HISTIOCYTIC COLITIS IN BOXERS AND OTHER LARGE BOWEL DISEASE
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The large intestine is responsible for absorption of water, sodium, chloride and short chain fatty acids, whilst it secretes potassium and bicarbonate. The colon has a physiological barrier (mucus layer) and a significant commensal bacteria population. Colonic bacteria produce short-chain fatty acids (SCFA), and this can contribute up to 10% of the animal’s energy requirements. In dogs the majority of the colonic bacteria are anaerobes (90%), whilst in cats approximately half are anaerobic. Large intestinal diarrhea can occur by a number of mechanisms. In an otherwise normal colon without well-developed flora (e.g. neonates), excess sugars are not converted to SCFA and cause an osmotic diarrhea. In the normal colon with well-developed flora, but overloaded with readily fermentable carbohydrate, the luminal pH falls, lactic acid is produced, and osmotic diarrhea also develops. Diarrhoea may also occur if the large bowel is inherently diseased, and this may be independent of SI disease. Hallmark clinical signs of colonic inflammation or ‘colitis’ include (from most to least common):

- Mucoid faeces
- Tenesmus (straining to defecate)
- Haematochezia (fresh blood in the faeces)
- Mucoid faeces
- Constipation/obstipation
- Dyschezia
- Rarely associated with weight loss, but vomiting can occur in cats

<table>
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<tr>
<th>Differential Diagnosis for LI diarrhoea (colitis)</th>
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<tr>
<td>Fibre-responsive/Idiopathic colitis</td>
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<td>Inflammatory bowel disease:</td>
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<tr>
<td>Lymphocytic-Plasmacytic Enteritis</td>
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<tr>
<td>Histiocytic Ulcerative Colitis</td>
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<td>Eosinophilic colitis</td>
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<tr>
<td>Granulomatous colitis</td>
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*Clostridial perfringens* associated diarrhoea
*Trichuris vulpis* (whipworm)

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<th>Neoplasia:</th>
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<tr>
<td>Lymphoma</td>
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<td>Adenocarcinoma (although haematochezia</td>
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Animals presenting with colitis symptoms can be accurately diagnosed and successfully treated in most cases. A logical approach to diagnosis and a thorough understanding of possible pathogenesis in order to formulate a
treatment trial is necessary to ensure this. Good and accurate history along
with rectal examination is mandatory. Other investigations include faecal
analysis, metabolic screening and either colonoscopy and biopsy or
proctoscopy and biopsy. Full-thickness colonic biopsies are not indicated in
most dogs with mild colonic signs. If no systemic or physical abnormalities are
detected then a treatment trial could be used: faecal analysis or treatment with
fendbendazole (50 mg/kg sid 3-5 days) and fibre supplementation
(Metamucil). A failure to respond to treatment would then necessitate further
investigation.

This treatment approach is not recommended in Boxer dogs presenting with
colitis, as they are predisposed to a form of inflammatory bowel disease (IBD)
called Histiocytic Ulcerative Colitis (HUC), although the disease has also been
reported in other breeds. Typically affected dogs are usually less than 2 years
old at presentation. The clinical signs of HUC are usually severe and often
associated with weight loss or poor growth. Haematochezia is a prominent
component. Diagnosis of HUC is based on histological documentation of a
mucosal infiltrate of plasma cells, lymphocytes and Schiff-positive
macrophages within the colon. Traditionally prognosis has been considered
guarded when traditional immunosuppressive and dietary therapy has been
used, although spontaneous resolution has been reported\(^1\). There has
however been a paradigm shift in the thinking about the pathogenesis of this
disease, resulting in a different treatment approach. It appears that HUC is in
fact an example of dysbiois, where functionally distinct bacterial strains can
lead to a form of IBD, and this new state of knowledge confers a much better
prognosis for this disease.

Published reports have documented clinical resolution in dogs treated with
enrofloxacin alone at 5 mg/kg/day for 6-8 weeks\(^2,3,4\). Some of our dogs have
now been disease-free for over 30 months following on treatment course.
When this disease was first identified in the 1960’s\(^5\), an infectious aetiology
was proposed and investigation concentrated on organisms such as
Mycoplasma, but failed to identify a causative organism\(^6\). Recent evidence
about the immunological cell distribution present in the colonic mucosa of
dogs with HUC\(^7\) correlates well with this new thinking about one possible
pathogenesis of IBD. There is increasing evidence that suggests that IBD may
be a consequence of an abnormally exuberant immune response to normal
intestinal flora\(^8\). This appears to occur in genetically susceptible individuals,
and such an abnormal response may occur in the Boxer dog. Adherent and
invasive E coli have been demonstrated to be present within the colonic
mucosa of affected dogs, but not in controls\(^9,10\). Comparisons can be made
with spontaneous Crohn’s disease in people, where an increased immune
response to enteric bacteria occurs\(^11\). It has further been established that
these bacteria are no longer present following treatment with enrofloxacin
(unpublished observation).

\(\text{Fibre-responsive colitis}\) is an idiopathic condition of dogs, in which clinical
signs of colonic inflammation are present, but histological evaluation of colonic
biopsies is unremarkable. This disease carries a good to excellent prognosis and responds well to soluble fibre supplementation or low-residue diets. Cats do not appear to be affected by this condition. Fibre supplementation may be beneficial by promoting colonic transit via stimulation of segmental contractions, altering the bacterial population in the lumen, increasing the production of SCFA or by absorbing large amounts of faecal water in its own right.

**Lymphocytic-plasmacytic colitis** may be part of a diffuse IBD in dogs, but is more common in cats as an isolated condition. Diagnosis is based on histopathology, and hypersensitivity is considered a possible cause in many cases. Initial treatment should consist of feeding a hypoallergenic or hydrolysed diet with added omega-3 fatty acids. If there is a poor response then fibre supplementation or a change to a low-residue diet may result in improvement. In rare cases immunosuppression (with prednisolone as for IBD) or sulfasalazine may be required. If animals are still refractory to this treatment increasing immunosuppression or considering the use of loperamide or probiotics may be of benefit. However, if this is necessary I think it is wise to reconsider the original diagnosis. **Eosinophilic colitis** is rare and generally always requires immunosuppression. **Granulomatous colitis** may also occur, but is extremely uncommon and often results in masses that may require surgical excision. In endemic areas elimination of infectious aetiologies is vital prior to starting the strong immunosuppression also required.

Colitis due to *C perfringens* may a relatively common cause of colitis (and may also be associated with other intestinal signs such as vomiting)\(^1\)\(^2\). It is often triggered by stress such as a hospital stay, and there are suggestions it may actually be a nosocomial infection\(^1\)\(^3\). Unfortunately this condition is notoriously difficult to diagnose as *C perfringens* is a normal colonic inhabitant and the use of toxin assay (RPLA), culture and faecal spore numbers has been shown to be unreliable at diagnosing this condition\(^1\)\(^4\). Improved diagnostic sensitivity can be obtained by measuring *C perfringens* enterotoxin by ELISA in combination with PCR detection of enterotoxigenic strains in faeces after heat or alcohol shock treatment\(^1\)\(^5\). It is controversial as to whether there is a necessity for antibiotics as fibre supplementation (to decrease colonic transit time and improve segmental contraction) may be the treatment of choice. Empirical antibiotic usage should be metronidazole or tylosin if required. *C difficile* has also been reported as a possible cause of nosocomial diarrhoea in cats, but its true pathogenesis is unknown\(^1\)\(^6\).

**Pythiosis, protothecosis and histoplasmosis** have all been reported to affect the colon and cause inflammation. The mucosa generally becomes quite nodular and there may be significant abdominal lymphadenopathy. Generally animals are significantly unwell with these conditions and diagnosis is based on demonstration of the organisms within the colonic mucosa as well as positive culture results. Generally these diseases should be considered only in highly endemic areas.
Irritable bowel syndrome (IBS) is commonly diagnosed in people, and may well be a significant cause of large intestinal signs in dogs, but it is virtually impossible to diagnose definitively in companion animals. IBS is a functional disorder causing deranged motility and abnormal pain perception. Clinical signs are often triggered by stress, and the condition has been associated with psychiatric illness in people. The hallmark clinical signs in dogs are mucoid diarrhoea, increased faecal frequency, signs of faecal urgency or abdominal discomfort. IBS can only be diagnosed in dogs by complete exclusion of all other organic intestinal disease that can produce similar clinical signs. Confidence in your diagnosis must be present as individual dogs have varying responses to treatment is variable and clients may become frustrated if they are not led to expect this. Treatment consists of a combination of dietary manipulation (fibre supplementation to improve normal motility), reduction of environmental stressors, motility modifiers such as loperamide and anti-spasmodic agents.

References