most affected kittens are healthy, alert and active, and the only outward signs of illness are the presence of anal hyperemia or swelling, and painful defecation. Most infections are diagnosed in young kittens with chronic diarrhea (average age 9 mo), but infection can occur in cats of any age. Cats that are exposed to the organism are highly likely to become infected, and infection is likely to be persistent. In a recent study, all 8 cats that were exposed to the trophozoites became infected – the organism was cultured from their feces throughout the 200 days of the study. However, infection with *T. foetus* does not necessarily correlate with the degree of clinical signs, as there are many cats that culture positive to the organism but are completely asymptomatic. The prevalence of this infection in the general population is unknown, but at a large international cat show, 31% of the cats (36/117 cats) were affected. The infection can be easily misdiagnosed as giardiasis unless the observer is trained to recognize the differences in the two species, and co-infection with *Giardia* spp. has been documented in 12% of cats. Infections are most commonly found in young cats from crowded housing conditions (shelters, catteries, rescue groups or cat “collectors”) which may reflect an increased opportunity for exposure or, alternatively, due to environmental stress and immature immune function in young cats.

Diagnosis of this infection can be made by one of four different approaches. These are listed in order from relative ease of using the test and expense: 1) direct examination of the feces for the trophozoites, 2) fecal cultures for the organism (using the InpouchTF kit, Biomed Diagnostics, White City, OR), 3) PCR of feces (must be submitted to specific labs, Dr. Gookin’s lab at NC State University is the best), and 4) colonic mucosal biopsy. The fecal smear test has the lowest sensitivity (14%), and errors in diagnosis can be made by inexperienced observers. However, it is still the easiest and potentially fastest way to make a definitive diagnosis. The InPouchTF kit is more sensitive than the fecal exam, but takes up to 12 days to grow the organism for diagnosis. The samples can be sent to lab for culture, or the culture kits can be obtained and used in the practice setting. Because other trichomonad species can grow in the pouch, PCR testing of the cultured organisms may be needed. PCR testing is the most
sensitive and specific method of diagnosis, but is also more expensive and results take longer to obtain as there are only a few labs that can do this test.

Therapy of cats with trichomonosis is difficult, as there is no readily available, approved drug for the treatment of the infection. Metronidazole and other antibiotics have been used in both experimentally and naturally infected cats, but are completely ineffective in clearing the infection. Because members of the nitroimidazole family of antimicrobials would be expected to be effective against trichomonads, other drugs from the family have been tested. Ronidazole (powder-on feed antibiotic used in treatment of turkey cankor) at a dose of 10-30 mg/kg q12-24h po has been shown to clear the infection in both naturally infected and experimental cases of the disease. This drug is not approved for use in cats, and is also potentially hepatotoxic and neurotoxic, and thus should be used only in circumstances where the owners understand the risks and a definitive diagnosis has been made. This antibiotic should not be used empirically to treat cats with undiagnosed diarrhea, as numerous anecdotal reports of neurotoxicity have been reported with its use in cats – especially at doses higher than recommended above or for longer than 14 days. All other antibiotics and antiparasiticidals, including tylosin, enrofloxacin, azithromycin and fenbendazole, have not been shown to be effective against *T. foetus*, and in some cats may exacerbate diarrhea by altering the normal flora, or result in delay of clinical remission. Clinical remission of the diarrhea has been shown to occur in many infected cats, usually by 2 years of age, even if they are not treated. However, many cats that have this infection are not acceptable indoor pets due to the malodorous feces they produce. At this time there is no evidence that this organism is zoonotic, but it certainly is infectious to other cats, and thus appropriate infection prevention measures should be instituted.

**Giardiasis**

*Giardia* spp. is a frequent cause of diarrhea in cats and kittens, with a prevalence rate reported to be at 4 percent nationally, but the infection rate is much higher in shelters or catteries where it may be nearly 12%. In many adult cats, *Giardia* spp. infections are subclinical or transient, but in kittens, infection is classically associated with an acute onset of malodorous, pale, mucoid diarrhea. The diagnosis is relatively straightforward when the trophozoites or cysts are identified on fresh fecal smears or a flotation. However, because the cysts are shed intermittently, and they can be misidentified or confused with other fecal artifacts, the sensitivity of this approach is only about 50%. The sensitivity increases to 90% if zinc sulfate flotation is used to examine 3 separate fecal samples. Recently, a SNAP Giardia test kit (IDEXX laboratories) for detection of *Giardia* cyst wall protein 1 (GCWP-1) in canine and feline feces has been made available for use as an in house diagnostic test for diagnosis of the infection. The test has not been performance tested in large numbers of field studies, but if the sensitivity is found to be > 90% (e.g. like commercial ELISA microplate readers used in commercial labs), the ease, simplicity and cost will make this test a great addition to the veterinarian’s diagnostic armamentarium. Treatment of giardiasis in cats and kittens has not changed drastically for many years, and includes specific anti-protozoal therapy combined with environmental control. Metronidazole, at a dose of 25 mg/kg po q12h for 7 days, continues to be a highly effective therapy for the disease in affected cats. Fenbendazole has been anecdotally reported to be effective in cats at a dose of 50 mg/kg po q24h, but only one clinical study has been reported and in that study the cats were co-infected with cryptosporidium, and the response to treatment was less optimal (50%). So, the true effectiveness of this drug against *Giardia* spp. is not known. Finally, experimentally infected cats were effectively treated with a combination product containing febantel (DrONTAL Plus, Bayer Animal Health). In that study, the kittens did not have diarrhea from the giardia infection, but the giardia antigen tests became negative after therapy, suggesting complete removal of the organism. One note of caution is suggested as this drug is not approved for use in cats, primarily because neurologic signs were observed in some cats when the drug was administered them during initial testing. Because re-
infection is a major cause of persistence or recurrence of infection in a household, cattery, or shelter setting, institution of appropriate environment control measures is essential. These measures include environmental decontamination (cleaning of all floors, cages, litter pans and surfaces that have been in contact with feces with quaternary ammonium or Clorox containing disinfectants), coat cleaning (bathing or shaving of long haired cats), and isolation of affected animals during the diarrheic phase to prevent infection by co-grooming, etc. Because this organism is zoonotic, appropriate education about handling of infected cats and kittens is an important aspect of the environmental control procedures implemented.

Cryptosporidiosis

*Cryptosporidium parvum* is a coccidian parasite that infects the microvilli of the intestinal epithelium of kittens and immunosuppressed cats. The disease caused by this infection can range from an asymptomatic carrier, to mild, transient illness, to prolonged, life-threatening malabsorption syndromes. The some adult cats, the organism can cause intestinal infiltrates similar to those observed with classic inflammatory bowel disease, and because the organisms are very small, unless special stains are used, may be not diagnosed. Because cryptosporidiosis has a high prevalence rate in cats (8-87% by serology), diagnosis should be made by detection of the organism in feces using an ELISA test or with immunofluorescence assays on feces. The organisms can be observed in feces at high power, but they are extremely small (< 4 um), and are easily missed unless special stains or assays using immunofluorescence and careful observation are employed. Further complicating the diagnosis, the organisms are shed intermittently, and thus, infected cats can often have negative fecal fluorescence exams. Because cryptosporidiosis is zoonotic, the person handling the needs to use appropriate precautions when handling the infected feces, such as wearing gloves and cleaning any utensils with disinfectants (bleach). Treatment of kittens infected with cryptosporidiosis is very difficult, as the drugs proported to be effective against this organism are either toxic or ineffective in cats (e.g. paromomycin, nitrazoxanide). Tylosin, metronidazole and other commonly used antimicrobials are ineffective in eradicating the organism. They may improve diarrhea if a bacterial component is active, but in most cases they are not helpful. However, azithromycin (dose 5-10 mg/kg po q24h) is effective in humans, and although its effectiveness in cats is unknown, should be considered.

Other Infectious Causes of Kitten Diarrhea

Other causes of diarrhea that should be considered in kittens include several viral diseases: feline panleukopenia virus, hemorrhagic calcivirus, rotavirus, astrovirus, enteric coronaviruses and feline infectious peritonitis. Feline panleukopenia is the most clinically important intestinal virus of this group, and affects primarily unvaccinated kittens and cats causing fever, depression, anorexia, vomiting and diarrhea. Diagnosis is usually based on the clinical signs and history, but the canine parvovirus antigen test cross-reacts with the feline virus and thus can be used for confirmation. Treatment of this and any viral enteritis in kittens is symptomatic and supportive. Because young kittens are prone to dehydration and hypoglycemia, fluid therapy and nutritional support are key aspects of the supportive care. Bacterial causes of diarrhea include salmonellosis, campylobacteriosis, clostridial infections, and occasionally yersiniosis, tyzzer's disease (Bacillus piliformis), and colibacillosis. Diagnosis of bacterial infections causing diarrhea in kittens or cats is very difficult, primarily because pathogens can be isolated in similar rates from both diarrheic and non-diarrheic feces. Other infectious causes of diarrhea include fungal diseases such as histoplasma, however, these are more likely to occur in adult cats. Most of the parasitic causes of diarrhea in kittens are typical, e.g. hookworms, roundworms, and strongyloides, and be easily found on fecal flotation, however, therapeutic de-worming should still be performed in kittens that have diarrhea, even if the fecal is negative.
Anatomic/Mechanical Causes of Diarrhea
The curious and investigative nature of kittens makes particularly at risk of ingestion of foreign substances that may result in the development of diarrhea or vomiting. In most cases, obstructions or intussusception cause vomiting, but the more distal the problem in the GI tract, the more likely diarrhea may be the primary clinical signs. The mechanical or anatomic causes of diarrhea to be considered in kittens include developmental abnormalities (e.g. short bowel syndrome), mechanical dysfunction (e.g. obstruction or intussusception), or foreign bodies (e.g. bones, string, plants, hair, etc). In general, the diagnosis of these conditions will require radiographs or other imaging techniques, but string foreign bodies can occasionally be diagnosed by finding the string entrapped at the base of the tongue or by palpation of the intussusception. For most of the problems in this category, surgical resolution of the problem is required.

Nutritional Causes of Diarrhea in Kittens
The use of diet to assist in the management of diarrhea is not a new concept. Nevertheless, the type of diet used to help manage the problem has become an increasingly complex issue. In many, if not most cases of simple diarrhea (especially in kittens), the best approach is to feed a highly digestible diet or change the diet to one with fewer additives, flavorings, or other substances than may be associated with food intolerance. These types of diets are designed to provide food that is easy to digest (moderate to low fat, moderate protein, moderate carbohydrate), may have additives to improve intestinal health (soluble fibers, omega 3 fatty acids, increased anti-oxidant vitamins, etc), and contain no gluten, lactose, food coloring, preservatives, etc. There are many different brands available that fall under the category “highly digestible”, but, the key is to remember that they are not all alike. In particular, the protein digestibility of the diet chosen is one of the key factors they may determine the success of the diet. This information can be difficult to access, but in general, meat source proteins are more digestible than plant source, animal proteins are more digestible than meat by products. Meat meals are a good source of protein. Also, to increase digestibility of foods in cats, decrease the number and amount of carbohydrates in the food – a single source carbohydrate food is better than foods with many different sources, highly digestible carb sources are better than complex plant source carbs. Thus, when one diet from this category not accepted by the kitten, is ineffective, or seems to make the diarrhea worse, you cannot assume that all diets in this category will be ineffective. The highly digestible diets from different pet food manufacturers have a wide variety of different formulations: different protein and carbohydrate sources, different levels of fat, and a variety of additives designed to promote intestinal health (FOS, MOS, omega 3 fatty acids, antioxidant vitamins, soluble fiber, etc). If one type of highly digestible diet has been fed for at least 2 weeks with minimal response, then is it entirely reasonable to either try another diet from a different source, or try an entirely different dietary strategy (e.g. high protein/low carb, novel antigen, hydrolyzed, etc). Another consideration in kittens is that the diarrhea may be due to carbohydrate intolerance or bacterial changes resulting from diet changes. Thus, feeding a canned food diet, which contains less carbohydrates may result in the resolution of the diarrhea, or addition of probiotics or prebiotics to help influence the microflora are also reasonable therapeutic options.

Inflammatory or Immune-Mediated Causes of Diarrhea

Inflammatory Bowel Disease
Inflammatory bowel disease (IBD) in cats is a commonly diagnosed condition of adult cats that may represent multiple diseases. IBD is characterized by persistent
clinical signs (vomiting, diarrhea or weight loss) consistent with GI disease that occur concurrently with histologic evidence of mucosal inflammation. There are a number of possible causes of intestinal inflammation that must be considered in the diagnostic process, including infectious, food sensitivity/intolerance, hyperthyroidism, neoplastic or protozoal and parasitic. These should be investigated thoroughly or empirical therapy instituted prior to settling on the diagnosis of idiopathic IBD. Food sensitivity can be particularly difficult to distinguish from IBD or other intestinal disorders. In a recent study, food sensitivity was reportedly responsible for at least 30% of all feline gastrointestinal problems. Thus, appropriate food trials are an extremely important component of both diagnosis and therapy of cats with GI disease or suspected IBD. In addition to food trials, the diagnostic plan for a cat with chronic diarrhea should include multiple fecal examinations or therapeutic deworming, assessment of thyroid and FeLV/FIV status, and intestinal vitamin (cobalamin) status. Serum cobalamin levels in cats commonly decrease with severe distal bowel disease, and in cats with hypocobalaminemia, the diarrhea will not resolve until replacement therapy is instituted. Cobalamin therapy (250 ug/cat IM q week) in some cats may be lifelong, while in others, once the clinical disease resolves the supplementation can be discontinued. In addition, radiographs and ultrasound are important in assessment for the presence of infiltrative diseases such as FIP granulomas, histoplasmosis or lymphosarcoma. But, ultimately, intestinal biopsies, either obtained endoscopically or at an exploratory surgery are essential – both for the diagnosis of IBD and for ruling out other specific causes of the clinical signs. In humans, recent studies indicate a strong association of development of IBD with a breakdown of normal tolerance mechanisms, host susceptibility and the enteric microflora. It is quite likely that these same factors are important in feline IBD, and in studies using experimental models of IBD, the resident microflora are essential cofactors in driving the inflammatory response. Further, modulation of the enteric microenvironment in humans with IBD has been shown to reduce proinflammatory cytokines in the mucosa and thus, decreases the inflammation. Unfortunately, accurate, readily accessible methods of assessing the bacterial numbers and species populating the small intestine are not yet available. In addition, studies in cats with IBD assessing modulation of the enteric flora (using probiotics, prebiotics, or other specific therapy for cytokines) are only in the early stages of study. At this time, therapy of IBD in cats continues to include inflammatory suppression and antibiotic therapy. The most effective therapies for IBD include steroids (prednisolone or methylprednisolone 1-2 mg/kg po q12h po) or other drugs that interrupt the pro-inflammatory pathways that are active in the gut. In cats that are intolerant of steroids, or in those in which steroids are no longer effective, immunosuppressive therapy may be necessary, and is often effective. The two drugs that most commonly recommended in this setting are cyclosporine and chlorambucil. Antibiotic therapy with metronidazole (5-10 mg/kg po q12h) has been effectively used for a number of years and continues to be recommended for initial therapy of IBD. There is also a widely held belief that metronidazole is effective, not only because of its antibacterial properties, but because of concurrent immune modulation properties. There is some data to support these ideas, however the specific role of metronidazole in therapy of IBD is still not completely known. Finally, general agreement exists among gastroenterologists that elimination diets or novel protein, highly digestible diets are beneficial in cats with IBD. Nevertheless, agreement also exists that dietary management alone is seldom successful, thus control of the aberrant inflammatory process and bacterial components are still necessary. Further, at this point in our understanding, we still do not know which components of the diet (protein, carbohydrate, minerals, etc) are important in the pathogenesis or therapy of IBD, or if other aspects of nutritional support (fatty acids, probiotics or other nutriceutical therapy) may reduce the inflammatory response. There is increasing data in human IBD that probiotics and anti-oxidant, prebiotic nutraceuticals may be important components of therapy.
Adverse Reactions to Food

Food sensitivity and food intolerance are the most common adverse reactions to food in cats. Food allergy or hypersensitivity is an adverse reaction to a food or food additive with a proven immunologic basis. Food intolerance is a non-immunologic, abnormal physiologic response to a food or food additive. Both can be responsible for diarrhea or vomiting, but vomiting is a more common presenting complaint. Food poisoning, food idiosyncrasy and pharmacologic reactions to foods also come under this category of adverse reactions to food. The specific food allergens that cause problems in cats have been poorly documented, with only 10 studies describing the clinical lesions associated with adverse food reactions. In these reports, over 80% of the reported cases were attributed to beef, dairy products or fish in cats. The incidence of food allergy versus food intolerance in cats is unknown. However, intolerance to carbohydrates, specifically disaccharides, is a well known cause of diarrhea in cats due to low level disaccharidase activity (or loss of activity in enteritis). The diagnosis of both food sensitivity and intolerance is based upon a dietary elimination trial. The major difference between these two types of adverse food reactions is the length of time on the diet that is required to achieve a response (cats with food sensitivity require 6-12 weeks on the elimination diet before an improvement will be seen). Alternatively, in cats with food intolerance, resolution of signs usually occurs within days of the diet change (unless there is concurrent bacterial floral disruption or other factors influencing the response).

There are a variety of commercially available and homemade elimination diets, as well as diets formulated with hydrolyzed proteins, that may be used in cats with suspected food sensitivity or intolerance. The key is to select a diet that has a novel or hydrolyzed protein source (based on a careful dietary history), that is balanced and nutritionally adequate (commercial diets are best for this), however, homemade elimination diets may be needed to find an appropriate test diet. If a homemade diet must be used for long term therapy, a complete and balanced diet containing the necessary protein sources should be formulated by a nutritionist. In most cats with food sensitivity, avoiding the offending food is the most effective therapy and will result in complete resolution of signs. However, short term steroid therapy can be used to decrease the concurrent intestinal inflammation until the appropriate food sources can be identified.

Finally, some cats with diarrhea will respond to placing them on a high protein, low carbohydrate diet (canned growth or diabetic formula foods). The reason why cats respond to these diets is not completely known, but may be related to carbohydrate intolerance or to changes in the bacterial flora that result from some foods. While this hypothesis remains to be proven in cats and kittens, there is increasing anecdotal evidence that in kittens and adult cats with idiopathic diarrhea, feeding a canned diet containing high protein and low carbohydrate content is beneficial. This may be beneficial for a variety of reasons, but is a prudent therapy option. Obviously, all cases of diarrhea in kittens or cats will not resolve by use of dietary manipulation alone, but in many of these cats dietary therapy is an important component of therapy that should be carefully
considered and implemented, and adjusted to meet the needs of the pet and its situation.

Neoplastic Causes of Diarrhea

Alimentary lymphoma is a complex disease in cats, and although most lymphomas are believed to be caused by clonal expansion of B cells, there are a variety of presentations of this disease that make diagnosis or treatment difficult. The types of lymphoma described in cats include small cell lymphoma, lymphoblastic lymphoma, T cell lymphoma, and mixed cell tumors. The most common form, small cell lymphoma, creates the most difficulty in diagnosis, because it cannot be reliably distinguished from IBD using histopath alone and the lesions can be quite focal, so it can be easily missed. Because of the difficulty in making the definitive diagnosis with histopath alone, further analysis of the cells using specific markers is recommended. This form of lymphoma is very slow growing because it has a low mitotic index, and many cats will live for 1-2 or more years with appropriate immunosuppressive therapy. Lymphoblastic or other forms of lymphoma are more aggressive, highly malignant forms, and although they may respond to chemotherapy, they tend to have much shorter periods of remission and are associated with greater morbidity because of the risk of intestinal perforation. The interested reader should refer to the more recent reviews for specific therapy of alimentary lymphoma.

References


