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The term ‘inflammatory bowel disease’ (IBD) is applied in veterinary medicine to idiopathic inflammation arising from any area of the gastrointestinal tract. The predominant types of IBD described in dogs are lymphocytic plasmacytic, eosinophilic and granulomatous. Several theories exist about the pathogenesis of IBD including: an autoimmune response to a luminal or mucosal antigen; a dysfunctional immune response to a commensal bacterium; and an infection with a pathogenic organism that either remains in the tissues resulting in chronic inflammation, or creates ongoing dysregulation of the immune response after resolution of infection.

The treatment of canine and feline IBD is largely empirical due to the poor understanding of aetiopathogenesis and lack of therapeutic trials, and treatment strategies have been based upon extrapolation of human research. Corticosteroids, sulphasalazine, azathioprine, antibiotics and dietary trials are currently the mainstay of treatment for all histological types of human IBD, either singly or in combination. The efficacy of such therapeutics in canine and feline IBD has not been determined, and there is no discrimination between drugs prescribed for either induction or maintenance of remission.

Current treatment protocols most often involve the use of immunosuppressive doses of corticosteroids to reduce intestinal mucosal inflammation and achieve clinical remission. However, a number of dogs and cats treated in this manner have either no response at all to the drug or they relapse after weeks to months of treatment. In addition, treatment with prednisolone often results in unacceptable adverse effects, specially in dogs, which is another reason for withdrawal of therapy.

In human medicine, failure to respond to medical treatment with steroids is observed in 20–30% of patients with IBD. A recent retrospective study of 80 dogs with IBD revealed that about 15% of cases had intractable disease.

For those intractable cases cyclosporine A could be a solution, accord the results of Allenspach et al (2006) who probed this drug in 14 steroid-refractory IBD canine patients. The clinical efficacy study showed that administration of cyclosporine (5 mg/kg PO q24h) for a period of 10 weeks was effective in 11 of 14 cases (78%). In this period of time, 9 dogs were complete responders after 10 weeks of treatment, 3 were partial responders, and 2 dogs had to be euthanized during the study because no clinical improvement was observed.

Studies have suggested that chronic or repeated episodes of intestinal mucosal inflammation may result in carcinogenesis. Antinflammatory therapy may protect against dysplasia and carcinoma reducing inflammation, altering the state of increased cell turnover and proliferation and altering mucosal cytokine and adhesion molecule profiles. Reducing inflammation also may modify intestinal floral bacteria by direct effects of bacteria on colonic mucosa or by altering the production of short-chain fatty acids, which may be anticarcinogenic. 5-ASA drugs can be protective through antioxidant, antiproliferative, and proapoptotic effects. 5-ASA drugs (sulphasalazine, mesalamine and olsalazine) can function as a free radical scavenger, an antioxidant, inhibitor of lipoygenase (and hence reduce leukotrienes), and via effects on prostaglandin 15-hydroxydehydrogenase, can reduce prostaglandin production.

**Melatonin:** the analysis of extrapineal sources of melatonin have highlighted the gastrointestinal (GI) tract as a major source of this factor, with concentrations of melatonin as much as 100 times that found in blood and 400 times that found in the pineal gland. GI melatonin may have a direct effect on many GI tissues, influencing the regeneration and function of epithelium, modulating the immune milieu in the gut, and reducing the tone of GI muscles by targeting smooth muscle cells.

At least 13 experiments in rodents have shown that melatonin administration reduces the severity of colitis. These effects were attributed to a variety of mechanisms, including inhibition of nitric

**Probiotics** have been the topic for research in IBD for quite some time, because they may exert several protective effects by altering the mucosal immune response resulting in less inflammation, prevention of colonization by intestinal pathogens, improving the intestinal epithelial barrier, stimulation of antinflammatory cytokine production and secretion of antibacterial substances. So far, the current literature has not been conclusive on the effect of probiotics in the treatment of IBD.

**Prebiotics** are nondigestible (oligo)saccharides, defined as "selectively fermented ingredients that allow specific changes, both in the composition and/or activity of the gastrointestinal microflora that confers benefits upon host wellbeing and health." Prebiotics are not digested in the upper gastrointestinal tract and reach the colon intact, where they are selectively fermented by residential microbiota into short chain fatty acids (SCFAs) and lactate. Several substances are claimed to be prebiotics, but so far only fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), lactulose, and inulin have met the following criteria: 1) be neither hydrolyzed nor absorbed in the upper part of the gastrointestinal tract; 2) be selectively fermented by 1 or a limited number of potentially beneficial bacteria in the intestine; and 3) be able to alter the colonic microflora toward a healthier composition.

Supplementation with antioxidants improved antioxidant status in human patients with Crohn’s Disease in remission. In addition, supplementation with n-3 fatty acids plus antioxidants significantly changed the eicosanoid precursor profile, which may lead to the production of eicosanoids with attenuated proinflammatory activity. An immunomodulating formula containing n-3 fatty acids and/or antioxidant may have the potential to play a role in the treatment of IBD. Recently, several studies reported that the antitumor necrosis factor-alpha antibody, **infliximab (IFX)**, is effective for refractory Crohn’s disease cases. Ruemmele et al. (2009) study confirms and extends previous findings in adult and pediatric Crohn’s disease (CD) patients, in that IFX is a potent and safe inducer of remission in otherwise treatment-resistant CD patients with a moderate to severe disease course. This trial clearly indicates that a scheduled 2-month treatment interval is more appropriate for disease control, and not associated with more adverse events compared to an on demand basis IFX therapy.

**Methotrexate (MTX)** is an alternative immunosuppressant to thiopurine analogs (azathioprine and mercaptopurine) in the treatment of IBD human patients. MTX is an antimetabolite interfering with DNA synthesis, although the antiinflammatory effect is unclear. A recent study demonstrated the efficacy of parenteral (intramuscular) MTX in the induction of remission in refractory CD but also show that oral MTX is ineffective in maintaining remission.

**References:**


Geerling et al., 2000. Nutritional Supplementation with N-3 Fatty Acids and Antioxidants in Patients with Crohn's Disease in Remission: Effects on Antioxidant Status and Fatty Acid Profile. Inflamm Bowel Dis 6(2): 77-84.

