G – Gastroenterology
SMALL INTESTINAL DIARRHEA – CAUSES AND TREATMENT

Frédéric Gaschen, Dr.med.vet., Dr. habil., DACVIM, DECVIM-CA

School of Veterinary Medicine
Louisiana State University
Baton Rouge
Louisiana
USA
fgaschen@vetmed.lsu.edu

When presented with a dog or a cat with diarrhea, it is useful attempt to identify which segment of the intestine is affected. Although many animals with small intestinal involvement will at some time show signs of large bowel diarrhea, the presence of large bowel diarrhea alone is associated with a different approach and, possibly, a better prognosis. A table summarizing the clinical signs associated with small and large bowel diarrhea can be found in the summary of the lecture on large intestinal diarrhea.

Small intestinal disease will ultimately lead to decreased absorption of nutrients through the small intestinal mucosa and to severe systemic consequences leading to malnutrition and weight loss. Dogs and cats with diarrhea of small intestinal origin are usually presented with a variety of associated clinical signs, reflecting the secondary involvement of numerous organ systems. On the other hand, small intestinal diarrhea may also occur secondary to a variety of non-gastrointestinal diseases such as polysystemic infections, endocrine diseases (e.g. hypoadrenocorticism in dogs or hyperthyroidism in cats), renal disease, various toxins and drugs, etc. This is why, once parasitism has been ruled out, a broad-based diagnostic approach including blood analyses and abdominal imaging (and any other test deemed appropriate for the affected animal) is always recommendable in severely affected dogs and cats with small intestinal disease.

This presentation will focus on describing the most frequent small intestinal diseases. Systemic diseases with secondary involvement of the gastrointestinal (GI) tract will not be further discussed. The veterinarian should first attempt to rule out the presence of any *GI parasites* using the appropriate parasitological test. Then, a precise *dietary history* should be available: dietary indiscretion is a frequent problem leading to acute diarrhea in young but also in adult dogs. In fact, many cases come with a previous history of similar problems, or have been seen ingesting potentially harmful food. In chronic cases, food intolerance (including food allergy) is a very frequent problem that needs to be ruled out early in the work-up.

Anomalies: the most frequent anomaly associated with the digestive tract and leading to diarrhea is exocrine pancreatic insufficiency. The clinical signs are quite specific (production of large amounts of yellowish or grey feces of decreased consistency, weight loss, and flatulence, often associated with a ravenous appetite). Diagnosis is easily confirmed by evaluating the serum trypsin-like immunoreactivity (cTLI). Treatment consists of enzyme replacement often with dietary modification with a low fat, easily digestible diet.

Infections: viral infections such as parvovirosis (dogs) and panleukopenia (cats) typically cause severe, acute small intestinal disease in non vaccinated young animals. Currently, feline panleukopenia is less frequently encountered than canine parvovirosis. The viruses attack the small intestinal crypt cells and severely damage the intestinal epithelium. Treatment is mostly symptomatic with aggressive fluid therapy, broad spectrum systemic antimicrobials, antiemetics and analgesia. Secondary electrolyte disorders such as hypokalemia should be prevented, and animals watched for the occurrence of secondary intussusception. Early refeeding (small amounts, naso-gastric feeding tube) is recommended as soon as vomiting has subsided.

With few exceptions, bacterial infections appear to be a rare cause of small intestinal disease in dogs and cats. The small intestinal lumen naturally harbors a variety of bacteria in limited numbers. This resident bacterial flora has important functions in preserving anatomical structures and enhancing physiological processes necessary for the proper digestion and absorption of food.

The small intestinal flora also plays a role in preventing colonization by pathogenic bacteria, and enhances the development of the enteric immune system. Enteric bacterial infections have been documented in small animals. Responsible enteropathogens include *Campylobacter* spp., *Clostridium perfringens* and *difficile*, *Salmonella* spp., *Yersenia* spp., and some strains of *E. coli.* However, some of these bacterial species have not only been isolated in feces of dogs and cats with diarrhea, but also in healthy animals. To further complicate matters, pathogenic bacteria may just be "opportunists" in small animals with intestinal diseases due to an unrelated cause. If enteropathogenic bacteria are not the actual source of the animal's problems or if they represent an incidental finding, indiscriminate use of antibiotics is not recommended as it may lead to development of resistant strains with possible public health relevance. Even though the pathogenicity of many of these bacteria is subject to controversy, a risk for the transmission of zoonotic infections to humans exists after contact with sick dogs and cats, but more importantly also after contact with healthy animals shedding such enteropathogens. These important facts have contributed to a sometimes confusing situation making diagnostic and therapeutic decisions difficult. Additional research is needed to more clearly establish the role of enteric pathogens in canine or feline intestinal diseases.

Numerous reports have shown that *C. jejuni, C. upsaliensis*, and other enteric *Campylobacter* spp. may be present in the feces of healthy and diarrheic dogs and cats. *Campylobacter* infections appear to be less frequent in cats than in dogs. In Sweden, *Campylobacter* spp. were isolated in 76% of young healthy dogs < 12 months of age, but only in 39% of adult and older healthy dogs. *Campylobacter* spp. can also infect human beings, and cause abdominal discomfort, fever and diarrhea which may be bloody. Recovery occurs frequently spontaneously but antibiotic treatment may be required. Based on recent studies, risk factors for human infection include eating poultry that was cooked at home, drinking water from a well or from a lake/river, and daily contact with a dog. Therefore, fecal shedding of *Campylobacter* spp. by healthy pets seems to represent an important source of infections in people. The therapeutic approach of dogs with proven fecal shedding of *Campylobacter* spp. depends on the health status of the patient (i.e., healthy vs. showing gastrointestinal signs). Among healthy dogs, those sharing home with immune-compromised people or with infants should probably be treated. In dogs showing diarrhea, vomiting, and/or other signs compatible with small intestinal disease, appropriate antibiotic therapy is recommended, even though the causal relationship of *Campylobacter* spp. infection and the clinical signs may be difficult to establish. The antibiotics of choice are erythromycin (in dogs 20 mg/kg p.o. BID for 2-3 weeks) or fluoroquinolones (e.g. enrofloxacin 5 mg/kg p.o. BID for 7-10 days) at the usual dosages. The prognosis for full recovery is generally good. If the infection is secondary to another underlying intestinal condition, recovery may also depend on identification and treatment of that condition

Idiopathic inflammatory bowel diseases (IBD):

In small animal gastroenterology, the term IBD groups various chronic intestinal diseases of unknown etiology leading to chronic enteropathies. These diseases may be further differentiated on the basis of the histological appearance of the inflammatory infiltrate: lymphocytic-plasmocytic, eosinophilic, neutrophilic or granulomatous. The clinical signs are characterized by chronic small and/or large bowel diarrhea. The diagnosis is made by elimination of all other identifiable causes of diarrhea including food intolerance and ARD.

In dogs, severe IBD could lead to protein-losing enteropathies. Affected dogs can be presented because of diarrhea associated with the consequences of hypoproteinemia (strong hypoalbuminemia, often with panhypoproteinemia) causing effusions and edema. Often, histological exam of the intestinal mucosa reveals lymphangiectasia with inflammatory infiltration. Even though it has been reported to occur specifically in certain breeds (Soft Coated Wheaton Terrier, Norwegian Lundehund, possibly also Yorkshire Terrier etc.), the cause of this syndrome remains unknown. Generally, treatment consists of feeding the dog with a highly digestible diet with low fat content together with treatment of IBD (see under). In severely affected dogs, intensive care with aggressive fluid therapy aiming at restoring adequate oncotic pressure may be necessary. The prognosis is generally guarded to poor when severe systemic clinical signs are present.

Current treatment protocols for canine IBD most often involve the use of immunosuppressive doses of corticosteroids (CS) for several weeks followed by slow tapering to reduce the intestinal mucosal inflammation and achieve clinical remission. The usual protocols for predniso(lo)ne usage recommend dosages of 1-2 mg/kg BID for approximately 2-4 weeks, followed by a slow tapering period over weeks to months. However, a number of dogs treated with immune suppressive doses of CS will show either no response at all to the drug or will relapse after weeks to

months of treatment. At high dosages, CS have numerous side-effects such as PU-PD which may become unbearable for the owners, especially in large breed dogs. In difficult cases that require prolonged CS therapy but are sensitive to its side-effects, the more expensive drug budesonide has been used with good anecdotical success (3.0 mg/m2, resp. 0.5-3.0 mg per dog, depending on body weight, once daily or every other day). In humans, budesonide undergoes a first pass hepatic extraction of approximately 80-90%. Therefore, only a fraction of the absorbed compound reaches the systemic circulation, theoretically decreasing the side-effects. It has been documented that budesonide suppresses the hypothalamic-pituitary-adrenal axis in dogs with IBD

Other immunosuppressive agents such as azathioprine, chlorambucil, cyclophosphamide at the usual dosages are used alone or in combination with CS. They may (a) decrease the required dosage of CS and the associated side-effects, or (b) allow the dogs to be weaned off CS as soon as possible. Moreover, these drugs are also used cases of steroid-refractory canine IBD. However, they may have a delayed onset of action (weeks to months until maximal effect). Recently, we described the use of cyclosporine A (5mg/kg once daily) in CS-refractory dogs with IBD, leading to clinical improvement in 12/14 dogs.

As is the case in dogs, IBD in cats is an exclusion diagnosis. Other causes of chronic enteropathies have to be systematically ruled out, and a compatible infiltrate has to be present in the intestinal mucosa. The most common inflammatory infiltrates include lymphocytes, plasma cells, or eosinophils. Contrarily to what is observed in dogs, diarrhea may not be the most common clinical signs associated with feline IBD. Initially, cats may show loss of appetite/anorexia and/or chronic vomiting with weight loss. In severe cases, cats are emaciated or cachectic, and abdominal palpation reveals rigid intestinal loops and/or presence of enlarged lymph nodes. The diagnostic approach is similar to that of dogs. Treatment may occur in several steps: in mild cases start with a diet change to a novel protein ("hypoallergenic") diet. Metronidazole may be administered simultaneously (62,5 mg/cat 1x daily during 10-20 days). Resistant cats or those with severe disease are given immunosuppressive doses of prednisolone (1-2 mg/kg initially BID). Cats are usually less sensitive to side-effects of corticosteroids than dogs (exception: diabetic cats). If the treatment using high doses of prednisolone is successful after 10-15 days, the doses are decreased stepwise until the minimal effective dose can be reached (total duration approx. 3 months). Resistant cats can benefit from the addition of other immunosupressants to the protocol (e.g. chlorambucil 2mg p.o. every 4 days).

It is important to know that most cats with chronic intestinal disease are likely to develop cobalamin deficiency due to intestinal malabsorption. Cobalamin has important functions in virtually all body cells, and chronic deficiency can lead to a variety of non-specific clinical signs. This is why parenteral supplementation is usually recommended in chronic feline enteropathies, particularly if serum cobalamin concentration is lower than 300 ng/l. Injections of vitamin B complex are not sufficient due to low cobalamin concentration. Injectable cobalamin is available in 1 mg/ml strength, and should be administered s.c. at a dose of 0.25 mg weekly to cats up to 5 kg for 6 weeks, then every other week for 6 weeks, finally monthly for 2 months.

Neoplasia: Gastrointestinal lymphoma diffusely infiltrates the intestinal mucosa, and preferably affects older cats (generally > 7 years old). In the last years GI lymphoma has become the most prevalent form of feline lymphoma in many areas. According to a recent study, 54% of feline lymphomas affect the abdomen, and 75% of those involve the gut. However, 10 to 46% of affected cats do not show any gastrointestinal signs (they essentially present with decreased appetite or anorexia, and weight loss). Chronic diarrhea however remains a frequent reason for presenting the cat to a veterinarian. Diagnosis may require "full thickness" intestinal biopsies, as the histological differentiation between IBD ansd small cell lymphoma can be very challenging for the pathologist. Well differentiated tumors seem to respond well to "simple" chemotherapy protocols during numerous months, but blast forms are more difficult to treat. Generally, the prognosis depends on the tumor response during the first weeks of chemotherapy. If only a partial or no remission is achieved, the success chances of chemotherapy are compromised.

A list of references can be obtained by sending an e-mail request to the author.