Idiopathic inflammatory bowel disease (IBD) is characterized by chronic gastrointestinal signs associated with diffuse accumulation of lymphocytes and plasma cells in the lamina propria and morphologic abnormalities of the intestinal mucosa and epithelium. Lymphocytic-plasmacytic mucosal inflammation may be diffuse or selectively involve the stomach, small intestine or colon; and is the most common endoscopic abnormality found in dogs and cats with chronic vomiting and diarrhea.

The etiology of IBD in dogs and cats is unknown, but the pathogenesis is believed to involve genetic factors, interactions of dietary antigens and enteric microflora with the mucosal immune system, and altered permeability of the mucosal barrier. In IBD the intestinal mucosal immune system seems to be reacting inappropriately to antigenic stimulation from dietary constituents and commensal bacterial flora. Chronic inflammation of the bowel may become uncontrolled and self-perpetuating when loss of mucosal integrity and increased permeability allow bacterial and dietary antigens to enter the lamina propria where they incite ongoing immune stimulation and inflammation. Studies in naturally occurring IBD in dogs and cats have found altered subpopulations of mucosal immune cells, increased proinflammatory cytokines, increased acute phase proteins, altered mucosal permeability, and changes in bacterial microflora. However, it is unclear whether some of these observations reflect primary causal abnormalities or the nonspecific consequences of chronic GI inflammation.

Precise criteria for the definitive diagnosis of IBD in dogs and cats have not been established. In general, the presumptive diagnosis of idiopathic IBD is based on 1) chronic GI signs greater than 3 weeks in duration; 2) characteristic lesions of IBD in mucosal biopsies; 3) incomplete response to dietary trials, anthelmintics, and antibiotics; and 4) exclusion of identifiable causes of chronic inflammation of the GI tract based on thorough diagnostic evaluation. This last criterion recognizes that lymphocytic-plasmacytic inflammation is a nonspecific lesion, and only a thorough diagnostic work-up can establish that it is truly idiopathic and not merely an inflammatory response to an undiagnosed condition. In addition to endoscopic mucosal biopsy of the intestines, diagnostic evaluations should be directed toward exclusion of parasitic and infectious diseases, extraintestinal diseases (e.g., organ failure, hypoadrenocorticism, or hyperthyroidism), and diet-responsive disease. Well planned dietary trials are required to diagnose dietary hypersensitivity.

TREATMENT

Treatment of IBD is focused on modifying the diet and intestinal flora to decrease the antigenic stimulation of the GI tract, and medical therapy to modulate the local immune response and control inflammation. In most IBD cases, an underlying cause cannot be identified, and the most effective treatment approach is a sequential series of therapeutic trials beginning first with a fenbendazole trial to exclude undetected Giardia
or helminth infections; then if signs persist, a diet trial using a novel protein or hydrolyzed protein diet to exclude dietary hypersensitivity; then if signs persist, an antibiotic trial using metronidazole or tylosin to modify the intestinal flora; and then finally if signs persist, an antiinflammatory regimen of a corticosteroid is initiated, usually combined with dietary modification (e.g., commercial GI diet, novel protein diet, or hydrolyzed protein diet). If diet and corticosteroids fail to control the disease, metronidazole or tylosin may be added for antibacterial and potential immunomodulatory activity. Metronidazole can also be used as a single drug to induce or maintain remission in mild cases. For refractory large bowel involvement, sulfasalazine or mesalamine may be used for local antiinflammatory effects in the colon. For the most refractory cases, immunosuppressive agents such as chlorambucil (cats), azathioprine (dogs), or cyclosporine can be combined with a corticosteroid. Adjunctive therapy includes cobalamin supplementation, prebiotics, probiotics, omega-3 fatty acids, and environmental enrichment (indoor cats).

**Dietary Therapy**

Various strategies for dietary modification have been used for treatment of IBD, including limited antigen (single novel protein) diets, hydrolyzed protein diets, fiber-enriched diets, and diets with adjusted fatty acid levels. In some animals with IBD, dietary modification produces a complete or partial resolution of the signs and sometimes regression of the lesions. Potential explanations for a beneficial response to dietary modification include the effects of the diet on composition of the microflora, mucosal morphology and function, and exposure to foodborne antigens or additives.

Dietary hypersensitivity or food allergy is an immunologically mediated adverse reaction to a protein component in food. A well-controlled dietary trial using a protein elimination diet is the basis for diagnosis of dietary hypersensitivity as a cause of IBD. The diet is changed to a well-defined, additive-free, digestible diet that contains hydrolyzed protein or a single novel source of protein not found in the patient’s normal diet. Hydrolyzed protein diets consist of minimally antigenic oligopeptides instead of intact proteins. Alternatively, novel protein sources can be used, such as turkey, duck, lamb, rabbit, venison, fish, or tofu. Novel protein diets can be home-prepared diets or commercial single-source novel protein diets, which are more convenient and balanced for long-term feeding. Intake of all other foods and sources of antigen must be completely eliminated throughout the feeding trial, including table scraps, treats, and medications with antigenic additives, such as probiotics and flavored vitamin supplements. The goal is to feed the trial diet for a minimum of 4 weeks. One study using commercial novel protein diets in a strict dietary elimination trial followed by antigen challenge testing found that 29% of cats with chronic idiopathic gastrointestinal problems had dietary hypersensitivity, most commonly involving beef, corn, and wheat.

**Probiotics and Prebiotics**

Considering the emerging importance of the intestinal microbiota in intestinal disease, there is growing interest in the role of intervention using probiotics and prebiotics. Probiotics are nutraceuticals containing live microorganisms that beneficially affect host health by improving the intestinal microbial balance. To have an effect, probiotics must contain adequate numbers of viable bacteria that survive transit into the intestine. Loss of viability in processing is a significant issue for over-the-counter probiotic products, but the quality of
commercial brand name veterinary probiotics is excellent. Prebiotics are nondigestible food ingredients (e.g., fructans, lactulose, galactooligosaccharides) that beneficially affect the host by selectively promoting the growth and/or activity of desirable populations of intestinal bacteria.

Numerous studies are published that demonstrate the effects of probiotics and prebiotics on fecal microbiota, fermentation end products, and fecal consistency in healthy dogs and cats, but placebo-controlled studies to establish efficacy in gastrointestinal disease are lacking. Using molecular techniques it has been shown in dogs and cats treated with a multistrain probiotic that the increased numbers of the probiotic species are detectable in the feces throughout the treatment period, but this effect rapidly disappears after discontinuation of treatment and the microbiota returns to baseline. Probiotics are extremely safe and free of adverse side effects. It is important to recognize that the results obtained with one probiotic strain (or product) may not be equivalent to the effects of other probiotic strains. Also, beneficial effects of a probiotic in one particular disease or condition does not necessarily mean the probiotic will be effective in other diseases.

**Cobalamin Therapy**

Cobalamin deficiency can occur with IBD, especially in cats, presumably the result of malabsorption of the vitamin in the ileum, and cobalamin deficiency can impair intestinal mucosal regeneration and cause mucosal atrophy, exacerbating diarrhea and making the patient refractory to the usual anti-inflammatory therapy. Hypocobalaminemia (serum cobalamin < 200 ng/L) is treated with subcutaneous injections of cobalamin (cats/small dogs - 250 µg; medium dogs - 500 µg; large dogs - 1000 µg), given weekly for at least 6 weeks, then every other week for 6 weeks, and then monthly.

**Metronidazole and Tylosin**

Metronidazole (10 to 15 mg/kg PO q12h) and tylosin (10 to 20 mg/kg PO q12h) are sometimes beneficial for IBD as single agents or in combination with corticosteroids. The beneficial effects might be attributable to intraluminal antibacterial action (reduction of bacterial-derived antigens) or to the immunomodulating effects of these drugs. Metronidazole tablets have an unpleasant bitter taste and provoke salivation, nausea, and sometimes vomiting. A liquid formulation of metronidazole benzoate is better tolerated by cats, or tablets can be split and placed in gel capsules. Dosages of metronidazole exceeding 50 mg/kg/day, especially for prolonged periods (weeks), have occasionally caused signs of reversible central nervous system toxicity characterized by weakness, ataxia, disorientation, seizures, and cortical blindness.

**Corticosteroids**

For initial medical therapy of IBD, oral prednisone and prednisolone are the most consistently effective and preferred therapy: in dogs at 1 to 2 mg/kg q24h or divided; and in cats at 2 to 4 mg/kg q24h, or 5 mg total dose/cat q12h, PO. Prednisolone is the active form of the steroid and preferred over the prodrug prednisone in cats. Clinical improvement using this dosage should be noted within 1 to 2 weeks. After 2 weeks of remission, the dosage is tapered in 2- to 4-week increments to the lowest effective alternate-day dosage (usually 0.5 to 1.0 mg/kg). Dexamethasone (0.2 mg/kg PO q12–24h) is sometimes more effective than
prednisone or prednisolone. In cats that are impossible to medicate orally, periodic injections of methylprednisolone acetate (20 mg IM or SC q2–4 wk) may be substituted for oral treatment.

Budesonide (Entocort; total daily dose of 1 to 3 mg PO for dogs and 0.5 to 1 mg for cats) is an alternative corticosteroid for refractory cases. Budesonide has selective mucosal anti-inflammatory activity with less steroidal side effects due to first-pass liver metabolism. In dogs, enough budesonide is absorbed to suppress the hypothalamic-pituitary-adrenal axis, but steroidal side effects are generally less than with conventional steroids.

Corticosteroid therapy may be discontinued on a trial basis after 8 to 12 weeks of remission; however, continuous alternate-day therapy is often required indefinitely to prevent relapse. In animals refractory to corticosteroids alone, combination with metronidazole, tylosin, or an immunosuppressive drug may be necessary.

Mesalamine and 5-Aminosalicylic Acid Derivatives
Orally administered 5-ASA derivatives (sulfasalazine, olsalazine, mesalamine) are designed to be minimally absorbed during passage through the small intestine, which allows them to reach the colon where they have a targeted nonsteroidal anti-inflammatory effect. Because they have limited activity in the upper GI tract, they are only beneficial in animals with colonic IBD (colitis). In general, these drugs are not as effective as corticosteroids for controlling IBD in dogs and cats.

Chlorambucil in Cats with Refractory IBD
In cats with IBD that is refractory to prednisolone alone, combining prednisolone with the alkylating agent chlorambucil (Leukeran; 2 mg total dose per cat, PO q48–72h; or 20 mg/M² once every 2 to 3 weeks) may provide greater immunosuppression and be more effective for inducing remission of the disease. In addition to treating refractory IBD, the addition of chlorambucil may enable use of a lower dose of corticosteroid to control the disease, thereby minimizing steroidal side effects. The chlorambucil-prednisolone combination is also an effective treatment for low-grade small cell lymphoma; thus, this combination can be used in cats where histopathologic differentiation between IBD and small cell lymphoma is inconclusive. The CBC should be monitored periodically in cats on chlorambucil. Chlorambucil is preferred over azathioprine in cats because azathioprine can be associated severe myelotoxicity in cats.

Azathioprine, Chlorambucil, or Cyclosporine in Dogs with Refractory IBD
In dogs with severe or refractory IBD, azathioprine, chlorambucil, or cyclosporine can be added to the corticosteroid regimen. Azathioprine is given at 2 mg/kg PO q24h for 2 weeks, then 1 to 2 mg/kg PO q48h combined with prednisolone. The CBC and liver enzymes should be monitored periodically in dogs on azathioprine. In dogs with concurrent protein-losing enteropathy, prednisolone combination with chlorambucil (4 to 6 mg/M² body surface area PO q24h for 2 weeks then q48h) was more effective than azathioprine-prednisolone. Cyclosporine (Atopica; 5 mg/kg PO q24h), a potent immunosuppressive drug that inhibits interleukin-2 and T-cell recruitment, has been found to be effective for controlling steroid-refractory
IBD in dogs. Transient inappetance and vomiting are common side effects of cyclosporine, but these typically resolve within 1 to 2 weeks.

**Monitoring Treatment with Clinical Activity Indexes**

Clinical activity indexes for IBD and chronic enteropathies in dogs and cats are now being used routinely to gauge the severity of clinical disease, to guide the initial choice of therapy, and to evaluate response to therapy. Depending on the index used, clinical scores are assigned for attitude/activity, appetite, vomiting frequency, diarrhea (consistency and frequency), weight loss, hypoalbuminemia, effusion/edema, pruritus, serum liver enzymes, hypocobalaminemia, and endoscopy lesions. The use of the following index systems in monitoring IBD treatment will be discussed: The Canine IBD Activity Index (CIBDAI), the Canine Chronic Enteropathy Clinical Activity Index (CCECAI), and the Feline Chronic Enteropathy Activity Index (FCEAI).

**References**


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