CHRONIC LARGE BOWEL DIARRHEAS

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Distinguishing Small Bowel Diarrhea From Large Bowel Diarrhea

The first question in a patient with diarrhea is whether it is acute or chronic disease. Most acute diarrheas are self limiting and only need supportive therapy to help them resolve faster. If the diarrhea becomes chronic, then you know that this is not a self resolving disease; therefore, diagnosis is necessary in order to resolve the problem. When faced with a chronic diarrhea, the next question is whether the patient has large intestinal disease or small intestinal disease. It is important to realize that diarrhea is simply increased fecal water. Severe, life-threatening small bowel disease may cause minimal or no diarrhea if the colon can absorb enough water to make the feces firm or solid by the time they are evacuated. In particular, if the patient has been in a cage and unable to exercise (a potent stimulus for defecation), the feces may be normal despite significant intestinal disease. It is only when the colon's water absorbing capacity is exceeded that diarrhea occurs. Even when small bowel disease does cause diarrhea, the weight loss from nutrient malabsorption may precede diarrhea by months.

Use the history to help differentiate large bowel from small bowel disease. Weight loss, especially in the face of a reasonable appetite, strongly suggests nutrient loss from the small intestine. Hepatic disease can closely mimic intestinal disease in this regard, but the intestines are usually a better place to start looking. Weight loss (or loss of body condition as reflected in the hair coat) is probably the most important area to look at in differentiating large bowel from small bowel disease. Any animal with chronic small intestinal disease that is clinically significant should have weight loss or loss of condition. Any animal with chronic diarrhea and no loss of weight or condition has large bowel disease until proven otherwise. Some animals with severe large bowel disease will have weight loss, but these have more severe causes (usually infiltrative) of diarrhea and therefore usually also have hematochezia, mucus, hypoalbuminemia and/or marked tenesmus.

Red blood in the feces (hematochezia) comes from the large bowel or the ileum. This finding is specific but insensitive for large bowel diarrhea. Mucus in the feces comes from the large intestine or ileum. This finding is specific but insensitive for large bowel diarrhea. Tenesmus and dyschezia suggest large bowel disease; however, any animal with chronic diarrhea can have anal irritation causing mild tenesmus. Vomiting can occur with either large or small bowel disease.

Causes Of Large Bowel Diarrhea

The most commonly diagnosed chronic large bowel diseases causing diarrhea in dogs in our practice are so-called irritable bowel syndrome (IBS) (which is NOT the same as irritable bowel disease in people), fiber-responsive colonic dysfunction (which is probably a subset of irritable bowel syndrome), dietary intolerance (by which I am referring to allergic as well as non-allergic dietary problems), clostridial colitis (which might be better called “tylosin-responsive colitis”), parasites, fungal infections (i.e., histoplasmosis and pythiosis) and schistosomiasis (i.e., heterobilharzia). The most commonly diagnosed large bowel diseases in cats in our practice are fiber-responsive disease, dietary intolerance, antibiotic-responsive colitis and inflammatory

bowel disease (IBD), especially lymphocytic-plasmacytic infiltrates. Fortunately, colonic histoplasmosis is much less common in cats than it is in dogs.

Parasites

The first concern in a diagnostic work up is parasites. Whipworms can be very difficult to demonstrate on fecal flotation. Direct fecal examination will be more useful than fecal flotation if the flotation solution is not dense enough to ensure that the whipworm ova will float. Also, remember that whipworms can be periodic egg shedders. Whipworms can be very easily missed by fecal flotation; therefore, it is appropriate to treat any dog with chronic large bowel disease with fenbendazole. I have seen several cases of whipworms that were diagnosed during colonoscopy because fecal examinations were non-diagnostic. Tritrichomonas is primarily a problem of cats, but very, very rarely will be seen in dogs.

If the diarrhea persists after eliminating parasites from consideration, the next question is whether to try a therapeutic trial or perform tests. If the patient is hypoalbuminemic, lost substantial weight, or is a Boxer or a French Bulldog, then extensive diagnostics aimed at infiltrative diseases, especially histoplasmosis, pythiosis, heterobilharzia, histiocytic ulcerative colitis, and cancer are indicated. Otherwise, a therapeutic trial (e.g., dietary therapy or empirical antibiotic therapy) plus modest diagnostics (e.g., fecal examination) may be particularly helpful. It is worth noting that many of the more common diseases affecting the colon are better diagnosed with a therapeutic trial than with an extensive diagnostic work up that includes blood tests and endoscopy/biopsy. The main therapeutic trials are usually a fiber-supplemented diet, an elimination diet, anthelmintics, and/or antibiotics (e.g., tylosin or amoxicillin). Good therapeutic trials are better at diagnosing some of the more common large bowel disorders of dogs than are endoscopic examinations and biopsies.

Clostridial Colitis

Clostridial colitis might better be called "antibiotic-responsive colitis". It is a very important disease in the dog, but we are not sure how important or common it is in the cat. We think that it is caused by toxigenic strains of *Clostridium perfringens*. However, even when a toxigenic strain of *Clostridium perfringens* is established in the colon, it does not generally produce disease unless there is sufficient toxin being produced due to upregulation of toxin production in the bacteria. Toxigenic strains upregulate the amount of enterotoxin produced when they sporulate, and it is this toxin which damages the colonic epithelium and produces diarrhea.

Diagnosing clostridial colitis is not as "easy" as it was a few years ago. One cannot reliably diagnose clostridial colitis by finding spores in the feces on fecal cytology, performing quantitative cultures for *Clostridium perfringens*, or assaying for clostridial enterotoxin in the feces. Looking for fecal spores is an especially easy screening procedure, and the spores can be detected with a variety of stains. However, just as the disease can wax and wane unexpectedly, the presence and number of spores may likewise vary. Biopsy is not that helpful; there may or may not be histologic changes in the colonic mucosa in animals with clostridial colitis. Besides, the histologic lesions seen with clostridial colitis are nonspecific, and cannot be reliably differentiated from IBD or dietary allergy/intolerance. We used to think that the most definitive method of diagnosing clostridial colitis was to assay the feces for the presence of toxin; however,

this is relatively expensive and is no more sensitive or specific than other tests.

Many of us currently just treat for the disease and observe the clinical response. Typically, the patients are treated with tylosin and a high fiber diet simultaneously (even if they have been shown to not respond to a high fiber diet in the past). While this approach can cause a problem when there are two things happening concurrently (e.g., clostridial colitis PLUS dietary intolerance), it seems to currently be one of the better ways to diagnose clostridial colitis. Response to amoxicillin or tylosin may be one of the best ways to presumptively diagnose clostridial colitis. Many patients with clostridial colitis do not respond to metronidazole.

Tylosin is an antibiotic that seems to be consistently effective against *Clostridium perfringens*. This is a wettable powder that is used to treat poultry. Animals that respond to tylosin and a high fiber diet usually do so within 3-7 days. The initial dose of Tylan is 10-40 mg/kg bid (20 mg/kg seems to be a good place to start). Most patients that respond can be slowly weaned off the drug and maintained on a high fiber diet alone. It is important to note that you will not eliminate Clostridium perfringens from the patient, and very rarely, some patients seem to need to be tylosin for life. Tylosin tends to have an unpleasant taste and needs to be mixed into the food, and sometimes it is better to put it into capsules and give it that way instead of putting it on the food. Amoxicillin is also effective in almost all animals with clostridial colitis. Many animals with chronic clostridial colitis that cannot be completely removed from tylosin therapy can be well controlled with one treatment of amoxicillin or tylosin every 2-3 days.

Metronidazole is very effective against anaerobic bacteria in general, but metronidazole is inconsistently effective in animals with clostridial colitis, possibly because metronidazole does not reliably achieve therapeutic levels throughout the feces.

Some dogs that are tylosin responsive also respond to fiber supplementation, which makes sense because fiber will usually remain relatively intact until it reaches the colon where it may have profound effects on the microenvironment of the colonic bacterial flora. The goal is not necessarily to eradicate *Clostridium perfringens* from the animal (you probably can't do that even if you wanted to); rather, it is to prevent the bacteria from elaborating and releasing its toxins. The preferred long term therapy of clostridial colitis is to maintain the animal on a high fiber diet which controls signs and not have to give antibiotics; however, not all animals can achieve this level of control.

Fecal Transplantation

Fecal transplantation has seemingly been beneficial in some cases of clostridial colitis. It is reasonable to try, although at this time there is not a consensus as to the best way to perform this procedure.

Dietary-Responsive

We will use the term "dietary-responsive" to include both dietary allergy (an immune process) and dietary intolerance (a non-immune process). Dietary-responsive disease is more common than many suspect, especially in cats with chronic large bowel disease. You cannot count on finding eosinophils in the blood or the colonic mucosa of animals with dietary allergies; most

patients with dietary intolerance have minimal histologic changes or have nonspecific lymphocytic and/or plasmacytic and/or eosinophilic infiltrates. Because the histologic findings are nonspecific, it is typically preferable to try elimination diets prior to performing colonoscopy. The biggest problem in these patients is finding an effective diet. We often see cases in which the right thing was done (i.e., an elimination diet was used), but was so poorly planned or implemented that the effort was wasted. Hydrolyzed diets are a good place to start; many (not all) dogs with dietary hypersensitivity respond to hydrolyzed diets. If the patient does not respond to a hydrolyzed diet, then a novel protein diet should be tried. It is critically important to carefully investigate the history and see what the patient has eaten in the past. However, sometimes it is difficult to find a diet that is "right" for a particular patient. This might be because you do not know if the problem is an allergy or an non-allergic intolerance. In some cases, all of our well-planned hypoallergenic diets failed but a chance try at some commercial brand works. It is easy to do a poor job of feeding a “hypoallergenic” diet and thereby make the client so discouraged with dietary therapy that they end up requesting costly work ups when a good dietary trial done at the beginning would have worked. Also, if you do a thorough work up and do not find a reasonable cause of the diarrhea, it is probably a dietary intolerance or allergy, and you will have to simply try diet after diet until you finally find the right one.

Histiocytic Ulcerative Colitis

Histiocytic ulcerative colitis, also known as “Boxer colitis” is being seen more commonly now than it was 5-10 years ago. First described about 30 years ago, it was a horrible, progressive disease of young Boxers (and sometimes related breeds, such as the French Bulldog) that invariably had a terrible prognosis. The signs are those of severe large bowel disease (lots of hematochezia and fecal mucus) plus weight loss. Diagnosis is made histologically by finding PAS-filled macrophages in the mucosa. Recently, it has been discovered that this is an antibiotic-responsive disease caused by enteroadherent strains of *E. coli*. Initially, enrofloxacin seemed to be particularly effective but any number of antibiotics would work. Unfortunately, there has been an upsurge in antibiotic resistance of the *E. coli* responsible for this disease. Most strains are no longer sensitive to enrofloxacin. Therefore, it is recommended that mucosal samples (not fecal samples) be taken for bacterial culture and sensitivity analysis. The biggest problems are that a) many people (clients and veterinarians) are reluctant to biopsy the dogs because they assume that any disease so severe must have a bad prognosis, and b) many pathologists have never seen it and miss it, even when it is fairly obvious to the experienced eye. It is best to biopsy the dog instead of giving empirical enrofloxacin therapy since other treatable diseases may be present (e.g., histoplasmosis) that also can be successfully treated if therapy is begun in a timely fashion. If antibiotics are given, it is important to treat for several weeks (at least 8) to ensure eradication of the bacteria lest resistant strains be selected for and allowed to cause a relapse that is more difficult to control than the initial presentation. Unlike some diseases, failure to eradicate the infection with the first choice of antibiotics is almost uniformly associated with subsequent resistance to the antibiotic(s) used initially.

New Or Less Common But Important Diseases

Recently, we have seen miniature Dachshunds with what is initially diagnosed as multifocal inflammatory polyps. However, FISH analysis shows that these are bacterial in origin (something now shown by special histologic stains). At least some of them respond exceedingly

well to aggressive antibiotic therapy. However, relatively few have been seen so far, so broad-sweeping statements are not appropriate.

Histoplasmosis can be a very important cause of large bowel diarrhea in dogs (and rarely in cats). The urine antigen test is reasonably sensitive and specific, but I have seen false negative and false positive results. It is safest to perform a colonic biopsy to rule this out. Be aware that in its early stages, it can closely mimic more mild colonic diseases such as dietary-responsive, fiber-responsive, and clostridial colitis.

Protothecosis seems to be recognized more frequently over the last several years. It typically causes a severe colitis, but it is easy for pathologists to miss it as many have not seen it before. I've even seen cases where it was erroneously diagnosed as "coccidiosis".