Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease is an immune related disorder in which the intestines are chronically or intermittently inflamed. A synonym for inflammatory bowel disease that is abbreviated the same way is 'irritable bowel disease'. Affected dogs may be presented with a history of vomiting, diarrhea, weight loss or a combination of these signs. There is a great deal of variation in the severity, duration, response to therapy, and long-term effects of IBD among dogs.

While IBD exists in different forms, the most common is lymphocyticplasmacytic enteritis **(Figure 6.2)**, which means that the inflammation of the small intestine (enteritis) is associated with increased numbers of two white blood types that are linked to the immune system (i.e., lymphocytes and plasma cells). These are the primary immune cell types that are identified in biopsies of the affected sections of the small intestine. Lymphocytes are the cells that detect and kill viruses, fungi, and even tumor cells. When they are exposed to infectious agents, including bacteria and some complex molecules like foreign proteins and complex carbohydrates, they can transform into cells that produce antibodies. These cells are called plasma cells. Lymphocytes also interact with other immune and inflammatory cells to create the body's active defense system that helps protect people, dogs, and other animals against disease.

IBD also affects other parts of the gastrointestinal tract. For example, the condition known as lymphocyticplasmacytic colitis **(Figure 6.3)** primarily affects the colon (the dog's large intestine). There also is a rare condition characterized by inflammation caused by a different type of white blood cell. This condition, called granulomatous enteritis/gastritis, affects the small intestines and/or stomach **(Figure 6.4).**

Canine IBD, especially granulomatous enteritis/gastritis, is similar in some respects to the human disorder, known as Crohn's disease. Humans with Crohn's disease experience many of the same symptoms as dogs with IBD and are often treated in the same manner. In fact, much of our veterinary knowledge of IBD comes from research on Crohn's disease using dogs and other animals with spontaneous and experimental disease as translational animal models. Because Crohn's disease is thought to have a genetic component, veterinary researchers are examining the same possibility in dogs.

How does a dog develop IBD?

Over the past few decades, several theories have been proposed regarding the cause of IBD. These include vascular abnormalities that disrupt the function of the intestines, overproduction of mucus, an overactive gut, an infectious agent, or a dog with the equivalent of 'hyperactivity disorder'. Currently, it is understood that IBD is an immune-related disorder, with strong evidence for a genetic predisposition in some breeds and alterations in the bacterial flora in the intestines, otherwise known as the microbiome. For example, single nucleotide polymorphisms have been identified in genes that encode for specific innate immune factors in German Shepherds (Allenspach et al, 2010). There also is evidence for a shift in the bacterial populations in dogs with intestinal inflammation from gram-positive to gram-negative organisms, although at this point it is unknown if these changes are the cause or the result of the inflammation.

In a healthy dog, the small and large intestines, which includes the colon, have their own local part of the immune system. This purpose of the immune system in the gastrointestinal

Common Clinical Findings
Vomiting
Diarrhea
Weight Loss
Reduced Serum Cobalamin

tract is to protect the body against viruses, bacteria or other antigens (unwelcome outsider proteins and complex molecules) that may be consumed in the dog's food and water. The healthy intestinal tract is inhabited by a wide range of bacteria, many of which are important for the health of the dog. These 'resident' bacteria, otherwise known as normal flora, help restrict the other microbes and antigens to the lumen of the intestine; in essence, the resident bacteria serve as a barrier against the unwanted microbes and antigens from gaining access to the circulation. Under normal circumstances, the intestinal immune system ignores the resident bacteria, allowing them to do their job.

However, in animals with IBD, a problem has developed in one of three areas: the local intestinal immune system or its regulation (the body may be attacking itself or the resident bacteria), the integrity of the intestines themselves (through some type of injury), or the balance of normal flora in the intestines has been disrupted. Any of these problems can trigger an unwanted immune response that becomes excessive and selfperpetuating.

What are the clinical signs associated with IBD?

The most prominent clinical signs in IBD are vomiting, diarrhea and weight loss. In general, dogs in which the small intestine is affected have large volume diarrhea, vomiting and weight loss, whereas those involved with the large intestine are constipated, strain or frequently defecate small amounts of feces containing blood and mucus. Often the clinical signs seem to come and go randomly, particularly in the early stages of the disease. During that time, affected dogs may appear perfectly healthy except for a change in stool consistency and frequency. A common effect of gastrointestinal inflammation is failure to absorb cobalamin (vitamin B12), a vitamin that has an important role in many biochemical reactions. Consequently, serum concentrations of cobalamin often are used to characterize the severity of the disease process. As cobalamin is absorbed in a specific segment of the small intestine, abnormal serum concentrations of cobalamin also help to localize the disease.

If the disease is undiagnosed or left untreated, some dogs may lose weight, and develop vitamin and mineral deficiencies that manifest as malnutrition. Another long-term problem that can occur is lymphangiectasia (dilation of lymphatic vessels), which can eventually result significant protein loss and the development of tissue masses in the affected area.

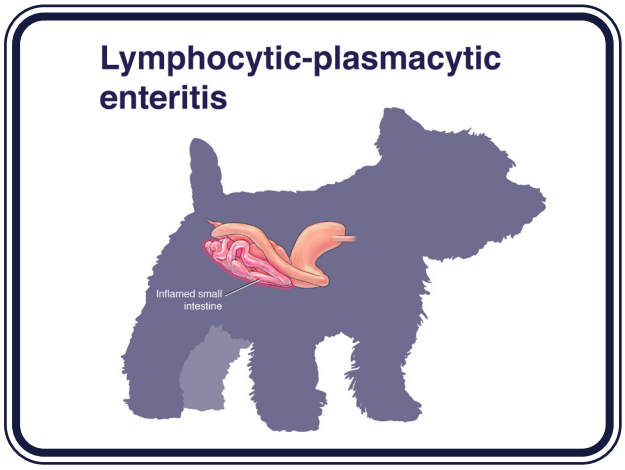

Figure 6.2 - The most common form of inflammatory bowel disease affects the small intestine (enteritis).

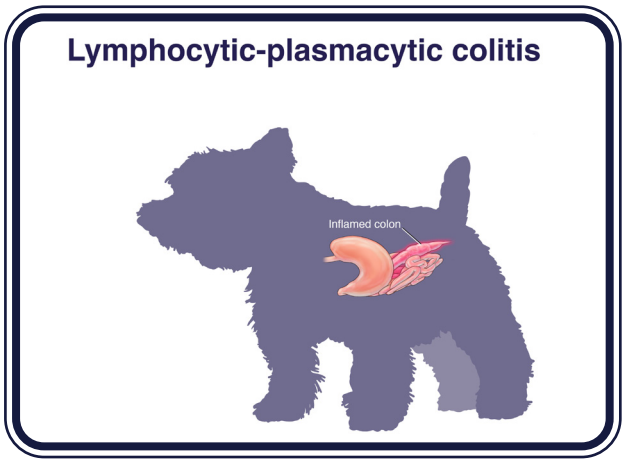

Figure 6.3 - This form of inflammatory bowel disease primarily affects the colon (colitis).

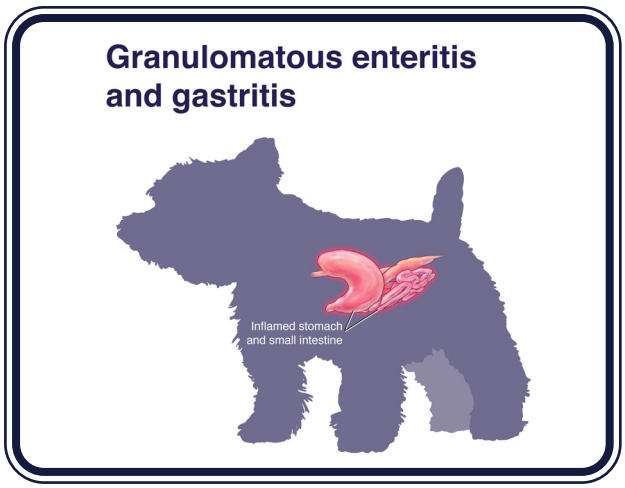

Figure 6.4 - This rare form of inflammatory bowel disease affects the small intestine and or stomach (enteritis and gastritis).

How is IBD diagnosed?

The diagnosis of IBD is made by eliminating other possible causes for the dog's clinical problems. Clinical signs of vomiting and diarrhea may be associated with other clinical diseases, such as intestinal parasites, food allergies, dietary changes, and stressors of any kind. Determining the cause requires a battery of tests. For example, a fecal test will be performed to help rule out the potential role of parasites, such as Giardia. Blood work will be performed, and may reveal an increased population of immunerelated cells, indicating inflammation. Abdominal ultrasound and xrays, taken either with or without a concurrent barium enema, may provide information about the status of the intestine. While both approaches may reveal other abnormalities, neither is very helpful in making a diagnosis of IBD, but may reveal other problems.

An important diagnostic test used to diagnose IBD is a thorough examination of the intestines with a flexible videoendoscope. A videoendoscope is a long cable with a camera on one end and a viewing port on the other. The camera-end of the videoendoscope is passed into the dog's gastrointestinal tract to allow the veterinarian to view the tissue lining the inside of the intestine and to take a biopsy, if necessary. In a 2015 study, Slovak and colleagues developed and prospectively validated an endoscopic scoring system for veterinarians to use to assess the severity of disease in dogs with IBD.

Having identified inflamed areas, the veterinarian can obtain small samples of the tissue using a special biopsy instrument that is passed through the length of the videoendoscope and controlled from the outside. This procedure requires sedation, anesthesia, and is invasive, time-consuming and can be expensive. The biopsy samples are placed in a tissue fixative and prepared for microscopic examination by a veterinary pathologist, who will determine if they contain an excessive number of immune cells. It is important for the pathologist to have access to several biopsy specimens, as the inflammatory response either may be localized or diffuse. If the microscopic findings do not correlate with the dog's clinical signs and other findings, a full-thickness intestinal biopsy may be obtained during more invasive exploratory abdominal surgery. This approach allows the pathologist to more fully evaluate the intestine for changes in the small intestinal villi or mucus and goblet cells in the large intestine. For some affected dogs, this is the only way a definitive diagnosis of IBD can be made.

A major differential diagnosis in dogs with some of these signs is a specific cancer affecting the intestine called malignant lymphoma. Making this diagnosis requires collaboration between the clinical veterinarian and a skilled pathologist, as the most common features of this neoplastic disease is the presence of an increased number of abnormal lymphocytes in the biopsy tissue. A major differentiating feature of IBD is the presence of mixed populations of normal lymphocytes, plasma cells, and sometimes cells like neutrophils and eosinophils (Craven, et al, 2004). If there is any doubt about the diagnosis, it is an excellent idea to obtain a second opinion from another veterinary pathologist.

A veterinarian may also used the canine IBD activity index to "score" a patient's clinical signs and determine the severity of the disease (Jergens 2004; Jergens et al, 2003, 2010). Using this approach, the veterinarian assigns a number from 1 to 3 for each of six clinical signs: attitude/activity, appetite, vomiting, stool consistency, stool frequency and weight loss. The total score is used to determine if the disease is considered clinically insignificant, mild, moderate or severe. This index is based on similar approaches designed to quantify Crohn's disease in humans and can be used to assess a patient's progress with treatment.

Although routine blood tests typically are not very helpful in making a definitive diagnosis of IBD, the low serum protein and cholesterol concentrations that typically are measured in dogs with IBD provide evidence of a protein-losing intestinal abnormality. While this is not a way to definitively diagnose IBD, this is certainly one of the major reasons routine bloodwork is performed in patients with chronic gastrointestinal signs. Other abnormalities that may be identified in a small number of dogs with IBD are decreased numbers of circulating platelets; this abnormality was present in 2.5% of affected dogs in one study (Ridgway, et al, 2001). Treatment of these dogs for IBD resolved the low platelet count. In another case report, two dogs were identified with anemia, presumably due to blood loss through the gastrointestinal tract (Ristic, et al, 2002).

Treatment of IBD

Unfortunately, relatively little is known about the effectiveness of particular treatments for IBD. As a result, treatment is based on empirical evidence and the clinical experience of the veterinarian. Treatment of IBD is usually multifaceted and will likely include a combination of diet changes, antibiotics and immunosuppressive drugs, including the use of corticosteroids such as prednisone. Management of dogs with IBD using medications alone is not recommended and usually is of limited value.

Dietary changes: One of the most important components

of treating a dog with IBD is to change the dog's diet. This can be done by switching to a completely different diet, to reduce exposure to certain antigens that might be present in the current feed. Similarly, commercial diets may be fed that contain hydrolyzed proteins that are smaller than typical proteins so as not to be recognized as antigens. Many veterinarians recommend feeding a highly digestible, rice-based diet that contains readily digestible fats and restricted amounts of fiber. Other dietary changes that can be made include altering the relative levels of omega3 and omega6 fatty acids (to reduce inflammation), and feeding prebiotics, such as inulin, or probiotics, such as Lactobacillus. The positive results obtained in recent studies in which dietary modifications were made in dogs with lymphocytic-plasmacytic enteritis underscores the importance of restricting exposure to antigens; in those studies, more than 60% of dogs responded positively and many did not require prolonged treatment with immunosuppressive drugs (Mandigers et al, 2010; Luckschander, et al, 2006).

Antibiotics: Antibiotics are administered to dogs with IBD in the hopes of reducing the amount of bacterial antigens present in the intestinal lumen and to control any bacterial overgrowth that might exist. Regardless, the aim is to reduce the intestinal immune response and local inflammation that are associated with IBD. The most commonly used antibiotics are tylosin or metronidazole, which in addition to its antibacterial effects also may help modulate the immune response. The beneficial responses that occur in some dogs with antibiotic therapy strongly suggest that these animals have what is called antibiotic-responsive enteropathy.

Immunosuppressive drugs: Based on the apparent role played by the immune system in the development of IBD, corticosteroids are given to suppress this response. Unfortunately, administration of these drugs is associated with a variety of ill effects, including gastric ulcers, increased appetite, increased urination, obesity, muscle weakness, and development of diabetes. Consequently, veterinarians are interested in pharmacologic agents that modulate the immune system, but cause fewer side effects. Because similar problems occur in human IBD patients administered corticosteroids, a relatively new drug called budesonide has been developed which is as effective as another commonly used corticosteroid, prednisone. In a recent clinical study comparing budesonide and prednisone in 40 client-owned dogs, Dye et al, (2013) reported that both drugs resulted in similar remission rates (>75%) but the frequency of adverse effects also was similar between the groups.

If the response to corticosteroid therapy is poor, many veterinarians also use azathioprine, cyclosporine A, and/or mycophenolate mofetil, which are immunosuppressive drugs sometimes used to treat autoimmune diseases and cancer. The most common side effect of treatment with azathioprine is bone marrow suppression, whereas gastrointestinal side effects tend to occur with the use of cyclosporine A and mycophenolate mofetil. In one study, Allenspach and coworkers (2006) administered cyclosporine A to 14 dogs that had not responded well to corticosteroid therapy, and reported concurrent improvements in clinical signs in 12 dogs and a decrease in the number of lymphocytes in intestinal biopsies obtained from these animals.

Cobalamin supplementation: Human patients with chronic gastrointestinal diseases often require monthly injections of vitamin B12 to address the low circulating concentrations of this vitamin, and a similar situation exists in dogs with chronic enteritis, such as IBD. In a 2016 study, Toresson and colleagues studied 51 dogs with chronic enteritis and low serum cobalamin concentrations, and reported that oral administration of cobalamin effectively normalized the concentrations. While these results are promising, the authors suggested that more in-depth studies need to be performed before oral supplementation can be recommended as part of the routine treatment for affected dogs.

It is critical for owners of dogs with IBD to realize that managing this disease requires a lifelong commitment. The prognosis for a dog with IBD depends on the severity of the disease and the progression at the time of diagnosis. While a change in diet and close monitoring of the dog may be all that's needed to manage many affected dogs, for others the situation may be quite different. Therefore, it is important for owners to be aware that this is a disease that is unable to be cured, instead it can be managed long-term, with the goal of achieving remission.

Current Research About Inflammatory Bowel Disease

Maggi G, Chiaradia E, Vullo A et al. Serum D-Lactate Concentrations in Dogs with Inflammatory Bowel Disease. Animals (Basel) 2024 Jun 6;14(11):1704.

The D-enantiomer of lactic acid (D-lactate) is normally produced by bacteria in the gastrointestinal tract. In humans, increased D-lactate concentrations are related to gastrointestinal disease, including short bowel syndrome and malabsorptive syndrome. This study was performed to measure serum D-lactate in 18 dogs with (IBD) and 10 healthy dogs. We found no significant difference in serum D-lactate between dogs with various degrees of IBD and healthy dogs. However, the wide variability in D-lactate concentrations in dogs with IBD and increased serum D-lactate concentrations in dogs with confirmed dysbiosis encourage further studies on this topic to understand potential factors influencing the serum D-lactate in dogs affected by IBD.

Diaz-Reganon D, Sainz A, Rodriguez-Franco F et al. Assessing the Quality of Life of Dogs with Inflammatory Bowel Disease and Their Owners. Vet Sci 2023 Jun 21;10(7):405.

The aim of the study was to assess the quality of life of dogs with IBD and the impact on the life and relationship of the owner. An online questionnaire based on a Likert scale score (1-10) was designed to assess items related to these areas. Responses from 30 dog owners with the disease and 80 healthy dogs were included in the study. Affected dogs had significantly lower overall quality of life, health, and level of activity. Owners of dogs with IBD reported lower overall quality of life. The scores for how their dog's quality of life might affect their own quality of life, how much their dog limited their social life, leisure time, or daily activities, and how often they felt burdened by caring for their dog were significantly higher in the IBD group than the healthy group. IBD has a negative impact on affected dogs and their owners regardless of the severity of the disease.

Linta N, Pey P, Toaldo MB et al. Contrast-enhanced ultrasonography in dogs with inflammatory bowel disease. J Vet Intern Med 2021 Sep;35(5):2167-2176.

Contrast-enhanced ultrasonography is used to evaluate vascularity of the gastrointestinal wall in neoplastic and inflammatory diseases. This study was performed to compare its use in the evaluation of duodenal perfusion in 42 dogs with inflammatory bowel disease and 20 clinically healthy dogs. This study showed that contrast-enhanced ultrasonography discriminates between affected dogs and healthy dogs by evaluation of time-intensity curves, but did not provide useful information for monitoring therapeutic response. The qualitative assessment identified no significant differences between healthy and affected dogs, or between dogs before and after treatment.

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