Inflammatory Bowel Disease in Cats

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Inflammatory bowel disease (IBD) is used to describe a group of gastrointestinal (GI) diseases commonly diagnosed in adult cats. The prevalence and cause of IBD are unknown. Idiopathic by definition, IBD is characterized by inflammation of the stomach, small intestine, and/or large intestine with associated GI signs, including vomiting or diarrhea lasting more than 3 weeks. IBD is not remedied by food trials or definitively ruled out using most diagnostics. IBD can be confirmed only by biopsy.

Types of Inflammatory Bowel Disease
The types of IBD are classified by the principal inflammatory cells infiltrating the GI tract. Most of these cell lines can be found in cases of IBD, but certain ones are more common. Lymphocytic-plasmacytic IBD, which infiltrates the lamina propria, is most common. Eosinophilic IBD and suppurative IBD are less common, typically invading one of two layers of the intestinal tract. Neutrophilic IBD and granulomatous IBD are rare.

Pathophysiology
No studies have confirmed the etiology of IBD in cats. Therefore, information on the cause of IBD has been based on human and murine studies. Although significant clinical and histologic differences exist between cats and humans, the pathogenesis of IBD is thought to be similar in both species.

The development of IBD is hypothesized to be due to interplay between (1) a disturbance in the GI mucosal barrier, (2) mucosal immunity, and (3) mucosal microflora. In a normal GI tract, a healthy epithelial lining protects the mucosal barrier with innate and adaptive immune responses to insults. Receptors on and within epithelial cells control the innate and adaptive immune responses and affect the interplay between the mucosal barrier, immunity, and microflora. Malfunctioning receptors disrupt homeostasis. Abnormal numbers of mucosal microflora may also be involved in the pathogenesis of IBD. Bacterial populations that are likely to induce inflammation increase in number, and commensal bacteria decrease in number. Large numbers of mucosal bacteria are associated with a faulty mucosal barrier, a cytokine mRNA response, and increased clinical signs.

Clinical Findings
Clinical signs of IBD can vary significantly among patients, depending on the anatomic location of the associated inflammation. Signs can appear and disappear sporadically. Vomiting and diarrhea are the most common signs. If the small intestine is inflamed, abdominal discomfort may be detected on palpation. Cats with inflammation of the large intestine may be painful on rectal palpation. In severe cases, the following can be present: weight loss, appetite changes, poor haircoat, mucoid feces, tenesmus, increased frequency of defecation, and hematochezia.

Male and female cats share the same disease predisposition. The mean age for development is 5.2 years. Siamese and exotic breeds appear to be at increased risk of developing lymphocytic-plasmacytic IBD, but no definitive breed predilection has been reported. The pancreatic and biliary ducts are combined in cats,
so IBD, lymphocytic cholangitis, and chronic pancreatitis can be associated with each other.12,13 Other than the cited breed associations, genetic influences have not been identified in cats; however, a gene mutation identified in humans may be applicable to cats.14

**Diagnosis**

IBD is diagnosed by ruling out other causes of inflammation. The following must be investigated in a step-by-step manner, but not necessarily in the following order: infectious or parasitic pathologies, food sensitivity or intolerance, endocrine or metabolic disturbances, foreign bodies, or neoplastic diseases of the GI tract (BOX 3). Empirical treatment should be initiated for suspected conditions. After the possibility of these diseases and conditions has been eliminated, the following clinical criteria must be met to confirm a diagnosis15:

- The cat has shown chronic GI clinical signs for at least 3 weeks
- Other conditions (BOX 3) have been eliminated as likely causes of the inflammation
- Food trials and antibacterial and anthelmintic treatment provide incomplete relief of clinical signs
- The cat has responded well to antiinflammatory and/or immunosuppressant medications
- Biopsy shows evidence of mucosal inflammation consistent with IBD

**Laboratory Findings and Diagnostic Imaging**

Laboratory findings can rule out other disorders1,10 and support a diagnosis of IBD. In IBD of the small intestine, serum biochemistry panels may show hypercholesterolemia, hypocalcemia, and hypomagnesemia. Hematology may show neutrophilia with or without a left shift. Anemia may be present because of chronic inflammation or chronic blood loss. These findings are not as common in IBD of the large intestine. The C-reactive protein level, which surges in response to inflammation, may be increased in severe IBD of the small or large intestine.16 Fecal α1-protease inhibitor activity tests can be used to detect protein-losing enteropathies before hypoproteinemia is apparent.17 Cats with IBD often have high trypsin-like immunoreactivity concentrations, which points toward simultaneous pancreatic disease. Increased hepatic values are frequently seen.

Cats with IBD sometimes have low serum folate and cobalamin concentrations.18–20 Folate is absorbed by the proximal small intestine, and cobalamin is absorbed in the ileum. These test results are consistent with a diagnosis of IBD and may help determine the location of the inflammation.

Radiography, including contrast studies, has limited value, except to rule out a foreign body; however, ultrasonography is an important diagnostic measure. Thickening of the large and small intestinal walls and enlarged lymph nodes are common ultrasonographic findings.21 They are characteristic of inflammatory disease processes but are not specific to IBD. Ultrasonography can provide information on the location and severity of lesions, suggesting whether a biopsy should be performed endoscopically or surgically.

**Food Trials**

To diagnose IBD, food allergies and intolerances must be ruled out. Except for very mild IBD, the disease does not respond to dietary manipulation alone. However, idiopathic GI signs resolve in up to 50% of cats placed on an elimination diet.21 These cats are presumed to have a food allergy or intolerance instead of IBD. At presentation, some cats are too fragile to begin a food trial and need immediate empirical treatment, which eliminates a food trial as a diagnostic possibility. If a food trial is permissible, a 4- to 6-week trial is recommended, although shorter trials have been adequate1,10,22

**Histopathology**

Histopathology is the only way to confirm IBD. However, histopathologic findings vary significantly among pathologists.23 Until recently, a lack of standard criteria clouded agreement on the normal histology of cats with IBD. Guidelines, including pictorial templates and standard reporting forms advocated by the World Small Animal Veterinary Association Gastrointestinal Standards Group (www.wsava.org/StandardizationGroup.htm), aim to reduce the subjectivity of histology.24 With the use of objective criteria, a sample of mucosa can be identified as normal or diseased. If diseased, a sample can show the severity of the disease, morphologic abnormalities, and predominant inflammatory cells.

Biopsy samples are most simply obtained using endoscopy, which is less invasive, less expensive, and more appropriate for frail cats. However, endoscopy allows sampling of only the mucosal layer of the proximal GI tract. Full-thickness and extraintestinal biopsies are important diagnostic tools25–27; if they are not obtained, a diagnosis may be missed or a misdiagnosis can be made (e.g., IBD can be easily confused with lymphoma). Although surgical and laparoscopic biopsies are complex, they are preferred.

Clients should be encouraged to allow a biopsy before any other diagnostic procedure or therapies. Obtaining a biopsy sample is
sometimes difficult because of financial restrictions or poor condition of the patient. Clients should be made aware that biopsies performed after therapy has begun may not be diagnostically accurate. Furthermore, cats with undiagnosed diseases such as lymphoma may initially respond well to IBD treatment, obscuring the true diagnosis.

**Treatment**

Well-controlled studies examining the efficacy of IBD treatment are absent. Instead, treatment relies on clinical experience. Treatment is aimed at reducing the antigenic source of inflammation and suppressing the inflammatory response. Treatment focuses on diet, supplementation, and pharmaceutical therapies.

**Diet and Supplementation**

According to the definition of IBD, an affected cat has an incomplete response to dietary modification. However, cats with mild IBD may be food-responsive because dietary antigens play a role in its etiology.2,4 Dietary changes can play a key role in IBD therapy. Food intolerances or allergies may develop secondary to IBD, so a dietary change may be called for in these situations. In more severe IBD, dietary changes should be used in combination with other IBD therapies. Low-antigen, easily digested diets from a single protein source may decrease the antigen load on the GI tract. Cats with eosinophilic IBD may respond well to a hypoallergenic diet, while a high-fiber diet may be helpful in colonic IBD.1,10

The therapeutic use of probiotics and prebiotics is gaining popularity. Prebiotics are live microorganisms that may help protect the mucosal barrier and balance microorganisms in the intestines. Prebiotics are nondigestible materials in food that may support growth of resident gut bacteria and suppress the immune response.

Human and canine IBD studies support the use of prebiotics and probiotics.26,27 Little research has been done on cats, but initial studies and clinical experience have shown the use of probiotics to be of value.28 The limited feline studies on the use of prebiotics have found no significant changes to bacterial flora.29 Further feline studies exploring their use may document therapeutic value.

Cats with IBD, especially those with weight loss, often have low cobalamin levels because of intestinal malabsorption. A low cobalamin level affects GI function, contributing to clinical signs.18,19 Cobalamin deficiency can be treated with subcutaneous injections. If this deficiency is not corrected, an affected cat continues to show clinical signs despite pharmaceutical and dietary intervention.

Folate deficiency in cats can result in anemia, anorexia, and lethargy.20 Folate (400 µg PO q24h for 6 weeks) should be given to compensate for decreased proximal intestinal absorption.33

**Pharmaceutical Treatment**

Although they can have adverse effects, corticosteroids are the pharmaceutical cornerstone of IBD therapy because they disrupt the inflammatory pathways of the GI tract. Prednisone, prednisolone, and methyl-prednisolone are recommended. Budesonide has been useful in humans and dogs with IBD, but clinical use of the drug in cats has had variable success.1,10 No studies have examined the effectiveness or long-term risk of using budesonide in cats.

Cats with refractory clinical signs or steroid-induced morbidity require additional management. The cytotoxic drug chlorambucil is an adjunct to steroid therapy and can be given until remission occurs.1,10 Leukopenia is an uncommon adverse effect of chlorambucil, so regular blood work is important.34 The use of cyclosporine has been helpful in dogs, and anecdotal evidence supports use of this drug in cats. Latent infections such as toxoplasmosis may appear with the use of cyclosporine in cats.1,10,35

Metronidazole is an antimicrobial that affects the innate and adaptive GI immune responses. Although this drug’s mechanism of action is not completely understood, the drug is known to help balance intestinal microflora, reduce obligate anaerobe load, and reduce inflammation. The use of metronidazole benzoate is recommended because anorexia and hypersalivation have been linked to the use of metronidazole hydrochloride.36–38 Metronidazole benzoate contains 60% metronidazole, so the drug must be dosed at 25 mg/kg instead of 15 mg/kg.37 Metronidazole should not be used indefinitely because of the risk of neurotoxicosis, genotoxicosis, and liver insufficiency.39–40

**Prognosis**

The prognosis for cats with IBD is frequently positive. Mild cases may respond to metronidazole therapy alone, and remission can

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**Key Points**

- IBD is diagnosed by ruling out other causes of GI distress and is confirmed by biopsy.
- IBD is thought to result from dysfunctional interplay between the mucosal barrier, mucosal immunity, and microflora.
- Treatment of IBD may involve dietary change and/or medication. Strict owner compliance is required, and recurrence is possible.

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**Glossary**

**Adaptive immune system**— composed of specialized lymphocytes, this system recognizes pathogens it has previously encountered, providing immunity to anticipated pathogens.

**Innate immune system**—a body’s first line of defense, this system does not have specialized cells and, therefore, does not provide long-term immunity to challenges.

**Nucleotide-binding oligomerization domain containing 2 (NOD2) receptor**—a type of pattern-recognition receptor, NOD2 proteins work intracellularly to activate an immune response; NOD2 receptors specifically recognize muramyl dipeptide, which is found in certain strains of bacteria.

**Pattern-recognition receptor (PRR)**—proteins that recognize molecules unique to a specific microorganism.

**Toll-like receptor (TLR)**—a type of PRR, TLRs play a critical role in the body’s immune system response; they recognize microbes that have invaded the intestinal tract mucosa and stimulate a response from the immune system.
extend for long periods.1, 10 Cats are unlikely to immediately develop serious metabolic side effects from steroid use.1 In some cases, the prognosis is poor. A decreased cobalamin level is associated with weak response to treatment.14,19,32 C-reactive protein may be a marker of the prognosis because increased levels in humans correlate with chronic and refractory inflammation.41 Research has raised the possibility that alimentary lymphoma in cats is the result of previous IBD.1,10 Disease markers such as C-reactive protein can be incorporated into clinical indices, which are valuable for assessing the course of a disease. Such indices exist for canine and human IBD, and a clinical index called feline chronic enteropathy activity index (FCEAI) was recently developed for cats with enteropathies13,42 (Box 4). The numeric scores can be used to measure the initial assessment, predict the response to treatment and the possibility of remission, and determine a prognosis. The clinical signs and severity of IBD vary significantly in cats, so numeric scores can more accurately define disease activity for clinical and research purposes.

Client Education

The technician’s role in educating clients about IBD is a valuable part of a cat’s recovery. The time-consuming nature of diagnosing IBD and stabilizing an affected patient makes client communication particularly important. Technicians should be able to clearly answer client questions about the diagnostic process, the disease, and the reasonable expectations. Remissions and setbacks are common with IBD, so technicians should offer support when clients are feeling uncertain about their cats’ progress. Clients may resist changing their pets’ diet and routine. Some researchers have speculated that cats and dogs with IBD may be unresponsive to treatment because of client noncompliance with food restrictions or with administration of medications.49 Clients may hastily stop drug treatment if adverse effects appear or if clinical signs of IBD disappear. Technicians should show clients how to properly medicate their cats, discuss potential adverse effects, and emphasize the need for long-term treatment. Technicians play an important role in supporting clients to ensure compliance with using a new food and/or medication.

Conclusion

Technicians are likely to frequently see cats with IBD. By understanding the pathogenesis and management of this disease (including potential adverse effects and nonmedical supplements), technicians can support clients in a possibly lifelong commitment to managing IBD.

References

38. Davidson G. To benzoate or not benzoate: cats are the question. *Int J Pharm Comp* 2001;5(2):89-90.
43. Jergens AE. Controversies in canine/feline IBD II. *Proc 79th Western Veterinary Conference* 2007.
1. Feline IBD is thought to result from interplay between all of the following except
   a. a defective mucosal barrier resulting in an influx of microbes and food antigens.
   b. dysregulation of an immune response.
   c. a food intolerance or allergy.
   d. poor balance of endogenous microflora.

2. Findings associated with inflammation of the large intestine may include
   a. pain on rectal palpation and an increase in the C-reactive protein level.
   b. thickening of the large and small intestinal walls and enlarged lymph nodes on ultrasonography.
   c. a decrease in the folate concentration.
   d. a and b

3. In their role as client educators, technicians should
   a. explain the cause of IBD by discussing TLRs, NOD2 receptors, and recent research.
   b. show clients how to properly medicate their cats but refrain from discussing adverse effects because this information may hurt client compliance.
   c. talk to clients about food trials and the amount of time it may take for their cats to respond.
   d. tell clients that many cats respond to metronidazole therapy alone and that setbacks in recovery are not very common.

4. Which of the following can be used for long-term pharmaceutical treatment of IBD without adverse effects?
   a. budesonide
   b. a combination of prednisolone, prednisone, and methylprednisolone
   c. metronidazole
   d. none of the above; all these drugs have adverse effects

5. A low cobalamin level in a cat with IBD is associated with
   a. poor ileal and colonic absorption.
   b. a good response to treatment.
   c. continued clinical signs and a weak response to treatment.
   d. a food allergy, so feeding a novel protein is recommended.

6. Laboratory findings in IBD of the small intestine may include
   a. hypercholesterolemia, hypercalcemia, and hypomagnesemia.
   b. erythrocytosis, hypercholesterolemia, and hypercalcemia.
   c. an increase in band cells, anemia, and hypermagnesemia.
   d. a low cobalamin level, anemia, and hypomagnesemia.

7. The World Small Animal Veterinary Association Gastrointestinal Standards Group has guidelines aimed at ________ feline IBD.
   a. standardizing the use of probiotics and prebiotics for treating
   b. reducing histologic inconsistencies for diagnosing
   c. standardizing recording documents for pathologists in diagnosing
   d. b and c

8. The most common clinical signs of feline IBD are
   a. lethargy, inappetence, and diarrhea.
   b. vomiting and diarrhea.
   c. regurgitation, diarrhea, and pain during abdominal palpation.
   d. a low cobalamin level and inappetence.

9. A defective NOD2 receptor
   a. binds with TLR and pathogenic bacteria.
   b. disrupts mucosal immunity by increasing TLR signals to the cerebellum, which starts a cytokine cascade.
   c. does not recognize pathogenic bacteria.
   d. b and c

10. A clinical index can
    a. give clients a score representing their cats’ health.
    b. help determine the location and severity of inflammation.
    c. help predict a cat’s prognosis and response to treatment.
    d. help determine the cause of IBD.