Feline Small Cell Lymphosarcoma Versus Inflammatory Bowel Disease: Treatment and Prognosis

Christian Eriksson de Rezende, DVM, MS
Suliman Al-Ghazlat, DVM, DACVIM
BluePearl Veterinary Partners
New York, New York

Abstract: Feline inflammatory bowel disease is a diagnosis of exclusion and a common cause for chronic gastrointestinal signs such as weight loss, variation in appetite, vomiting, diarrhea, and lethargy. Patients with intestinal small cell lymphosarcoma can present with identical clinical signs, and differentiating between these two conditions can be a challenge. A companion article discusses the value of performing immunohistochemistry and polymerase chain reaction testing on intestinal biopsy samples for this purpose.

Treatment for presumptive or diagnosed inflammatory bowel disease (IBD) includes dietary modification, antimicrobials with immunomodulatory properties, and glucocorticoids. For small cell lymphosarcoma (SCLSA), treatment with chlorambucil in conjunction with corticosteroids results in a favorable prognosis compared with other forms of lymphoma.

The Role of Dietary Modification

The use of a highly digestible diet with a novel source of protein is recommended for feline patients with suspected or confirmed IBD and may help by limiting the antigenic stimulation of the intestine's mucosal immune system. The use of a hydrolyzed protein diet can also be effective, although these diets may be less palatable than those using a novel source of protein. In a 2001 study of cats with chronic gastrointestinal (GI) signs attributed to food allergies, IBD, or an unknown cause, approximately 50% of cats fed novel-protein diets showed resolution of clinical signs. Some studies also indicate that cats with food allergies or IBD may have significant improvement in clinical signs (e.g., vomiting, diarrhea) in as few as 4 to 8 days after dietary modification. Other sources argue that a period of 8 to 12 weeks may be needed before concluding that dietary modification is not helpful. It is essential that the pet receive only the trial food during this time (e.g., no treats, flavored drugs, or flavored chew toys should be given).

Novel-protein diets may help ameliorate clinical signs and potentially delay the need for immunosuppressive therapy for cats with IBD; however, the use of additional therapeutic interventions may be inevitable. For example, one study showed that although cats diagnosed with IBD had an improvement of clinical signs after being fed a novel protein diet, corticosteroids were necessary to sustain remission. In other research, a dietary trial alone was unsuccessful in controlling clinical signs in cats. Based on the current state of understanding regarding the pathophysiology of IBD, the use of a novel protein diet is still recommended early in the treatment process, knowing that it may not suffice to control clinical signs. If the patient is inappetent, an appetite stimulant (e.g., mirtazapine 2 to 3 mg/cat PO q72h or cyproheptadine 1 to 2 mg/cat PO q12h) may be necessary. Sometimes, immunosuppressive therapy in combination with glucocorticoids may need to be started before a dietary change can be accomplished.

Fiber-enriched diets have been reported to be useful in patients with colonic IBD, but there is no evidence that they are particularly helpful in patients with IBD affecting the small intestine.

The role of diet in the management of SCLSA should follow the same principles that apply to cats with disease of the GI tract. Dietary factors that should be considered include (1) using highly digestible nutrients (protein digestibility of >87%; fat/carbohydrate digestibility of >90%) and single protein and carbohydrate ingredients if possible and (2) avoiding additives or flavoring that could promote dietary intolerance. Diets containing a high-quality protein source are more easily digested and may result in improved assimilation of nutrients.

The use of omega-3 fatty acids has been described as adjunctive therapy in patients with inflammatory diseases because they may help decrease the concentrations of proinflammatory omega-6 fatty acids.
metabolites (e.g., prostaglandins, interleukin-1). Although studies have evaluated the use of fatty acids in the management of various feline disorders (e.g., atopic dermatitis, renal disease, osteoarthritis), we are not aware of trials assessing efficacy in the management of IBD. Because most commercial feline diets are augmented with omega-3 fatty acids, additional supplementation may not be necessary. Furthermore, omega-3 fatty acids can be unpalatable and cause diarrhea, and their long-term safety has not been determined in cats.

**Probiotics, Prebiotics and Synbiotics**

Probiotics have been defined as live microorganisms that confer a health benefit to the host when administered in adequate amounts. The proposed mechanisms for the benefits of probiotics in human IBD include their ability to prevent gut colonization by pathogenic bacteria, reduce inflammatory cytokine expression, enhance epithelial cell proliferation, inhibit apoptosis, and provide metabolic energy for enterocytes.

Probiotics are being investigated as an adjunctive therapeutic option in various conditions in people, such as allergies in children and recurring urinary tract infections. The use of probiotics has been shown to be efficacious in ameliorating symptoms and maintaining remission in such conditions as ulcerative colitis, pouchitis, and antibiotic-associated diarrhea in humans.

The efficacy of using probiotics for the specific management of feline IBD or SCLSA has not been established; however, reports have shown that probiotics can improve the intestinal environment and the function of the immune system. One study showed that the probiotic strain *Lactobacillus acidophilus* DSM 13241 favorably altered the intestinal microflora in healthy adult cats by increasing and decreasing the populations of beneficial (e.g., *Lactobacillus* spp) and detrimental (*Clostridium* and *Enterococcus* spp) bacteria, respectively. Beneficial immunomodulatory effects were also noted, such as altered lymphocyte and eosinophil populations and an increase in phagocytic activity of granulocytes. Cats receiving probiotics also had a lowered concentration of endotoxins. Another study identified higher percentages of CD4+ lymphocytes in vaccinated pathogen-free kittens treated with *Enterococcus faecium* SF68 when compared with controls. These studies support the potential for probiotics to favorably alter the GI microbiota and immune function of cats.

Once started, it is likely that probiotic therapy may need to be continued indefinitely. If stopped, the number of probiotic organisms may gradually decrease in the feces, possibly voiding some of the therapy’s beneficial effects.

The use of probiotics appears to be safe in animals but may need to be used with caution in severely immunosuppressed or critically ill animals, as human cases of bacteremia from probiotic strains such as *Bacillus subtilis* and *Lactobacillus* spp have been reported.

Choosing which probiotic to use can be challenging, as studies have shown that commercial products have a large variation in quality control. Products may not possess viable organisms or the recommended dose of at least 10^9 organisms. Additionally, products may frequently contain improper labels (e.g., misidentification of bacteria). For these reasons, practitioners should carefully evaluate the label, looking for the names and numbers of all organisms included and their expected viability, both when administered (shelf-life) as well as at the level of the intestine (protection from digestion). Due to a limited number of objective studies evaluating the efficacy of probiotics and prebiotics, we prefer products from reputable companies or those that have been independently clinically evaluated.

Prebiotics are described as “non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one, or a limited number of bacteria in the colon, thus providing host health.” Common prebiotics used in veterinary medicine include chicory (inulin) and beet pulp (incorporated into some commercial diets) and oligosaccharides such as fructo-oligosaccharide. The fermentation of these ingredients may help increase populations of beneficial gut bacteria (e.g., *Lactobacillus* and *Bifidobacterium* spp) that produce butyrate, a short-chain fatty acid that promotes colonic health. At this time, we are not aware of data that convincingly justify the use of prebiotics exclusively as an effective adjunct therapy for the treatment of IBD or SCLSA in cats. A recent meta-analysis evaluated the effects of various prebiotics on digestibility, short-chain fatty acid concentration, and gut bacterial populations in dogs fed various prebiotics (e.g., inulin, fructo-oligosaccharides). This study concluded that the use of prebiotics may increase the number of beneficial bacteria and levels of short-chain fatty acids that are beneficial for gut health.

Products called *synbiotics* contain both prebiotic sugars and probiotic bacteria. In a recent report, cats with chronic diarrhea had an improvement in their fecal scores after being fed a proprietary synbiotic for 21 days.

**Cobalamin**

Cobalamin (vitamin B12) is a required cofactor for normal nucleic acid synthesis and hematopoiesis. Vitamin B12 is absorbed by specific receptors located in the ileum; therefore, pathology in this area of the intestine can result in hypocobalaminemia. Although cobalamin supplementation does not treat the underlying GI disease (e.g., IBD or SCLSA), it appears to improve the clinical state of most affected cats; it may be required for optimal response to immunosuppressive therapy. It should be administered subcutaneously at a dosage of 250 µg once a week for 6 weeks, then every other week for 6 weeks, then monthly if serum cobalamin levels are <300 ng/L. We recommend that practitioners consider rechecking cobalamin levels after four injections to ensure that adequate...
Corticosteroids are the cornerstone of therapy for IBD and SCLSA and have multiple effects on the immune system. They decrease leukocyte chemotaxis and cause lymphocytes and monocytes to redistribute to the lymphatic system. They exert antiinflammatory effects by inducing lipocortin-1, an inhibitor of phospholipase A₂, thereby resulting in a decrease in inflammatory eicosanoids from arachidonic acid. 

**Immunosuppressive Therapy**

Corticosteroids are the cornerstone of therapy for IBD and SCLSA and have multiple effects on the immune system. They decrease leukocyte chemotaxis and cause lymphocytes and monocytes to redistribute to the lymphatic system. They exert antiinflammatory effects by inducing lipocortin-1, an inhibitor of phospholipase A₂, thereby resulting in a decrease in inflammatory eicosanoids from arachidonic acid. 

**Prednisolone**

Prednisolone has a higher bioavailability than prednisone in cats and is therefore the preferred form.  Although several tapering regimens are available for the treatment of IBD, a starting dose of 2 to 4 mg/kg/d (SID or divided BID) is used for 2 to 4 weeks. Once a favorable response is noted, the dose can be continued for an additional 2 to 4 weeks to ensure that the response was not fortuitous. At this time, a slow taper (e.g., dose reduction by 25% to 50% every 2 to 4 weeks) can be started with the goal of achieving the lowest effective dose that keeps the patient free of clinical signs. In some cases, prednisolone can be discontinued and the patient maintained on a novel protein diet and possibly an additional immunomodulatory agent (e.g., metronidazole). If a liquid corticosteroid formulation is used, ensure that it does not contain flavoring because additives of animal origin could interfere with disease remission.

The use of methylprednisolone acetate at 10 mg/kg SC every 2 to 4 weeks has been advocated for patients that do not tolerate oral medication. The frequency of injections can be decreased to every 4 to 8 weeks depending on response to therapy. Long-acting corticosteroids are not generally recommended because the drawbacks include unpredictable bioavailability, predisposition to the patient becoming refractory to the agent, and the development of diabetes mellitus.

**Budesonide**

Budesonide is an orally administered glucocorticoid that was developed for humans with enteritis affecting the ileum and proximal colon (e.g., Crohn disease). Budesonide undergoes extensive first-pass hepatic metabolism in humans (>90% of available drug is converted to less active metabolites) and therefore causes minimal systemic effects. The efficacy of this medication is somewhat less than that of conventional corticosteroids in humans. Studies evaluating the efficacy of budesonide in the treatment of IBD in companion animals are limited; however, there is some anecdotal evidence of success. A study of budesonide in dogs with IBD showed that a dose of 3 mg/m² did significantly suppress the pituitary-adrenal axis, which did not correlate with clinical signs of excess glucocorticoids. To our knowledge, there are no studies evaluating the efficacy of budesonide in cats with IBD; however, empirical dosages of 0.5 to 1.0 mg/cat/d have been suggested.

**Chlorambucil**

Chlorambucil is a nitrogen mustard derivative that acts as an alkylating agent. It cross-links deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), which ultimately interferes with protein synthesis. Some sources recommend reserving this medication for patients with severe or relapsing IBD. This medication is used in conjunction with steroids at a dose of 2 mg PO every other day or every third day in cats weighing >4 kg or <4 kg, respectively. It is important to monitor the patient’s complete blood count (CBC) every 2 to 4 weeks when using this protocol because this agent can cause bone marrow suppression and permanent damage. Particular attention must be paid to declining neutrophil or platelet counts.

**Cyclosporine**

Cyclosporine inhibits T-cell activation and survival by inhibiting the production of cytokines, such as interleukin-2, that are necessary for T-cell viability. It has been used in dogs with IBD that is refractory to steroid therapy. Cyclosporine is used for several dermatologic conditions in dogs and cats (e.g., eosinophilic granuloma complex, pemphigus complex) and, recently, as adjunctive therapy for cats with idiopathic pure red cell aplasia. Anecdotally, cyclosporine has been used to treat IBD in cats with some success at a dose of 5 mg/kg PO once to twice daily. A recent study looking at adverse effects of cyclosporine in cats treated for allergic skin disease (mean and median doses of cyclosporine were 5.25 mg/kg and 5 mg/kg, respectively) reported vomiting, diarrhea, anorexia, and weight loss as the most common adverse events. These effects may lead the clinician to reduce the dose or frequency or be severe enough to require discontinuation of the drug (discontinuation was reported in up to 10% of cats in the study). Other potential complications include hepatopathy, urinary tract infection, gingival hypertrophy, and, at very high doses, recrudescence of dormant toxoplasmosis.

**Azathioprine**

Azathioprine is a synthetic purine analog that interferes with DNA replication and transcription in cells of the humoral and cell-mediated branches of the immune system. This drug is generally not recommended for use in cats due to reported severe bone marrow suppression and idiosyncratic fatal leukopenia and thrombocytopenia. A dose has been published for treatment of severe or refractory IBD (TABLE 1), with improvement seen in 3 to 5 weeks.

**Antimicrobials**

Antibiotics can be used to treat conditions in which alteration of intestinal microbiota is desired (e.g., hepatic encephalopathy, IBD). Metronidazole is effective against anaerobic bacteria and protozoa and appears to affect cell-mediated immunity. The immunomodulatory effect of metronidazole is not clearly understood, but research has shown that it can induce DNA single-strand breaks in lymphocytes, suppress macrophage phagocytic activity by inhibiting macrophage tumor necrosis factor a production, and inhibit leukocyte-endothelial cell adhesion in venules.
Feline Small Cell Lymphosarcoma Versus Inflammatory Bowel Disease: Treatment and Prognosis

Table 1. Drugs Used for the Treatment of Feline Inflammatory Bowel Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism/Indication</th>
<th>Dose</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>Immunosuppression, antiinflammatory</td>
<td>2–4 mg/kg/d for 2–4 wk, tapered by 25% to 50% every 2–4 wk</td>
<td>Polyuria/polydipsia/polyphagia, Cardiomyopathy, Infection, Diabetes mellitus</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Immunosuppression, antiinflammatory; alternative for patients that refuse oral medication</td>
<td>10 mg/kg SC every 2–4 wk, tapered to every 4–8 wk</td>
<td>As with prednisolone</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Severe/refractory cases of IBD and SCLSA</td>
<td>Cats &gt;4 kg: 2 mg PO q48h</td>
<td>Bone marrow suppression, neurotoxicity</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Inhibits T-cell function; for severe/refractory cases of IBD</td>
<td>5 mg/kg PO SID to BID</td>
<td>Vomiting, diarrhea, hepatopathy</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Interferes with DNA synthesis; for severe/refractory cases of IBD</td>
<td>0.3 mg/kg PO q48h</td>
<td>Severe bone marrow suppression</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Anaerobic bacterial activity, antiprotozoal, immunomodulator</td>
<td>10–15 mg/kg PO BID</td>
<td>Neurotoxicity with chronic use</td>
</tr>
<tr>
<td>Tylosin</td>
<td>Antimicrobial, immunomodulator</td>
<td>40–80 mg/kg/d PO BID</td>
<td>Gastrointestinal disturbance</td>
</tr>
<tr>
<td>Cobalamin (B₁₂)</td>
<td>Hypocobalaminemia</td>
<td>250 µg SC/cat/ wk for 6 wk, then every other week for 6 wk, then monthly</td>
<td>Stinging at the injection site with some preparations</td>
</tr>
</tbody>
</table>

*IBD = inflammatory bowel disease, SCLSA = small cell lymphosarcoma

Generally not recommended for use in cats.

may be effective as a sole agent in patients that have mild intestinal inflammation or used in conjunction with a glucocorticoid. In the latter case, the steroid should be tapered to every other day before the dose of metronidazole is reduced and eventually discontinued.³ Neurotoxicity (disorientation, ataxia, seizures, blindness) is the main adverse effect and usually resolves when the drug is discontinued.

Tylosin is a bacteriostatic macrolide that is efficacious against gram-positive and gram-negative cocci and Mycoplasma spp. Escherichia coli and Salmonella spp are usually resistant to this macrolide. This antibiotic may alter the microflora favorably and may have antiinflammatory properties. It has been used more commonly to treat colonic IBD in dogs and cats.¹⁹

Specific Treatment for Small Cell Lymphosarcoma

Due to the indolent nature of SCLSA, treatment generally involves a glucocorticoid (prednisolone) used in conjunction with chlorambucil, which targets slowly dividing lymphocytes.³⁵ A standardized protocol does not exist, particularly with respect to the use of chlorambucil. The prednisolone regimen is typically started at an immunosuppressive dose (e.g., 2 to 3 mg/kg PO q24h or a standard dose of 5 to 10 mg/cat/d), and then reduced to 1 to 2 mg/kg/d once solid remission is achieved (resolution of clinical signs such as vomiting, diarrhea, and weight loss). Some clinicians maintain this daily dose for an extended time (e.g., 6 to 12 months) whereas others taper the corticosteroid regimen to every other day when remission is achieved.

Chlorambucil is used in a continuous dosing regimen (e.g., 2 mg/cat PO q48–72h) or as a bolus (20 mg/m² PO) every 2 to 3 weeks.³² The duration of clinical remission achieved with both regimens is comparable. Further studies are necessary to establish the optimal glucocorticoid/chlorambucil protocol, but administering chlorambucil every 2 to 3 weeks instead of every 2 to 3 days is a clear advantage. Stein et al.³¹ reported treatment delays due to adverse hematologic effects in three of 28 cats receiving chlorambucil as a bolus therapy (two cases of neutropenia and one case of thrombocytopenia). These adverse effects resolved and did not require additional therapy.³²

Permanent bone marrow damage can occur when alkylating agents are used long term; therefore, it is important to monitor cats on chlorambucil for dropping trends in neutrophil and platelet counts.³⁶ The CBC should be monitored during therapy. When using chlorambucil on a bi- or triweekly basis, a CBC is performed weekly for the first few doses of chemotherapy.³⁶ Once it has been established that the dose is safe for the patient, a CBC can be evaluated before each dose (every 2 to 3 weeks) and then
before every other dose (every 4 to 6 weeks).26 The drug should be discontinued if the patient’s segmented neutrophil and platelet counts are at or persistently below 1500 and/or 75,000 cells/mL, respectively.26 Rescue protocols using cyclophosphamide or combined therapy (cyclophosphamide, vincristine, prednisolone) have been used for patients that no longer respond to glucocorticoid–cholorambucil therapy.13

Prognosis
Incorporating immunohistochemistry (IHC) early in the diagnostic approach in conjunction with clonality evaluation in selected cases can significantly improve the ability to differentiate IBD from SCLSA and consequently establish a more accurate prognosis. All cases with a morphologic diagnosis of lymphoma or suspected lymphoma should be further evaluated by IHC. The presence of a monomorphic population of B or T lymphocytes supports the diagnosis of lymphoma. In cases in which a definitive diagnosis cannot be made, the clinician should request polymerase chain reaction testing for B and/or T cell clonality. If a clonal population is not present, then inflammation should be considered the most likely underlying disease process. Furthermore, if biopsies yield a morphologic diagnosis of IBD but the patient does not respond to conventional therapy, the clinician should consider repeating the biopsy or having the original samples reviewed in conjunction with IHC and PCR. The clinician must consider the quality and type of biopsy when interpreting results (e.g., full-thickness biopsies may reveal lymphocytic infiltration beyond the mucosa, which could be missed with endoscopic biopsy samples. In his recent study, Dr. Kiupel stresses that it is important to maintain a systematic approach to biopsy samples (histopathology followed by IHC and PCR) to increase the chances of achieving a correct diagnosis and selecting the best treatment.33

Feline IBD can be well managed with a combination of dietary modification and immunosuppression; however, the client must be informed that cure is unlikely and the objective of treatment is to minimize frequency and intensity of clinical signs. In one study, 79% of cats treated with a change in diet and prednisone responded favorably to therapy.14 A more guarded prognosis may need to be discussed with clients if the patient is severely debilitated and or has severe histologic GI lesions, eosinophilic enteritis, or hypereosinophilic syndrome.

In cases of refractory IBD, the clinician must determine if the client is being compliant with therapy (e.g., has the client altered the diet or decreased/discontinued drug therapy; is the client having difficulties medicating the animal). It is also possible that the patient has a more severe form of IBD (e.g., eosinophilic enteritis, hypereosinophilic syndrome). Alternatively, the patient may have comorbidities that were missed or have developed since the start of treatment (e.g., pancreatitis, cholangitis). Ultimately, the clinician must question whether the diagnosis of IBD is correct and whether the patient has SCLSA.34 In such cases, the clinician should consider collecting GI biopsy samples for histologic assessment followed by immunophenotyping and PCR for T-cell clonality if necessary, as discussed above.33

The prognosis for cats with SCLSA affecting the GI system or other organs is also favorable, with one study by Kiselow et al reporting a 92% response rate for a median of >2.5 years (TABLE 2).36 This study indicated that the median response duration time was longer (29 months) for cats that had a complete response to treatment compared with partial responders (14 months). Although this study did not find an association between response to treatment and overall survival, other studies showed longer survival times for cats that achieved complete remission.36–38 Kiselow et al identified a large percentage of cats that were hypocobalaminemic (78%), which was associated with a shorter duration of remission but not overall survival time. Patients that experience relapse may be rescued with therapy consisting of cyclophosphamide and glucocorticoids, resulting in a 100% response rate in one study.32

<table>
<thead>
<tr>
<th>Table 2. Summary of Treatment Protocols and Response Rates for Cats With Small Cell Lymphosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting Steroid Dose</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Prednisone 5–10 mg PO q24h</td>
</tr>
<tr>
<td>Prednisone 3 mg/kg PO q24h</td>
</tr>
<tr>
<td>Prednisone/prednisolone 2 mg/kg PO q24h</td>
</tr>
</tbody>
</table>

CR = complete remission, PR = partial remission

1 In this study of 17 cats, 12 cats were treated with a prednisone/cholorambucil protocol, two cats were treated with a multiagent chemotherapy protocol (modified Madison-Wisconsin), and three cats were treated with a combination of prednisone/cholorambucil and the chemotherapy protocol.
2 This remission reflects cats treated with prednisone/cholorambucil dual therapy, the multiagent chemotherapy protocol, or both.
3 Median survival time for patients that achieved complete remission.
4 Steroid therapy varied according to clinician preference. Sixty percent of cases received prednisone or prednisolone at 2 mg/kg PO once a day for 7 days. All cats were tapered to 1 mg/kg PO every other day until relapse.

References
3. Mandigers PJ, Biourge V, German AJ. Efficacy of a commercial hydrolysate diet in eight cats suffering from inflammatory bowel disease or adverse reaction to food. Tijdschr Diegengeskd 2010;135:668-672.
7. Caney S. Weight loss in the elderly cat. Appetite is fine and everything looks normal...
Vet learn.com | 2013 | Compendium: Continuing Education for Veterinarians™

Feline Small Cell Lymphosarcoma Versus Inflammatory Bowel Disease: Treatment and Prognosis

---

1. A novel protein diet may help reduce gastrointestinal symptoms in patients with inflammatory bowel disease (IBD) by
   a. decreasing the antigenic load to which the immune system in the disrupted intestinal barrier is exposed.
   b. providing probiotics that help reduce the population of harmful bacteria in the gut.
   c. providing prebiotics that help reduce the population of harmful bacteria in the gut.
   d. all of the above

2. Which is/are a proposed mechanism(s) for the benefits of probiotics in human IBD patients?
   a. helping to prevent gut colonization by pathogenic bacteria
   b. reducing expression of inflammatory cytokines
   c. helping to provide metabolic energy for enterocytes
   d. all of the above

3. What are prebiotics?
   a. concentrated cultures of beneficial bacteria
   b. nondigestible food ingredients (e.g., oligosaccharides) that are fermented by bacteria in the colon, yielding a growth advantage to beneficial gut bacteria and by-products of fermentation that may help local enterocytes
   c. proteins that bind to bacterial lipopolysaccharide, preventing activation of the immune system
   d. oligosaccharides that have a bactericidal effect against specific bacteria in the gut (e.g., Clostridium spp)

4. The use of prednisolone over prednisone is preferred in cats because prednisolone
   a. has a higher bioavailability than prednisone in cats.
   b. has more activity in the intestine with fewer systemic adverse effects than prednisone.
   c. is less likely than prednisone to induce diabetes mellitus in cats.
   d. all of the above

5. What is the diagnostic value of assessing serum cobalamin levels in feline patients with suspected IBD or SCLSA?
   a. Establishing that a patient has a low serum cobalamin level helps localize disease to the jejunum.
   b. A low serum cobalamin level helps differentiate between IBD and SCLSA.
   c. A low serum cobalamin level supports a diagnosis of ileal disease.
   d. Elevated cobalamin levels indicate that the ileum is normal and does not need to be biopsied

6. What is/are a possible long-term adverse effect(s) of metronidazole use in cats?
   a. skin disorders (e.g., alopecia, pemphigus-like lesions)
   b. arrhythmias and syncopal events in patients with occult heart disease (e.g., hypertrophic cardiomyopathy)
   c. renal insufficiency
   d. reversible neurologic signs (e.g., altered mentation, ataxia, seizures)

7. Which of the following immunosuppressive drugs should particularly be used with great caution in cats due to its potential to cause idiosyncratic fatal leukopenia and thrombocytopenia?
   a. azathioprine
   b. cyclosporine
   c. chlorambucil
   d. cyclophosphamide

8. If a patient suspected of having IBD based on clinical signs and imaging studies (e.g., thickened intestine on ultrasonography) does not respond to conventional therapy (e.g., elimination diet, glucocorticoids, antimicrobials), the clinician should
   a. confirm that the client is following the treatment recommendations.
   b. question the presumptive diagnosis of IBD.
   c. consider testing the patient for other diseases that may cause signs similar to those of IBD
   d. all of the above

9. How can complete blood counts help guide the use of chlorambucil for the treatment of feline gastrointestinal disease?
   a. The practitioner may have to temporarily or permanently discontinue it if the patient's neutrophil and/or platelet count goes below reference ranges.
   b. The drug must be stopped if the patient develops a mild nonregenerative anemia.
   c. Chlorambucil can cause a leukemoid response and should be discontinued if this occurs.
   d. This agent can cause an immune mediated anemia and should be stopped if agglutination of erythrocytes is observed.

10. The prognosis for feline patients with small cell lymphosarcoma affecting the GI system or other organs is
    a. similar to that for feline patients with large cell lymphosarcoma.
    b. superior to that for feline patients with IBD, with appropriate therapy.
    c. favorable, with a survival time >1 to 2 years.
    d. good only for patients that go into complete remission after starting glucocorticoid/chlorambucil therapy.