INFLAMMATORY BOWEL DISEASE (IBD) IN DOGS – DIAGNOSIS AND THERAPY

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA
Los Angeles, CA

Introduction
Inflammatory bowel disease (IBD) is not a specific diagnosis, rather it is a histological description of a syndrome resulting from a host hypersensitivity response to antigenic stimuli. In IBD there is an increase in the inflammatory cell population in the intestinal mucosa. The predominant inflammatory component can be lymphocytic-plasmacytic (most common type), eosinophilic, neutrophilic, or granulomatous. Primary causes of intestinal inflammation that should be considered include parasites, bacteria (specific agents or bacterial overgrowth), fungal disorders (e.g., Histoplasma, pythiosis), immune-mediated diseases, and food sensitivities. Many cases of IBD are likely idiopathic in nature. A presumptive diagnosis of IBD is made on the basis of history, physical exam and elimination of other disorders by laboratory tests and other studies such as radiography and ultrasonography. A definitive diagnosis can be made only by intestinal biopsy.

Clinical Course
The clinical course of inflammatory bowel disease can be characterized by diarrhea only, vomiting only, or both vomiting and diarrhea. Associated clinical signs that may also be seen, either singly or in combination, include weight loss, listlessness, borborygmus, flatulence, and abdominal pain. In some patients, inappetence may be the only sign, although this is more common in cats than dogs.

Inflammatory bowel disease is a common cause of chronic vomiting in dogs. Vomiting may be reported as a problem of recent onset or it can be an intermittent problem occurring over a period of several months or years before it becomes more frequent and severe. It is important for the clinician to recognize that vomiting may be the only major sign that occurs in a patient with inflammatory bowel disease. Gastric hypomotility can occur secondary to an infiltrative bowel disease such as IBD.

In some dogs with IBD, chronic intermittent or chronic intractable diarrhea is the major clinical sign. In these cases, the clinician must determine if the diarrhea is resulting primarily from small bowel or large bowel involvement, or is a mixed component of both large and small bowel.

Although inflammatory bowel disease is not breed specific, the Sharpei breed requires special consideration because they can develop a severe type of IBD. Most Sharpei dogs with IBD will present with a ravenous appetite, chronic diarrhea and weight loss. They often have intestinal dysbiosis (bacterial overgrowth) and other
intestinal problems as well. Shar-Peis with diarrhea, even for short durations of 3 to 4 weeks, due to IBD seem to be at increased risk of developing hypoproteinemia. Early clinical investigation in these patients should always include a complete blood count and complete biochemical profile.

If clinical investigation of a patient with chronic vomiting and/or diarrhea shows decreased albumin and globulin levels (panhypoproproteinemia), IBD of a moderate to severe degree should be one of the leading differentials. Lymphangiectasia, intestinal lymphoma, histoplasmosis, and pythiosis should also be considered. There is a regional geographic distribution with the latter two conditions. IBD is by far the most common cause of protein losing enteropathy in dogs. The presence of panhypoproteinemia indicates that the degree of disease is significant and likely chronic in nature. Many dogs with IBD will not develop hypoproteinemia, but for those that do, hypoproteinemia heralds severity and indicates that the disease is advancing. Steps to establish a definitive diagnosis should be expedited and an aggressive treatment regimen will likely be necessary.

**Diagnosis**

A presumptive diagnosis of canine inflammatory bowel disease is made on the basis of history, physical examination and the elimination of other disorders through laboratory tests and radiographic studies. The most important diagnostic procedure for a definitive diagnosis of IBD, however, is biopsy.

Baseline laboratory tests in dogs with chronic vomiting or diarrhea should always include a **complete blood count**, **biochemical profile**, **urinalysis** (as a means of assessing renal function and to evaluate for proteinuria), and **fecal examination for parasites**. Baseline tests are frequently normal or negative, but abnormalities that may be identified include mild nonregenerative anemia (anemia of chronic inflammatory disease); leukocytosis (20,000 to 50,000 cells/ul) without a left shift (suggests active chronic inflammatory disease); eosinophilia (mild to dramatic increase) in some dogs with eosinophilic enteritis; and hypoproteinemia. Any abnormalities of liver enzymes should also be noted.

Testing for parasites in dogs with diarrhea is best accomplished using zinc sulfate flotation with centrifugation. This is an excellent test medium for detection of nematode parasites as well as *Giardia*. **Zinc sulfate flotation with centrifugation** is superior to flotation with sodium nitrate, or flotation with zinc sulfate without centrifugation. Testing for *Giardia*-specific antigen in feces is also an excellent means of diagnosing giardiasis. In fact, *Giardia* antigen testing is very sensitive and can identify infections that may be missed on one or two zinc sulfate centrifugation tests with centrifugation or where there is incorrect interpretation of the identity of cyst structures (a common error in clinical practice). A fecal assay for *Clostridium perfringens* enterotoxin should also be done.

Although exocrine pancreatic insufficiency (EPI) is uncommon in dogs, it is always a good idea to do a **trypsin like immunoreactivity (TLI)** test on dogs with chronic
diarrhea to definitively rule out (EPI). Serum cobalamin (B12) and folate assays may be useful in evaluating dogs with chronic diarrhea, especially for intestinal dysbiosis (formerly referred to as intestinal bacterial overgrowth) and clinical hypcobalaminemia. Subnormal serum cobalamin concentrations may occur in association with small intestinal disease, EPI, dysbiosis, and inherited selective defects in cobalamin absorption. Serum folate concentrations may be increased in dogs with dysbiosis and decreased with infiltrative small bowel diseases.

A definitive diagnosis can be made only by biopsy, the single most important diagnostic procedure in the evaluation of chronic intestinal disease. Biopsy should be done to confirm diagnosis and determine type and extent of involvement. It is especially useful in determining treatment and prognosis. Endoscopic and surgical biopsies are discussed in a subsequent section.

Diagnostic Imaging of the Intestinal Tract
(Diagnostic Imaging section contributed by Dr. David S. Biller, DACVR, Kansas State University)

Normal Radiographic Anatomy of the Small Intestine
The small intestine should be evaluated for margination (serosal surface definition). The margin should be smooth. It will normally be visible due to fat in the serosa except when the animal is young (< 6 months) or emaciated or if abdominal fluid or cellular infiltrates are present. The normal diameter of the small intestine in dogs is < 2–3 rib widths, or less than the dorsoventral dimension of the second lumbar vertebral body.

The small bowel should be evenly distributed throughout the abdomen, occupying space not taken up by other organs. As organomegaly occurs, whether normal (distended stomach or urinary bladder) or abnormal (e.g., mesenteric lymphadenopathy, pancreatic enlargement, splenic mass), the intestine will be displaced. The direction helps to determine the differentials for the mass causing the displacement. In obese cats, it is common for the intestines to be localized in the ventral abdomen to the right of midline. The small bowel should have a smooth, continuous, curved appearance.

It is often necessary to have contrast studies (upper GI series) to identify normal or abnormal shape or diameter of small bowel. The radiopacity of the bowel loop is dependent on whether it is fluid-filled, gas-filled, or filled with a combination of fluid and gas. Fluid-filled loops of bowel appear as white rope-like structures. Gas-filled loops appear as black, thin-walled tubes. A small amount of gas above fluid appears as a narrow, radiolucent band with an apparent thickening of the bowel wall. A larger volume of gas reflects wall thickness more accurately and therefore bowel wall thickness should never be evaluated on survey films but only with use of contrast (whether negative or positive).
In dogs, barium should enter the duodenum in 13–20 minutes, the jejunum in 30 minutes, the jejunum and ileum in 60 minutes, and the ileocolic junction in 90–120 minutes. Barium should clear the upper GI tract and enter the ileum and colon in 3–5 hours.

The appearance of the mucosa or wall of the small bowel is best evaluated using positive contrast material. The mucosa should appear as a smooth, even surface or as a finely fimbriated edge. This fimbriation is due to barium dissecting between groups of aggregated villi. In normal young dogs, the mesenteric border of the duodenum has numerous or single, usually square or conical depressions, in the bowel overlying lymphoid follicles. These are pseudoulcers and considered normal. They are not seen in cats.

**Abnormal Anatomy of the Small Intestine on Survey Radiographs**

Ileus is an obstructive condition of the intestine and is either mechanical or functional. Mechanical ileus is also referred to as “dynamic” (or obstructive) ileus. It is usually simple and nonstrangulating. The radiographic signs may be influenced by the degree, location, and duration of obstruction. Dilatation of small intestine secondary to mechanical obstruction results from swallowed air and saliva and accumulation of mucosal secretions in the digestive tract.

Functional ileus, also referred to as paralytic or adynamic ileus, can be localized or generalized and may be a sequelae to mechanical ileus. The stages of development of functional ileus include muscle fatigue allowing stretching of the intestine, muscle ischemia secondary to stretching, and muscle necrosis. Functional ileus has numerous causes, such as extrinsic (which tend to be more generalized) that include spinal cord injury, reflex to pain, peritoneal trauma or irritation, or vascular compromise, and intrinsic (which is most often regional). Intrinsic causes include edema, amyloidosis, and acute inflammation or enteritis.

Survey radiographs of inflammatory bowel disease are usually normal or luminal fluid maybe increased.

**Abnormal Anatomy of the Intestinal Tract on Contrast Radiographs**

Intraluminal disorders usually appear as radiolucent areas surrounded by positive contrast medium. They often delay intestinal transit time and cause ileus proximal to their location. Intramural disorders should be evaluated with an upper GI series (positive contrast/barium).

The following questions should be answered while evaluating the upper GI series:

1. whether the lesion projects into the lumen, causes a narrowing or constriction;
2. whether the lesion projects away from the lumen, causing an enlargement of the diameter of the lumen as a result of a defect in the bowel wall;
3. whether thickening and rigidity of the bowel wall, irregularity at the serosal or mucosal surfaces, or a combination of these changes has occurred.
Radiographically, intramural disorders of the bowel may appear pedunculated, broad-based, smooth or irregular, and may expand the width of the bowel. Benign tumors tend to be smooth; malignant tumors tend to be irregular. The causes of intramural lesions include neoplasia, granuloma, abscess, scar, and hematoma. Inflammatory diseases of the small intestine (enteritis) tend to increase the rate of intestinal motility (i.e., reduced transit time). Chronicity and severe enteritis may cause irregularity of the mucosal surface; chronic enteritis may also decrease the width of the bowel lumen. Chronic and very severe enteritis can cause alterations or erosion of the mucosa.

Barium studies of patients with severe/chronic inflammatory bowel disease may be characterized by the appearance of thumbprinting. Thumbprinting is described as irregularly arranged mural based indentations into the contrast column.

**Ultrasonography of the Normal Gastrointestinal Tract**

Until recently, ultrasonography was considered to be a poor choice for evaluation of the GI tract because of the ultrasonographic barrier caused by luminal gas. Over the past 5 years, however, it has been applied successfully in diagnosis of a number of GI disorders, including gastric and intestinal foreign bodies, intussusception, uremic gastropathy, chronic pyloric hypertrophic gastropathy, enteric duplication, and GI neoplasia. It has proven useful not only in the diagnosis of morphologic GI disease but also in the evaluation of GI function. Maximizing resolution by using a high-frequency transducer is critical in the examination of the GI tract. Fasting the animal before ultrasonography also improves the results of the examination.

### Normal Wall Thickness in Dogs

<table>
<thead>
<tr>
<th>Site</th>
<th>Thickness</th>
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<tbody>
<tr>
<td>Stomach</td>
<td>3-6 mm</td>
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<tr>
<td>Duodenum</td>
<td>3-5 mm</td>
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<tr>
<td>Jejunum</td>
<td>2-4 mm</td>
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<td>Ileum</td>
<td>2-4 mm</td>
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<tr>
<td>Colon</td>
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*Larger dogs have thicker walls.*

Ultrasonography enables differentiation of the layers of the stomach, which alternate in echogenicity. Under optimal conditions, five separate layers can be identified. They are the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic). The submucosa and subserosa–serosa are hyperechoic because of the presence of relatively more fibrous connective tissue. The mean number of peristaltic contractions in the stomach is 4–5 per minute.

The ultrasonographic appearance of the GI lumen depends on its contents. In a collapsed state, the bowel lumen appears as a hyperechoic core (“mucosal stripe”) surrounded by a hypoechoic halo of bowel wall. This core represents mucus and small air bubbles trapped at the mucosal–luminal interface. When fluid is present in the bowel lumen, an anechoic area is present between the walls of the bowel that
appears tubular in long-axis views and circular in short-axis views. Gas in the GI lumen causes a highly echogenic interface with reverberation artifact. The presence of fluid in the bowel lumen improves the sonographer’s ability to evaluate the mucosal and submucosal layers of the GI tract, whereas the presence of luminal gas hinders it.

As with the stomach, the layers of the intestine alternate in echogenicity. Under optimal conditions, five separate layers can be identified: the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic).

Real-time ultrasonography should be included in the examination of enteric motility. The mean number of peristaltic contractions in the intestine is 4–5 per minute. Contractions are not seen in the colon.

**Ultrasonography of the Abnormal Gastrointestinal Tract Ileus**
Both mechanical and paralytic ileus have been described as ultrasonographic findings. Mechanical ileus occurs proximal to an area of obstruction; paralytic ileus can be generalized (e.g., viral enteritis, hypokalemia) or focal (e.g., duodenitis secondary to pancreatitis). When ileus is present, the bowel appears dilated and fluid-filled and GI motility is decreased or absent.

**Inflammatory Disease**
With inflammatory bowel disease, the intestine may be normal on ultrasound examination. The measurement of the intestinal wall thickness by ultrasound is neither specific nor sensitive for diagnosing IBD. Changes, especially those of severe or chronic disease, have been reported as focal to diffuse thickening, altered echogenicity, poor intestinal wall layer definition, and mild enlargement of adjacent lymph nodes. Mucosal echogenicity may remain hypoechoic, appear hyperechoic with striations or hypoechoic with speckles and be associated with but nonspecific for IBD. Jejunal lymph node thickness of > 6 mm maybe consistent with IBD but nonspecific for the type of disease. Round, enlarged, hypoechoic LNs maybe more consistent with neoplasia, while inflammatory lymph nodes may be enlarged but tend to maintain their normal shape.

The most common finding with inflammation is extensive and symmetric wall thickening with the layering retained. In comparison, neoplasia is usually localized with greater wall thickness and loss of normal layering. These categories can overlap, and therefore cytology or histopathology is required for definitive diagnosis. Acute enteritis or inflammatory bowel disease may demonstrate corrugation of the intestine on ultrasound examination.

**Intestinal Biopsy Techniques**
**Endoscopic Biopsy:** Endoscopy is a minimally invasive procedure in which multiple biopsies can be obtained and this procedure generally has greater client
compliance than with surgery because it is less invasive and less expensive than exploratory abdominal surgical procedures. Endoscopy offers a means of examining the upper and lower small intestine, stomach, and colon. It is especially advantageous because biopsies can be obtained early in the course of the disorder, at a stage when a client will likely be reluctant to agree to an exploratory surgery for their pet. Endoscopy also offers significantly reduced risk to the patient with hypoproteinemia. The degree of intestinal changes noted on biopsy also provides useful guidelines for both type and duration of therapy that will be needed to control the specific disorder.

Clinicians need to make sure they are taking an adequate number of endoscopic biopsy samples for accurate diagnosis. Even expert endoscopists report that in some cases one-fourth to one-third of the biopsies they take from a patient will have some degree of damage to the tissue that may preclude the samples from being useful or representative. Therefore, it is recommended that clinicians take 8 to 12 biopsy samples from the upper small intestine so that the pathologist will have enough tissue to work with. Also, it is recommended that both upper and lower GI endoscopy be done in dogs with chronic diarrhea. In this way biopsies from the ileum can be obtained by passing the endoscope along the full length of the colon and through the ileocolic orifice and into the ileum. When a pediatric diameter endoscope is used this is possible in most dogs over 4 to 5 kg. If the ileum can not be entered, it may be possible to obtain at least blind biopsies of the ileum by passing the endoscopic biopsy instrument through the ileocolic orifice with the endoscope tip positioned at the ileocolic sphincter area. Colon biopsies are always obtained as well during colonoscopy in order to evaluate for inflammation in the colon.

**Organ Biopsy via Laparoscopy or Laparotomy**

Organ biopsy is required to confirm canine IBD, and full-thickness samples procure tissue samples that will help the pathologist make the most accurate diagnosis. Full thickness intestinal biopsies can be accomplished by laparoscopic techniques or open abdominal surgery. Laparoscopic techniques have been well described for visceral organ biopsy. They are minimally invasive and well-suited for tissue procurement; however, laparoscopy is not yet readily available as a tool in most small animal general practice hospitals. Surgery on the other hand is an excellent way to obtain liver, pancreatic, and full thickness intestinal biopsies. In addition to biopsy, liver, pancreas and bile aspirates can be obtained for culture and cytology.

**TREATMENT OF INFLAMMATORY BOWEL DISEASE**

Successful treatment of canine inflammatory bowel disease depends on accurate diagnosis. The presumed pathogenesis of IBD involves antigenic stimulation and an inflammatory response mediated by the mucosal immune system. Therefore, therapy should include the suppression of the inflammatory response which requires the use of pharmacologic therapy. Removal of any antigenic source of inflammation...
is also necessary, and that is where dietary therapy is important. Food allergens can be a causative factor in some animals with IBD. The goal of dietary management is to reduce the antigenic stimulation of the intestinal immune system.

**Drug Therapy**

For patients with mild IBD, diet alone may be the only treatment needed. If, however, pharmaceutical therapy is also indicated, steroids may be used at a range of 0.5 - 1 mg/kg, divided BID for two to four weeks. The dose is then gradually decreased at two to four week intervals, and an attempt is made to achieve alternate or every third day therapy by two to three months or so. Some patients with mild IBD will respond well to metronidazole therapy, without concurrent use of corticosteroids (see below).

In moderate cases (based on biopsy changes and the patient’s overall condition), the steroid dosage should be higher (1.1 to 2.2 mg/kg per day for two to four weeks before an attempt to decrease the dosage is initiated). Moderate to severe and severe IBD cases are managed initially with prednisone at 2.2 to 3.3 mg/kg per day. Combination therapy is often used for dogs with moderate to severe IBD. Combination therapy includes prednisone and metronidazole, or in dogs with severe IBD and concurrent panhypoproteinemia (with a total protein level of 4.5 g/dl or lower) prednisone, metronidazole, and azathioprine are used concurrently.

Some dogs do not tolerate corticosteroids very well. For example, Arctic breeds and Rottweilers frequently cannot tolerate very high doses for an appreciable period of time. In these breeds I generally start with conservative doses of steroids, usually no higher than 0.5 to 1 mg/kg total per day. This may still be too high for some dogs. Metronidazole is sometimes used concurrently from the outset. For patients exhibiting severe steroid hepatopathy (panting, severe PU/PD, lethargy, weakness, and sometimes a decreased appetite) steroids should be stopped completely for 36 hours to allow for adequate metabolism and clearance. Steroids can then be resumed at approximately 25 percent of the initial dose. If prednisone is still poorly tolerated at this lower level, try oral dexamethasone next (0.01 to 0.02 mg/kg per day initially).

Some larger canine breeds do not tolerate prednisone well, but will often tolerate dexamethasone at 0.25 to 0.5 mg total, one to two times per day. Very large breeds such as Great Danes and others weighing 68 kg (150 lb) or more, will sometimes do well even on as low as 0.5 mg of dexamethasone, BID when there was initial difficulty in tolerating prednisone. In some cases, steroids simply cannot be used due to severe drug reactions in the patient and other drugs must be used.

When a patient is either poorly responsive to corticosteroids when used as outlined above, or if there is poor tolerance, the next best options are to try either budesonide or cyclosporine. Cyclosporine is described further below. Budesonide is a newer corticosteroid for use in humans. Budesonide is a glucocorticoid that also represents an alternative for management of IBD in dogs, especially in severe cases.
that have proven to be refractory to prednisone, metronidazole, azathioprine, and dietary management; or that are intolerant of the corticosteroids discussed above. It is one of a group of novel corticosteroids that have been in development for use in humans in an attempt to make available alternative preparations that will help limit toxicity associated with corticosteroid use. Others include fluticasone propionate, tixocortol pivalate, and beclomethasone dipropionate.

Budesonide undergoes high first pass metabolism in the liver and 90% is converted into metabolites with low corticosteroid activity. It has minimal systemic availability. The potential for typical corticosteroid side effects is significantly reduced as a result of decreased bioavailability and the resulting limited systemic exposure, which makes this a particularly attractive drug for use in humans and animals that are poorly tolerant of other corticosteroids. Budesonide also has a high receptor-binding affinity in the mucosa. It has been referred to as a “locally acting” corticosteroid.

Therapeutic results with budesonide have been promising in humans with Crohn’s disease, collagenous colitis and lymphocytic colitis, ulcerative colitis, either when administered as a retention enema or in oral form, and primary biliary cirrhosis. Budesonide has been used by some veterinary clinicians in recent years to treat IBD in dogs and cats. Dose recommendations vary. In humans, a range of 6 mg to 9 mg per day has been used during initial therapy. The following general recommendations have been made for dogs. In general, budesonide is administered to small dogs at 1 mg administered once per day. Medium size dogs receive 2 mg once daily. Large dogs receive a maximum of 3 mg once daily initially. Budesonide is available as a 3 mg capsule preparation and lower dosage forms are prepared by compounding pharmacists.

Budesonide can be used in combination with other drugs. Potential adverse effects include PU/PD, when budesonide is used at the high end of the dose range, and GI ulceration. These reactions have been observed in some human patients. These problems would be more likely to occur in dogs than in cats. It appears to be very safe when used at the levels listed above.

Metronidazole has both antibacterial and anti-inflammatory effects. It is very useful in treatment of IBD in dogs. In mild to moderate cases metronidazole alone may be sufficient to help control the intestinal inflammation. When used in combination with steroids metronidazole often allows for earlier reduction of the steroid doses. The dose of metronidazole for antibacterial and anti-inflammatory effect is 11 to 22 mg/kg BID. It is sometimes administered once daily to once every other day for maintenance therapy once the patient is deemed to be well under control but not yet able to be entirely without some form of drug therapy.

Use of azathioprine is generally reserved for severe IBD cases. Azathioprine has a potent immunosuppressive effect. Although azathioprine can cause bone marrow suppression, marrow suppression is rare when azathioprine is dosed accurately.
The canine dose is 2 mg/kg SID, orally. Azathioprine also has the potential to induce pancreatitis.

Azathioprine has a lag phase of 3 to 4 weeks, so it should be instituted early once a diagnosis of severe IBD is made. Azathioprine is usually used for 3 to 9 months in dogs. Once adequate control is achieved, the daily dose is decreased by 50%, and subsequently alternate-day therapy is used. A complete blood count and platelet count should be run to monitor for evidence of anemia, leukopenia, or thrombocytopenia at 3 week intervals for the first 2 months of therapy and then once every several months.

Many canine IBD patients are thought to have intestinal bacterial overgrowth as well, and they can often be helped with the use of antibiotics. The antimicrobial drugs used most commonly include metronidazole or tylosin. In some cases cephalosporins or enrofloxacin are used (not usually the first choice, however). Combination therapy with metronidazole plus enrofloxacin or metronidazole with tylosin is used in some cases, e.g., those with longer duration of signs or where there may be more significant patient compromise. In mild cases two to four weeks of antimicrobial therapy is frequently sufficient. If crypt abscesses are reported on the histopathologic exam antimicrobial therapy is used for a longer time in conjunction with appropriate anti-inflammatory therapy.

Tylosin is a macrolide, bacteriostatic antibiotic that has activity against most gram-positive and gram-negative cocci, gram-positive rods, and Mycoplasma. However, the gram-negative bacteria E. coli and Salmonella spp. are intrinsically tylosin resistant. Studies (Westermarck) have revealed that administration of tylosin leads to significant but transient changes in the composition of the small intestinal flora. It may be that tylosin promotes the growth of commensal bacteria whole suppressing deleterious bacteria. In addition to antimicrobial properties tylosin may also have anti-inflammatory The term “tylosin responsive diarrhea” has been coined as a result of observations that dogs with nonspecific diarrhea will often respond to tylosin therapy. Some cases are intermittent or chronic in nature. Dose range is 7 to 20 mg/kg orally every 12 to 24 hours (administer BID initially).

Use of other drugs may be indicated in some dogs with IBD. If large intestinal inflammation is present either metronidazole or 5-amino salicylic acid derivatives (sulfasalazine, osalazine, mesalazine) or both in combination will usually control large bowel diarrhea due to colitis. Corticosteroids are usually ineffective for controlling signs of large intestinal inflammation in dogs (although steroids are very effective for this purpose in cats). Other alternative therapies may include cyclophosphamide, chlorambucil, and cyclosporin. Omega 3 fatty acids (antiinflammatory effects) or vitamin E (antioxidant) may also be beneficial in some chronic cases.

Cyclosporine: Cyclosporine A (cyA) has been shown to be effective in steroid-resistant IBD in humans and also perianal fistula management in both humans and
dogs. Other uses in dogs have included management of atopic dermatitis and sebaceous adenitis. A study was undertaken to evaluate the pharmacokinetics and clinical efficacy of oral cyA treatment in 14 dogs with steroid-refractory IBD (Allenspach K, et al). Patient assessment included determination of a clinical activity score to assess severity of clinical signs before and after treatment. The total number of infiltrating lymphocytes and T cells in duodenal biopsies obtained via endoscopy were also assessed before and after treatment. Improvement was noted in 12/14 dogs. There was a significant improvement in clinical activity score and a decrease in T cell numbers, implying that T cell lysis is a possible mechanism of action. Results from this study suggest that cyA is an effective option for managing some dogs with steroid refractory IBD.

The anti-inflammatory effect of cyA in human IBD is believed to be due to suppression of activated T cells infiltrating the mucosa, thereby decreasing the amount of proinflammatory cytokines, and ultimately, the clinical signs of disease. The cyA dose used in the study of 14 dogs was 5 mg/kg SID. The sole therapy was cyA. Previous therapy had included immunosuppressive doses of steroids in all dogs (starting dose of prednisolone was 2.2 mg/kg/day, administered for a range of 6 to 14 weeks before the dose was decreased). Other drugs tried in most of the dogs included metronidazole (range of 2 to 38 weeks).

There were transient adverse effects observed in 5 dogs, most of which occurred in the first 1 to 2 weeks of therapy, after which time they abated. Adverse reactions included vomiting and inappetence (4/14 dogs), and gingival ulceration and alopecia followed by hypertrichosis in 1 dog. A lag phase of 7 to 10 days has been seen in humans before there are obvious signs of clinical improvement, and a similar finding was observed in the dogs in the study reported here.

The clinical efficacy study showed that cyA was effective in 11/14 of the dogs (78%). Nine dogs were considered complete responders after 10 weeks of treatment, 3 were partial responders, and 2 were nonresponders that had to be euthanized during the study because no clinical improvement was observed. Eight out of the 9 dogs that responded well initially were still doing well after 6 months to 2 years follow-up. One dog responded well for 14 weeks but then relapsed and declined with severe vomiting and was euthanized. Eight dogs were discontinued from cyA after 10 weeks of therapy. Three dogs were kept on therapy for 4, 6, and 36 months. These dogs had all shown significant improvement in clinical score but the owners elected to keep their dogs on therapy.

**Duration of Pharmacotherapy**

The duration of therapy that is required in dogs with IBD is quite variable. Patients with milder forms of IBD may need medical management for as little as 2 to 4 months. IBD in middle age to older dogs that is initially graded as moderate to severe can usually be managed quite successfully and can be maintained in remission but not often cured. However, in the author’s (T. Tams) experience young dogs that are diagnosed and managed early enough rarely require long-term therapy.
(more than 1 to 2 years). In some young dogs (3 to 4 years of age or less) with severe lymphocytic-plasmacytic enteropathy and marked hypoproteinemia, therapy can be successfully discontinued as early as 9 months to 1 year. As a general clinical rule of thumb, an attempt can be made to discontinue therapy after 2 to 3 months of successful control on twice-weekly medication. If signs recur, medication is resumed on a daily basis for 7 to 14 days before a gradual reduction program is started.

**Dietary Therapy**

As was mentioned earlier, the goal of dietary therapy in IBD is to reduce the antigenic stimulation of the intestinal immune system. Many pet food companies today provide myriad information on adverse food reactions and offer many good diets from which to choose. Dogs with IBD should be fed divided feedings, two or three times per day. The two main categories of foods used in dietary trials are novel protein diets and hydrolyzed protein diets.

A diet that is hypoallergenic is one that contains no additives or preservatives and has a single source of protein that is easily digestible. The protein source must be one that is "novel," meaning one that the dog has not eaten before. Examples of novel proteins now being used by pet food manufacturers include white fish, venison, rabbit, duck, salmon, catfish, and lamb. Manufacturers have been using lamb in their diets for many years now, so many dogs have eaten lamb containing diets. Dogs that have eaten lamb before should be tried on some other protein. It may be helpful to consider switching the initial novel protein to another source at six to eight weeks into the treatment course. When there is considerable inflammation and damage to the intestinal mucosa, the antigens that are in the new protein source can get absorbed and the animal may acquire an allergy to this protein. Switching them periodically could potentially alleviate this situation. The primary carbohydrate source used in hypoallergenic diets is either potato or rice.

**Treatment Failure**

An inadequate response to therapy is most frequently due to either incomplete diagnosis (i.e., the patient has more problems that have been diagnosed), the diagnosis is incorrect, or inadequate therapy is being administered (e.g., wrong drugs, or right drugs but incorrect doses). Veterinarians need to stress the importance of GI biopsy for dogs with disorders that do not resolve fairly early on therapeutic regimens which include dietary trials, antimicrobials, and management for any GI parasites that have been identified. In chronic cases, too often the empirical therapy route is tried for too long and ultimately the patient suffers for this approach. A thorough diagnostic approach will significantly increase the chances that therapeutic intervention will be successful. In dogs with IBD that are vomiting, a secondary gastric hypomotility problem should be considered, and gastric prokinetic therapy may prove beneficial. Sometimes anti-inflammatory medication doses are reduced too rapidly. It is better to use aggressive therapy, while carefully monitoring the patient, rather than be too conservative.
References


