Symposium Proceedings

Critical GI Updates

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PURINA VETERINARY DIETS
Protein-Losing Enteropathy: The Beginning of the End?
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Much more common in dogs than cats, protein-losing enteropathy often causes bouts of diarrhea but can also occur without this obvious sign.

Rational Approach to Chronic Diarrhea in Cats
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Chronic diarrhea in cats warrants a step-by-step approach to obtain a diagnosis and formulate an optimal therapeutic plan.

The Vomiting Cat: You Can Make It Stop!
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Vomiting can be caused by GI disease or extra-GI conditions that trigger peripheral or central neural pathways.

Skinny Old Cats
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A decline in body weight often occurs in senior cats without evidence of any underlying disease.
Intestinal protein loss is a sign of failure of digestive function that may result from severe acute or chronic inflammatory lesions or disruption of chyle absorption and intestinal lymph flow. While the exact mechanisms leading to intestinal protein loss have not been elucidated in the dog, three basic mechanisms defined for humans with protein-losing enteropathy (PLE) likely apply to canine PLE. Protein loss may result from:

1. Erosive or ulcerative mucosal lesions causing secondary exudation of proteins
2. Lymphatic dysfunction causing leakage of protein-rich lymph into the intestinal lumen
3. Mucosal changes disturbing the “mucosal barrier,” causing abnormal permeability and protein leakage into the lumen.
In some dogs, significant intestinal protein loss may occur without obvious diarrheic episodes.

This article focuses on chronic intestinal disorders associated with intestinal protein loss in dogs. PLE is much less prevalent in cats. In dogs, it is frequently associated with severe chronic idiopathic inflammatory enteropathies, such as inflammatory bowel disease (IBD), or with idiopathic intestinal lymphangiectasia (IL) in specific breeds.

**Diagnostic Approach**

Dogs with PLE often present with clinical signs of chronic intermittent small intestinal diarrhea with possible vomiting. In severe cases, dysorexia/anorexia and malnutrition with evidence of malabsorption and weight loss may be observed. However, significant intestinal protein loss and hypoalbuminemia may also occur without obvious diarrheic episodes. In some dogs, hypoalbuminemia may be detected incidentally during regular health screens. In the presence of severe hypoalbuminemia (serum albumin <2 mg/dL or 20 g/L, often ≤1.5 mg/dL or 15 g/L), the main owner complaint may relate to signs suggestive of significantly decreased oncotic pressure (eg, cavitary effusion, subcutaneous edema).

The first diagnostic challenge involves establishing the origin of the protein loss. To this effect, a minimal diagnostic database should be conducted (CBC, serum biochemistry panel, urinalysis). Renal protein loss (urinalysis, urine protein:creatinine ratio) as well as liver dysfunction (postprandial serum bile acids) must be ruled out. In addition, third spacing of serum proteins (eg, vasculitis) should be considered. Generally, PLE is associated with panhypoproteinemia resulting from nonselective protein loss. Hypoalbuminemia with normal or increased globulin concentration is suggestive of protein-losing nephropathy (PLN) or possibly liver dysfunction. While these rules of thumb are useful in practice, they should not be blindly relied on, as many exceptions can occur. For instance, a dog with significant systemic inflammation (eg, histoplasmosis) may present with hypoalbuminemia and hyperglobulinemia. Other common abnormalities of dogs with PLE include hypocholesterolemia, hypocalcemia (total and ionized), hypomagnesemia, and lymphopenia.

Once the gastrointestinal (GI) tract has been confirmed as the site of protein loss, further workup should include abdominal ultrasonography with a focus on the intestinal wall, in particular thickness and layering. The intestinal wall consists of five distinct layers that are normally visible on ultrasonograms. Hyperechogenic mucosal striations are frequently observed in dogs with PLE (Figure 1) and appear to be quite specific. It has been postulated that they may represent dilated lacteals, although they may also be attributable to dilated crypts often seen in PLE or to other structural changes. Striations should not be confused with hyperechogenic mucosal speckles that are only a nonspecific indicator of inflammation.

The final diagnosis of PLE relies solely on histopathologic analysis of intestinal biopsy specimens collected during endoscopy or exploratory laparotomy. Dogs with severe hy-
Dogs with severe hypoalbuminemia are poor anesthetic candidates, and it is sometimes preferable to avoid taking excessive risks and postpone these procedures. In addition, many dogs with PLE have bicavitory effusion, and thoracic radiography is recommended as a screening tool to confirm the presence of thoracic effusion, which may represent an additional anesthetic risk. Synthetic (ie, hydroxyethylated starches) and natural colloids (eg, plasma, human or canine albumin concentrates) are useful in acutely increasing oncotic pressure in critical cases. Despite the risk for anaphylactic reaction or other complications, slow transfusion of 5% human albumin (2 mL/kg/hr for 10 hr/day; 20 mL/kg total daily volume) has been successful for partial restoration of serum albumin concentration before general anesthesia.3

The decision regarding the preferred biopsy collection technique depends on a variety of factors, such as availability of the equipment and surgical or endoscopic skills of the veterinarian. Advantages of surgical exploration include the possibility of sampling several sites along the small intestine and obtaining full-thickness specimens. Surgical collection of intestinal specimens was not shown to be more risky in hypoalbuminemic patients,4 although a cautious approach is recommended (use of serosal patching).

Endoscopy allows relatively noninvasive collection of specimens limited to the mucosa, but good endoscopic skills are required. Visualization of the mucosa is an advantage, allowing targeted sampling of mucosal lesions (Figure 2). Traditionally, only the duodenum has been examined. Recent studies convincingly demonstrate that collecting both duodenal and ileal biopsy specimens is essential, as lesion distribution may be irregular and severe ileal lesions may occur in a dog with only mild (or absent) duodenal lesions.5 This added procedure may prolong anesthesia time: a colonoscopy is required to intubate the ileum or, if proceeding without aid of an endoscope, a forceps must be passed through the ileocolic junction to obtain mucosal biopsies blindly. However, the improved diagnostic yield often outweighs the inconvenience of a prolonged procedure.

**Differential Diagnosis**

Diseases frequently associated with PLE include IL,1,6 IBD,1,7 and chronic enteropathies characterized by significant mucosal architectural changes, such as dilation of small intestine.

![Figure 2A. Appearance of the duodenal mucosa at the time of endoscopy in a 4-year-old spayed Yorkshire terrier with PLE resulting from primary intestinal lymphangiectasia. The numerous white spots are thought to represent enlarged villi secondary to lacteal dilation.](image)

![Figure 2B. Endoscopic photograph of the duodenum in a 3-year-old mixed breed dog with IBD and severe protein-losing enteropathy. The mucosa has a very irregular, granular appearance. The histopathologic diagnosis was moderate to severe neutrophilic and lymphoplasmacytic enteritis with numerous crypt abscesses.](image)
intestinal crypts. Moreover, alimentary lymphoma and intestinal histoplasmosis may also cause PLE.

Intestinal Lymphangiectasia
The following breeds have been shown to be prone to primary IL: Yorkshire terriers, Chinese shar-pees, Maltese terriers, Norwegian lundehunds, and Rottweilers (in Europe). The pathogenesis of primary IL is poorly understood. It results from obstruction to the flow of lymph in the intestinal wall, which could conceivably be associated with abnormal intestinal lymphangiogenesis. However, acquired obstruction to normal lymph flow apparently is a more common occurrence, in the form of granulomas impinging on intestinal lymphatics with associated lymph leakage and/or intestinal lymphangitis. Secondary IL is commonly associated with significant intestinal mucosal inflammation (e.g., IBD, fungal diseases) and neoplasia ( alimentary lymphoma). Histopathologic mucosal changes include dilated lacteals in the mucosa (Figure 3) and deep-seated perilymphatic granulomas that can be seen in full-thickness biopsies. Lacteals are essential for fat absorption and their obstruction leads to severe dilation and tearing. Damaged lacteals empty their lipid- and protein-rich content into the intestinal lumen.

Inflammatary Bowel Disease
A detailed review of IBD is beyond the scope of this article; however, the term has been described as “a group of chronic enteropathies characterized by persistent or recurrent gastrointestinal (GI) signs and inflammation of the GI tract.” The inflammatory process in the GI mucosa may lead to protein loss by both preventing absorption of nutrients and compromising the integrity of the intestinal mucosal barrier, leading to exudation of proteins into the intestinal lumen.

PLE of soft-coated wheaten terriers is a specific form of IBD affecting this breed worldwide. In approximately 50% of these dogs, PLE and PLN occur concurrently. Mucosal lesions can be severe and include inflammatory infiltration, dilated lacteals, and deep-seated intestinal lymphangitis. While the pathogenesis is still poorly understood, a hypersensitivity component has been documented: clinical episodes can be triggered by specific proteins.
Crypt Disease
Since the first report of six dogs with crypt lesions by Willard and colleagues 12 years ago,8 crypt dilation and necrosis have been frequently associated with PLE.12,15 Crypt dilation, a mucosal architectural change, is observed relatively frequently in dogs with IBD and IL (Figure 4). In some cases, crypt dilation and abscesses may be the only detectable mucosal lesions in dogs with PLE. In a recent study of 58 dogs with chronic enteropathies,16 the author’s group showed that dogs with histologically documented small intestinal crypt abscesses are more likely than dogs with no such lesions to experience significant hypoalbuminemia from PLE, to show ultrasonographic changes of their intestinal mucosa, and to experience more severe clinical signs.

Therapy
The two main components of treatment in dogs with PLE are dietary modification and management of the inflammatory process.

Diet
Because dogs with PLE are in a catabolic state, adequate nutrition is essential. There are currently no published studies critically evaluating nutritional aspects of canine PLE; however, a large body of clinical experience is available.

Primary idiopathic IL
In dogs with primary idiopathic IL, dietary modification centers on feeding a highly digestible diet with low to very low fat content (10%–15% on a dry-matter basis) to prevent further dilation and rupture of lacteals. In addition, the diet should contain highly bioavailable dietary proteins and be low in crude fiber. While drug therapy may be administered for a few months (see below) and then discontinued in some cases, dietary therapy should probably be maintained for the length of the dog’s life.

PLE associated with underlying IBD
In dogs with PLE associated with underlying IBD, many veterinary gastroenterologists report good success with exclusive feeding of a diet consisting of hydrolyzed proteins. Novel protein diets are an alternative approach.

Acceptance of the diet is a critical issue, particularly in the most severely affected animals, which may be anorectic. For each patient, the veterinary team needs to identify the most palatable diet. Initially, it might be more important to feed a less optimal diet that the dog is interested in eating, then progressively transition to a more desirable diet.

Elemental diets contain only free amino acids, including glutamine with carbohydrates and reduced fat (eg, Vivonex TEN [Nestlé], Peptamen HN [Nestlé]) and provide the necessary nutrients with minimal risk for disease flare. In dogs with severe IBD and PLE, these diets may be administered by feeding tube. Attention should be paid to osmolality of the diet. Elemental diets are very expensive, and there are no published studies documenting their benefits in dogs with IBD.

Management of Inflammation
In dogs with primary IL, antiinflammatory glucocorticoid therapy (eg, prednisone at 1 mg/kg/day) is useful and often required for proper management. Its main desired effect is to decrease inflammation associated with lipogranulomas secondary to chyle leakage and, therefore, help restore adequate flow of intestinal lymphatics. Some dogs can be slowly weaned off antiinflammatory treatment over 2 to 3 months or longer.

Immunosuppressive Therapy
Immunosuppression is the basis for treatment of severe IBD with PLE. As a side note, it is important to remember that chronic immunosuppression may make animals more susceptible to developing severe infections after contact with pathogens or opportunistic microorganisms.

The first approach consists of administering prednisone or prednisolone using the fol-
lowing protocol: start with 2 mg/kg q12h for 3 to 5 days; then switch to 2 mg/kg q24h until the dog’s condition has significantly improved and appears stable. Subsequently the dose can be decreased in 2-week steps with 1 mg/kg q24h, then 1 mg/kg q48h, and so on. However, side effects of steroid therapy may compromise owner compliance.

**Budesonide** has gained popularity in the treatment of canine IBD. In humans, this corticosteroid is known to be locally efficient and undergo high first-pass hepatic metabolism. Therefore, systemic complications of steroid treatment are less likely. In dogs, the drug significantly influences the pituitary–adrenal axis. To date, budesonide use in dogs or cats with IBD has not been evaluated critically; only anecdotal reports are available. Furthermore, there are no data on the pharmacokinetics of the orally administered drug in pets. The recommended doses are 0.5 to 3 mg/dog q24h, depending on the dog’s size. The drug needs to be reformulated by a compounding pharmacist for use in small dogs. Concurrent use with other glucocorticoids is not recommended.

**Azathioprine**, a thiopurine drug, may be used in dogs with steroid-refractory IBD and those that relapse when prednisone treatment is tapered. This drug may also be combined with prednisone in initial treatment of severe cases of IBD. Azathioprine is generally well tolerated, but side effects include bone marrow suppression, hepatotoxicity, and pancreatitis. Regular monitoring of the CBC and serum biochemistry panel is advisable during the first weeks to months of treatment. The initial dose is 2 mg/kg q24h for 3 weeks, then 1 to 2 mg/kg q48h. Up to 3 weeks of treatment may be necessary for the drug to reach maximal effect.

**Chlorambucil** is an alkylating agent mostly used in conjunction with prednisolone in cats with low-grade alimentary lymphoma or refractory IBD. A recent study from the UK compared the survival of 27 dogs with chronic enteropathies and PLE with serum albumin concentration less than 1.8 g/dL or 18 g/L receiving a prednisolone and chlorambucil combination (n = 14) versus that of dogs treated with prednisolone and azathioprine (n = 13). At recheck, dogs receiving chlorambucil and prednisolone had gained more weight and their serum albumin concentration was significantly higher than in the other group. Also, survival was greatly improved using the chlorambucil combination. The recommended initial canine dose of chlorambucil is approximately 4 mg/m² q24–48h. The drug is available in 2-mg tablets, so it needs to be appropriately reformulated or compounded for small dogs. Side effects of chlorambucil are rare and include bone marrow suppression. A CBC to monitor for neutropenia should be conducted after 1 and 3 weeks of treatment and repeated q2–3mo or if the dog’s condition deteriorates.

**Cyclosporine** is an inhibitor of T-cell function. In a 2006 study, the pharmacokinetics of cyclosporine in dogs with IBD were not found to differ significantly from those of normal dogs. Fourteen dogs with steroid-refractory IBD were enrolled, and eight dogs (57%) went into complete remission within 4 weeks of treatment (5 mg/kg q24h PO). In addition, three dogs experienced partial remission, while two did not respond and were euthanized. One dog relapsed after 14 weeks of initially successful treatment. Transient adverse effects, including vomiting or loss of appetite in four dogs and hair coat changes and gingival hyperplasia in one dog, were seen during the first 2 weeks of treatment. Most side effects responded to temporary discontinuation, followed by dose reduction. Cyclosporine treatment was discontinued in 8 of the 11 responders, which subsequently remained free of clinical signs. The owners of the remaining three dogs elected to continue treatment for
several additional months, and the dogs remained apparently healthy.\textsuperscript{19}

Monitoring of whole blood or plasma concentration of cyclosporine is controversial. In dogs that regularly vomit 1 to 2 hours after oral administration, it is possible that serum cyclosporine concentration peak reaches toxic levels and splitting the daily dose may be beneficial.

\textit{Other immunosuppressive drugs}, such as mycophenolate mofetil, methotrexate, and leflunomide, have been used to treat immune-mediated or autoimmune diseases in dogs. Because of lack of data and possible gastrointestinal side effects, their use for treatment of IBD in dogs cannot be recommended at this time.

**Complications**

**Hypocobalaminemia**

Low serum cobalamin (vitamin B12) concentrations are commonly found in dogs with PLE, especially in the presence of underlying IBD. Deficiency in vitamin B12 has negative effects on intermediary metabolism and may delay proper healing of intestinal inflammation.

Hypocobalaminemic dogs are initially treated with weekly injections of vitamin B12 (250–1500 µg/dog SC) for 6 weeks. If the treatment is successful, the interval between injections may be increased to 2 weeks and continued for another 6 weeks.

**Hypercoagulability**

Recent studies using thromboelastography have revealed the high prevalence of hypercoagulability in dogs with PLE,\textsuperscript{20} which significantly increases the risk for potentially fatal thromboembolic events. The problem may be compounded by the prothrombotic effects of glucocorticoids, which are often used for treatment. Interestingly, hypercoagulability does not appear to resolve after successful treatment of PLE,\textsuperscript{20} raising questions as to the pathogenesis of this complication. In dogs with documented hypercoagulability, administration of low doses of aspirin (0.5–1 mg/kg q24h) and/or clopidogrel (1–5 mg/kg q24h) should be considered to prevent thrombosis. However, currently no study confirms the beneficial effect of such a therapeutic regimen.

**Hypocalcemia**

A significant decrease of total calcium is expected in dogs with moderate to severe hypalbuminemia, as 50% of total calcium is bound to albumin. However, ionized calcium may also be abnormally low in dogs with PLE.\textsuperscript{21,22} Low serum ionized calcium concentration occurred in association with low 25-hydroxyvitamin D and increased levels of parathyroid hormone in a recent series of dogs with PLE.\textsuperscript{22} The study authors postulated that hypovitaminosis D resulted from intestinal loss rather than malabsorption, as a control group of dogs with IBD without PLE had normal 25-hydroxyvitamin D levels and serum 25-hydroxyvitamin D concentration correlated with serum albumin concentrations.\textsuperscript{22} Correction of moderate to severe hypocalcemia with parenteral administration of 10% calcium gluconate and vitamin D is advisable to prevent onset of clinical signs. The calcium gluconate can be administered as follows: 1 mL/kg slowly IV over at least 15 to 30 minutes or in 1:1 dilution with saline SC to a maximum daily amount of 9 mL/kg, given in 3 to 4 doses. Concurrent hypomagnesemia may compromise the success of treatment and should be corrected.\textsuperscript{21}

**Prognosis**

In two European studies encompassing a total of 150 dogs with chronic enteropathies, hypalbuminemia (serum albumin <2 g/dL or 20 g/L) was associated with a less favorable outcome.\textsuperscript{23,24} This finding was confirmed in a preliminary report from a recent North American study, although outcome did not appear to be correlated to severity of hypalbuminemia.\textsuperscript{25}
Idiopathic Intestinal Lymphangiectasia

Preliminary reports from a few studies show high mortality among Yorkshire terriers with IL (50%-60%). However, results from the UK revealed that the presence of dilated lacteals was associated with a better outcome in a group of 27 dogs with PLE. In the author’s practice, a significant proportion of Yorkshire terriers with IL respond well to strict diet alone or with antiinflammatory doses of glucocorticoids. The proportion of refractory cases seems to vary according to geographic location. Unfortunately, to this day, no known parameters allow early segregation of dogs likely to be refractory to diet and steroid treatment. This strategy would be useful to initiate early aggressive treatment in difficult cases.

Crypt Disease

In a series of 58 dogs with chronic enteropathies, the author’s group found that the presence of crypt abscesses in the small intestine was associated with significantly shorter survival.

References

Diarrhea is generally regarded as the most consistent clinical sign of intestinal disease in the cat and one of the most frustrating maladies for many veterinarians to diagnose and manage. Incomplete resolution of the problem can result in frustration and dissatisfaction for the owner and potential suffering for the animal. Antibiotics are commonly administered injudiciously to diarrheic animals, with resolution of clinical signs often wrongly attributed to eradication of a putative infectious pathogen.

Chronic diarrhea is persistent or relapsing over a period of 3 to 4 weeks or longer. In contrast to acute diarrhea that is often self-limiting and does not typically require a comprehensive workup, chronic cases warrant a step-by-step approach to obtain a diagnosis and formulate an optimal therapeutic plan. The history and physical examination are paramount for determining whether the diarrhea is caused by primary disease of the gastrointestinal (GI) tract or secondary to extraintestinal diseases such as hyperthyroidism (Table 1).
Animals manifesting clinical signs of colitis often have concurrent disease in the small bowel and vice versa.

### TABLE 1
Common Differentials for Chronic Diarrhea in the Cat

<table>
<thead>
<tr>
<th>Primary GI Disorders</th>
<th>Extra-GI Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease (SI, LI)</td>
<td>Hyperthyroidism (SI)</td>
</tr>
<tr>
<td>Infiltrative neoplasia (SI, LI): lymphoma, mast cell tumor</td>
<td>Pancreatitis (SI, LI)</td>
</tr>
<tr>
<td>Endoparasites (SI, LI): helminths, Giardia, Tritrichomonas foetus, Isospora, Cryptosporidium</td>
<td>Exocrine pancreatic insufficiency (SI)</td>
</tr>
<tr>
<td>Food-responsive enteropathy (SI, LI)</td>
<td>Pancreatic neoplasia (SI)</td>
</tr>
<tr>
<td>Bacterial, viral, and fungal enteropathogens (SI, LI): Campylobacter, Salmonella, and Histoplasma spp; FeLV or FIV-associated enteritis</td>
<td>Liver failure (SI): uncommon cause of diarrhea</td>
</tr>
<tr>
<td>Intestinal obstruction secondary to strictures, intussusception (SI, LI)</td>
<td>Uremia (SI)</td>
</tr>
<tr>
<td>Ileus (SI)</td>
<td></td>
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SI = small intestine, LI = large intestine

### DIAGNOSTIC APPROACH

**History**

The history can indicate location, severity, and probable cause of the disease process. The categorization of diarrhea into small bowel or large bowel in origin is helpful for prioritizing certain differentials (Table 1) and for determining which segment of bowel to biopsy if indicated. Caution is warranted in this oversimplistic anatomic differentiation of the affected segment of bowel because animals manifesting clinical signs of colitis often have concurrent disease in the small bowel and vice versa. In addition, most veterinary gastroenterologists prefer to biopsy the small and large intestine when feasible to maximize diagnostic yield of the procedure.

A careful history should also indicate the presence of extraintestinal disease as the underlying cause of diarrhea and may identify important predisposing factors such as diet, environmental influences, or exposure to parasites, infectious agents, drugs, or toxins. Failure to consider the role of the diet or dietary supplements in precipitating or alleviating the GI disorder can result in delayed diagnosis or improper dietary recommendations. The history should also focus on the duration of the diarrhea, the appearance of the feces (color, volume, mucus, presence of fresh blood), worming and vaccination history, defecation frequency, aggravating or alleviating factors, and defecation urgency.

**Physical Examination**

The physical examination should emphasize detection of fever, cachexia, dehydration, weakness or lethargy, pallor (blood loss anemia), and effusions or edema (hypalbuminemia). Careful palpation of the cervical region for a thyroid slip is warranted, particularly in cats older than 5 years of age. Intestinal loops should be carefully palpated for masses (eg, large-cell lymphoma, mast cell tumors, GI stromal tumors [GIST]), leiomyosarcoma, granulomas associated with feline infectious peritonitis, foreign bodies), diffuse intestinal thickening (inflammatory bowel disease [IBD] or small cell lymphoma), distention, pain, or associated lymphadenomegaly. The liver should be carefully palpated, as hepatomegaly could reflect hepatic lipidosis, lymphoma, mast cell tumor, or another neoplastic process.

A rectal examination is not typically performed in awake cats but can be done using the little finger if the cat is sedated or anesthetized.

**Fecal Examination**

The following guidelines can help veterinarians maximize diagnostic yield of fecal examinations.

1. **Examine fresh fecal specimens**

Fecal flotation should be performed on fresh fecal specimens (<2 hours old) when possible to ensure that eggs, oocysts, and larvae do not develop beyond their diagnostic stages. Fresh fecal specimens can be refrigerated for up to 96 hours to facilitate preservation of eggs, oocysts, and cysts if immediate examination...
cannot be performed. Fecal specimens can be placed in 10% buffered formalin if more than 1 hour will elapse before analysis or refrigeration. Specimens fixed in formalin are suitable for concentration techniques, acid-fast stains, and immunoassays.

2. Perform centrifugation fecal flotation

Fecal flotation is excellent for recovering common nematode ova, oocysts of coccidia (including Cryptosporidium spp), and Giardia cysts. The most important considerations for fecal flotation include:

1. Choice of flotation solution and its specific gravity
2. Selection of standing versus centrifugal flotation
3. Transfer of the meniscus.

Three solutions in common use are zinc sulfate, Sheather’s sugar, and sodium nitrate (specific gravity, 1.18–1.2, 1.27, and 1.2, respectively). Sodium chloride is an unacceptable flotation medium even if used with centrifugation, as it will not float Trichuris ova. Aqueous zinc sulfate (ZnSO₄) with a specific gravity of 1.18 to 1.2 has been widely recommended: it will float cysts, oocysts, and most helminth eggs with a minimum of distortion and fecal debris.

Flotation with centrifugation is considerably more efficient than standing (gravitational) flotation (eg, Ovassay [Pfizer], Fecalyzer [EVSCO], Ovatector [Webster]), which may not detect parasite stages shed in low numbers. Quantitative comparisons have shown that egg counts achieved using flotation with centrifugation are 2.4 to 6.0 times higher compared with standing flotation. Once the flotation procedure is complete, the meniscus containing the parasite stages should be transferred by cover glass to a clean glass slide after approximately 10 minutes. The meniscus should be transferred by lifting the coverslip directly off the fluid surface and placing it on a slide. Meniscus transfer using a loop or glass rod is the poorest method; it reduces the sensitivity of any flotation technique because only a small portion of the parasites recovered are actually transferred to the slide.

3. Understand benefits and limitations of immunoassays

Giardia infection in adult cats and dogs is often subclinical or associated with early transient softening of the stool; however, acute diarrhea tends to occur in kittens and puppies shortly after infection. Diagnosis of Giardia infection traditionally has depended on microscopic identification of trophozoites or cysts in feces from affected animals. However, cysts may be shed intermittently and are very delicate, so this process can be difficult. Many artifacts (eg, grass pollen, yeast) mimic to varying degrees the morphology of Giardia cysts, so care must be exercised in differentiating these from Giardia. In a recent study, microscopy following fecal flotation identified only half of infected dogs and produced false-positive results in up to 25% of uninfected patients.

Direct immunofluorescence (DIF): DIF is often the standard against which other tests for Giardia are measured. The Meriluor Cryptosporidium/Giardia assay (Meridian Diagnostics) uses a fluorescein isothiocyanate (FITC)-labeled monoclonal antibody directed against cell-wall antigen of Giardia cysts (not trophozoites) in the feces. A positive result is indicated by apple green fluorescence of the cyst. Morphologic identification is necessary for this technique. Specimens sent to commercial laboratories for DIF should be fixed in 10% buffered formalin. Meridian’s DIF combines the Giardia-specific and Cryptosporidium parvum-specific antibodies in one reagent, so specimens can be examined for both parasites with a single test (Figure 1).
Enzyme immunoassay (EIA): Many veterinarians and reference laboratories have resorted to using ELISAs that rely on detection of *Giardia* cyst-wall protein 1 (GCWP 1). The ELISAs are advantageous because they are generally easy to perform and interpret. In addition, they do not rely on morphologic identification of cysts or oocysts via microscopy, thus saving technician time and potentially avoiding false-negative interpretations. The EIA tests can also detect GCWP 1 in the absence of detectable cysts. The SNAP *Giardia* Test (IDEXX Laboratories) is a rapid in-house enzyme immunoassay that can be performed on fresh or previously frozen feces or samples stored at 2°C to 7°C for up to 7 days. As the first commercially available EIA designed for cats and dogs, the SNAP *Giardia* Test has the added advantages of simplicity, rapid availability of results (8 minutes), and low cost. Despite the impressive performance characteristics of this rapid assay, it should not be used as a test to assess response to therapy in animals that have completed a recent course of anthelmintics because animals can remain positive for *Giardia* spp on the SNAP ELISA for several weeks following successful eradication of the parasite.

### 4. Recognize limitations and benefits of fecal PCR

Commercial reference laboratories can perform PCR testing for *Giardia* and *Cryptosporidium* spp, although the author recommends fecal flotation and DIF testing for the routine diagnosis of both organisms. An exception is the use of PCR for determining *Giardia* “assemblages,” which vary in their infectivity for animals and humans. Dogs have mainly assemblages C and D; cats have assemblages A1 and F; humans have assemblages A2 and B. Assemblages can be determined via PCR to determine the likelihood of zoonotic transmission from animals to humans, although the risk for transmission of *Giardia* spp to humans is generally very low.

### Fecal Enteric Panel

Proper collection and preservation of feces are frequently neglected yet important requirements for isolation of suspected bacterial enteropathogens. Approximately 2 to 3 grams of fresh feces should be collected into a clean, sealed, leak-proof cup or sterile container and transported to the laboratory as soon as possible to maximize survival of *Salmonella* and *Campylobacter* spp. Specimens should be processed within 2 hours after collection. If the laboratory is onsite, no transport medium is required. Transport media such as Cary-Blair Agar (Conda) or Amies Gel (Copan) should be used for specimens that cannot be cultured within 2 hours of collection.

Rectal swabs are suboptimal for bacterial isolation given the limited volume of feces obtained. Specimens should be kept cool at 4°C to 10°C, but not frozen. Fecal specimens submitted for ELISA testing of bacterial toxins should not be placed in a transport medium.

Fecal culture and toxin assays are typically a low-yield diagnostic procedure in animals with diarrhea because clinical documentation of enteropathogenic bacteria that can
cause diarrhea is clouded by presence of these organisms in apparently healthy animals. If bacterial enteritis or enterocolitis is suspected, the feces should be cultured or PCR should be performed for specific enteropathogens, such as *Salmonella* spp or *Campylobacter jejuni*. Fecal enteric panels should be reserved for animals that develop diarrhea after boarding or show attendance, those with acute onset of bloody diarrhea in association with evidence of sepsis, or when diarrhea outbreaks occur in more than one pet in a household.

Lastly, *Campylobacter* and *Salmonella* spp are potentially zoonotic organisms that can cause disease in immunocompromised humans. A recent study in 219 diarrheic cats and 54 nondiarrheic cats showed that *Campylobacter* was isolated from significantly fewer diarrheic (21/219 or 9.6%) versus nondiarrheic cats (15/54 or 27.8%; *p* = .001) and was detected in 74 of 131 cats (56.5%) via PCR. *Campylobacter jejuni*, *C. helveticus*, and *C. upsaliensis* were detected in 6.8%, 100%, and 44.6% of the 74 cats, respectively. Multiple *Campylobacter* spp were identified in 47.3% of these cats. All cats were ELISA-negative on fecal culture for *Salmonella* spp and *C. difficile* TcdA. *Clostridium perfringens* enterotoxin was detected through ELISA in 9 of 219 diarrheic (4.1%) and 1 of 54 nondiarrheic cats (1.9%; *p* = .69). This study underscored the limited diagnostic value of routine fecal cultures and toxin immunoassays for detection of enteropathogenic bacteria in diarrheic cats. Molecular-based testing was superior to fecal cultures for detection and identification of *Campylobacter* spp, but positive test results did not correlate to disease.

**Fecal Cytology on Stained Fecal Smears**

Stained fecal smears are commonly evaluated by veterinarians and veterinary technicians in an effort to identify the underlying cause of diarrhea by looking for spiral-shaped bacteria (*Campylobacter*-like organisms), white blood cells, and fecal endospores associated with *C. perfringens* (Figure 2). Unfortunately, diagnostic yield of stained fecal smears is extremely low, and the author does not recommend their routine use in practice for several important reasons: The lack of association between presence of endospores and presence or absence of diarrhea and between endospore count and enterotoxin results has been well documented. Spiral-shaped bacteria are commonly found in fecal smears from healthy and diarrheic cats and dogs, and the spiral-shaped bacteria can be representative of a *Campylobacter*-like organism, including *Helicobacter* and *Arcobacter* spp. The problem is that there are over 18 *Campylobacter* spp, many of which are nonpathogenic.

The mere presence of spiral-shaped organisms among other bacterial forms is of no clinical relevance and is not sufficient for diagnosis of *Campylobacter* infection. Most bacterial enteropathogens are associated with self-limiting diarrhea, and injudicious administration of antimicrobials could be more harmful than beneficial. Supportive therapy and appropriate hygiene measures should be considered in all cats with sus-
expected or confirmed bacteria-associated diarrhea. Antimicrobials should be administered only to animals manifesting systemic signs of illness.7

Tests of Intestinal Function
Low serum vitamin B12 or cobalamin has often been regarded solely in the context of its diagnostic utility in identifying dogs with small intestinal bacterial overgrowth. However, low serum vitamin B12 has been described in cats in association with a variety of GI diseases, including IBD.11 It is plausible that mucosal repair is impeded in initial management of IBD when vitamin B12 is deficient and its absorption impaired. Measurement of serum vitamin B12 in initial evaluation of cats and dogs with chronic intestinal disease, followed by parenteral administration if low serum cobalamin is identified, is pivotal for successful patient management. Cats are typically supplemented with 250 µg/dose SC for 6 weeks on a weekly basis, with supplementation continued on an as-needed basis.

Interpretation of Hematology & Serum Biochemistry Panels
The CBC may reveal peripheral eosinophilia secondary to endoparasitism, eosinophilic IBD, abdominal mast cell neoplasia, or lymphoma (paraneoplastic phenomenon).12 Anemia may result from enteric blood loss or from depressed erythropoiesis caused by systemic disease or chronic inflammation.

The serum biochemistry panel can provide additional information pertaining to the likely cause of diarrhea and help rule out extra-GI causes of diarrhea (renal disease, hepatic insufficiency). Protein-losing enteropathies represent a syndrome of intestinal disorders (severe IBD, lymphoma, intestinal ulceration) that typically manifest with abnormal loss of serum proteins across an inflamed or abnormally permeable intestinal mucosal barrier. Hypocholesterolemia can be seen secondary to malabsorption. A discordant BUN:creatinine ratio results from dehydration (prerenal azotemia), GI bleeding, high-protein meals, and cachexia. Elevated liver enzymes should be interpreted cautiously in cats with intestinal disease or pancreatitis because drainage of bacteria or endotoxin via portal circulation can precipitate a “reactive hepatopathy” secondary to extrahepatic disease.

Abdominal Imaging
Survey abdominal radiography is a relatively low-yield procedure in most cats with chronic diarrhea but is indicated in animals suspected of having partial obstructions caused by foreign bodies, intussusceptions, or masses, or in those with gas distention or displacement of the stomach or bowel. Abdominal ultrasonography is complementary to survey abdominal radiography; it is more sensitive for detection of abdominal masses, intestinal mural thickening (Figure 3), intussusceptions, and mesenteric lymphadenopathy.13 In addition, ultrasound-guided percutaneous biopsy or aspiration of masses is an effective diagnostic procedure. Contrast radiography and fluoroscopy are occasionally indicated for identifying partial obstructions and intestinal motility disorders, respectively.

Figure 3. Ultrasonographic study of a segment of jejunum from a cat with chronic diarrhea and weight loss. The diffusely thickened muscularis propria layer is consistent with IBD or small-cell lymphoma (arrows).
Endoscopy & Biopsy—Pitfalls & Recommendations

Endoscopy is a valuable procedure for diagnosis of intestinal mucosal disorders associated with morphologic changes, but it does not differentiate intestinal motility disorders, secretory diarrheas, or brush-border enzyme defects. In addition, lesions of the intestinal submucosa and muscularis propria layers of bowel can easily be missed and endoscopy is limited by the working length of the scope, precluding examination of the jejunum.

Regardless of the method used to procure intestinal biopsies, the interobserver variation among histopathologic evaluations of intestinal tissues from cats and dogs is unacceptably high. With the support of the World Small Animal Veterinary Association, the Gastrointestinal Standardization Group has proposed a histologic evaluation system that can be applied to all companion animal gastroenterologic disorders. Standardization should yield several obvious benefits, including uniform diagnosis of disease, staging of disease, and subsequent development of controlled clinical trials for treatment of canine and feline GI disorders.

COMMON CHRONIC ENTEROPATHIES IN CATS

Parasitic Infection

_Tritrichomonas foetus_ is an important and common protozoal pathogen that causes colitis, primarily in young pedigree cats living in confined areas such as catteries and shelters worldwide. Clinical signs associated with _T foetus_ infection in cats generally consist of a chronic or recurrent large intestinal diarrhea characterized by increased mucus, tenesmus, and increased frequency. Eradication of the infection can be frustrating, as 57% of cats diagnosed with _T foetus_-associated diarrhea persist in shedding the organism for up to 5 years following treatment. Various antimicrobials have been attempted to eradicate _T foetus_ infection with limited success. More recent therapeutic approaches have involved ronidazole (30 mg/kg q24h × 14 days), a 5-nitroimidazole with similar properties to metronidazole; however, clinical resistance to metronidazole, low efficacy of tinidazole, and documentation of in vivo and in vitro resistance to ronidazole in some cats are consistent with a high level of cross resistance of feline _T foetus_ to conventional 5-nitroimidazole drugs. Diagnosis of _T foetus_ infection in cats is best confirmed via PCR testing on feces or using a proprietary InPouch culture medium (BioMed Diagnostics). Both methods are vastly superior to the wet-prep technique.

Food-Responsive Enteropathy

Elimination diets containing novel, single sources of protein have proven effective in dogs and cats with a variety of chronic enteropathies, including small and large intestinal lymphocytic–plasmacytic, eosinophilic, and mixed cellular infiltrates or forms of IBD. One study of 16 feline cases of elimination/challenge–proven dietary hypersensitivity with chronic GI signs found that all 16 patients had mild to severe inflammatory infiltrates in at least one region of the bowel. The infiltrates were lymphocytic, lymphocytic-plasmacytic (most cases), or eosinophilic (2 cases). All cats responded completely to the elimination diet alone and offending foods were identified in all cases.

In a report of dogs with lymphocytic–plasmacytic colitis, clinical signs resolved in all 13 cases with introduction of an elimination diet, and of 11 dogs rechallenged with their original diet, 9 relapsed. In a further report of 6 cats with lymphocytic–plasmacytic colitis, all responded completely to an elimination diet.

The theoretical basis for protein hydrolysate diets is that reduction in immunogenic epitopes being presented to the mucosal immune system during dysregu-
Administration of probiotics to dogs and cats with IBD represents a novel alternative therapeutic modality that warrants further investigation. Probiotics have also been used to facilitate eradication of intestinal parasites.

Inflammatory Bowel Disease

Diagnosis of IBD is based on compatible clinical signs (chronic diarrhea, vomiting, weight loss, with or without borborygmus and flatulence) and exclusion of metabolic, infectious, neoplastic, and obstructive disorders of the gut. GI biopsies must show histologic evidence of moderate to marked infiltration of the GI mucosa by inflammatory cells (predominantly lymphocytes and plasma cells) and changes in mucosal architecture for a diagnosis of IBD to be rendered.

An association between the mucosal bacteria and intestinal inflammation has been provocatively demonstrated by Janeczko and coworkers in 17 cats undergoing a comprehensive workup for clinical signs of GI disease and 10 healthy age-matched controls.24 The number of mucosa-associated Enterobacteriaceae, Escherichia coli, and Clostridium spp organisms was higher in cats with signs of GI disease than in healthy cats, and total numbers of mucosal bacteria were strongly associated with changes in mucosal architecture and the density of mucosal infiltrates, particularly macrophages. In addition, the numbers of mucosal bacteria were associated with up-regulation of cytokine mRNA (particularly IL-1, -8, and -12).24 Management of feline IBD includes elimination or hypoallergenic diets, antimicrobials (tylosin, metronidazole) and/or immunomodulatory drugs (prednisolone, budesonide, chloram-bucil), and cyanocobalamin supplementation.

Probiotics

Probiotic refers to “a preparation of or a product containing viable, defined microorganisms in sufficient numbers, which alter the microflora in a compartment of the host and by that exert beneficial health effects on the host.”25 Administration of probiotics to dogs and cats with IBD represents a novel alternative therapeutic modality that warrants further investigation. Probiotics have also been used to facilitate eradication of intestinal parasites. A recent study documented the ability of the probiotic organism Enterococcus faecium SF68 (FortiFlora, Nestle-Purina, St Louis, MO) to antagonize Giardia intestinalis infection in mice. Oral feeding of E faecium strain SF68 starting 7 days before inoculation with Giardia trophozoites significantly increased the production of specific anti-Giardia intestinal IgA and blood IgG. This humoral response was mirrored at the cellular level by an increased percentage of CD4+ T cells in the Peyer’s patches and in the spleens of SF68-fed mice. The improvement of specific immune responses in probiotic-fed mice was associated with a diminution in the number of active trophozoites in the small intestine as well as decreased shedding of fecal Giardia antigens (GSA65 protein).26 Administration of a species-specific probiotic containing Lactobacillus Group 2 and Enterococcus faecium to 27 juvenile cheetahs predisposed to bacteria-associated enteritis was associated with a significantly increased
body weight, with no weight increase in the control group. In addition, administration of the probiotic was associated with improved fecal quality.

**Intestinal Lymphoma**

There are several classifications of alimentary lymphoma in the cat. Small-cell (well-differentiated lymphoma or low-grade lymphoma) is the most prevalent, representing 75% of alimentary lymphoma cases in cats. Recent studies have indicated that low-grade lymphoma is more likely to be T cell in origin and high-grade alimentary lymphoma is more likely to be B-cell lymphoma. Large-cell lymphoma (high-grade lymphoma, lymphoblastic lymphoma) tends to have a more rapid onset and progression, resulting in acute and often severe clinical signs. Lastly, large, granular cell lymphoma often starts in the alimentary system of the cat before rapidly spreading to other organ systems. As an aggressive form of lymphoma, it responds poorly to chemotherapy. The characteristic cells contain cytoplasmic granules that can be demonstrated on Giemsa stains and are believed to be of the T-cell/natural killer cell immunophenotype.

Immunohistochemistry and clonality are becoming more established for confirming GI lymphoma and differentiating it from IBD. Using these markers, an ultrasonographic pattern of diffuse thickening of the muscularis propria of the small intestine has been recognized in cats with small-cell, T-cell GI lymphoma or IBD and smooth muscular hypertrophy.

**Triaditis**

Triaditis is a lay term that refers to a syndrome of concurrent hepatic disease (cholangitis or hepatic lipidosis), pancreatitis, and intestinal disease (IBD or small-cell intestinal lymphoma) in cats. The association of these entities may reflect a common underlying disease mechanism. It is believed that the predominant signs of triaditis are attributable to hepatobiliary disease, with pancreatitis and IBD occurring as secondary complications. Despite the relatively high prevalence of triaditis in cats, the temporal nature of the relationship as well as the specific cause(s) of cholangitis, pancreatitis, and IBD have not been well elucidated.

Ascending passage of bacteria or bacterial products from the intestine is a plausible factor in the development of pancreatitis, and it is plausible that the retrograde ejection of bile through the pancreatic and common bile ducts during vomiting increases the risk for pancreatic inflammation and cholangitis. Interestingly, a recent study comparing histopathologic features, immunophenotyping, clonality, and fluorescence in situ hybridization (FISH) in 51 cats with lymphocytic cholangitis failed to document strong evidence implicating in situ bacterial colonization as a pathogenesis of lymphocytic cholangitis. A similar study critically evaluating the role of bacterial colonization in cats with neutrophilic cholangitis is warranted.

Weiss and coworkers reported an association between inflammatory liver disease and IBD, pancreatitis, and interstitial nephritis in 78 cats at necropsy. Although the temporal relationship between disease entities could not be established, all cats with cholangitis should be evaluated for concurrent IBD and pancreatitis. It is plausible that altered mucosal integrity secondary to IBD could enable access by inflammatory mediators, endotoxins, and microbial components to the portal circulation, with consequent deposition of immune complexes in the liver, activation of the complement system, and hepatocellular necrosis. Measurement of serum cobalamin concentrations is warranted in all anorectic cats, particularly those with IBD, pancreatitis, or hepatobiliary disease, given the high incidence of subnormal cobalamin concentrations in these cats.
References


Vomiting, one of the most common reasons for cats to be presented for evaluation, is often considered to be “normal.” There is some truth to the idea that cats vomit more readily from eating too much or too fast; eating foods that are unusual, especially food that contains toxins; or grooming (vomiting hair). However, such vomiting should not be routine. If it is, there is often an underlying cause that needs to be addressed. Adult and senior cats have different causes of vomiting than kittens do, but there are similarities in the approach to diagnosis of vomiting in cats of any age.

To simplify the process, it is sometimes helpful to separate the multitude of causes of vomiting into two more distinct groups: vomiting caused by diseases or disorders of the gastrointestinal (GI) tract itself or vomiting due to systemic or non-GI diseases and disorders that trigger either peripheral or central neural pathways (Table 1). Vomiting caused by primary
cats and discusses the best approaches to their treatment. Because it is an important factor, the role of diet in both diagnosis and treatment of vomiting is also discussed.

**Primary Gastrointestinal Disease**
The GI tract should always be carefully evaluated in a cat that is vomiting; however, vomiting is not pathognomonic for gastric or intestinal disease. Furthermore, while it is rare for laboratory evaluation (ie, hemogram, serum biochemistry panel, urinalysis) to provide the definitive diagnosis for primary GI disease, initial evaluation of the vomiting cat should include a minimum database of routine blood analysis and, if appropriate, thyroid testing, GI function testing, and viral serology—particularly in adult or senior cats with chronic (>3 weeks) vomiting. It is important to note that these tests may not reveal the primary problem but are necessary to determine basic physiologic status (ie, electrolyte, acid–base, fluid needs) and rule out other systemic diseases.

GI function testing includes that of feline pancreatic lipase immunoreactivity, feline trypsin-like immunoreactivity, cobalamin, and folate. These tests are important for assessing pancreatic function but also give an indication of small intestinal health, as cobalamin and folate are important indicators of intestinal dysbiosis or disease. If primary GI disease is considered likely based on physical examination, history, or normal laboratory results, then imaging (eg, radiographs, abdominal ultrasound) is indicated either to make a definitive diagnosis or identify abnormalities that require further diagnostic steps. This wide spectrum of potential causes of vomiting in cats increases the difficulty of making a definitive diagnosis. Nevertheless, it is important to carefully consider each of the potential differentials to prevent the problem from progressing to create further problems. This article provides an overview of the process of making a diagnosis of some of the more common causes of vomiting in cats and discusses the best approaches to their treatment. Because it is an important factor, the role of diet in both diagnosis and treatment of vomiting is also discussed.

**TABLE 1**
Approach to Diagnosis of Vomiting

<table>
<thead>
<tr>
<th>Primary GI Causes</th>
<th>Extra-GI Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric parasitic or infectious disease</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Gastric or intestinal neoplasia</td>
<td>Cholangitis or hepatic lipidosis</td>
</tr>
<tr>
<td>Gastric ulcers or erosions</td>
<td>Endocrinopathies (eg, hyperthyroidism, diabetic ketoacidosis)</td>
</tr>
<tr>
<td>Gastric motility disturbances</td>
<td>Infectious hepatopathies (eg, toxoplasmosis, feline infectious peritonitis, fungal)</td>
</tr>
<tr>
<td>Gastric outflow obstruction</td>
<td>Neoplasia (eg, lymphosarcoma, mast cell tumor)</td>
</tr>
<tr>
<td>IBD</td>
<td>Heartworm disease</td>
</tr>
<tr>
<td>Dietary hypersensitivity (allergy or intolerance)</td>
<td>Acute or chronic renal disease</td>
</tr>
<tr>
<td>Intestinal dysbiosis</td>
<td>Systemic infectious disease</td>
</tr>
<tr>
<td>Infectious or parasitic disease</td>
<td>Diseases of CNS, causing nausea</td>
</tr>
</tbody>
</table>

CNS = central nervous system, GI = gastrointestinal, IBD = inflammatory bowel disease

GI diseases includes such differentials as infectious, inflammatory, parasitic, anatomic (obstructive, trichobezoars), neoplastic (alimentary lymphoma), and drug-related or food-related (hypersensitivity, intolerance disorders).1-3 Cats that are vomiting due to extra-GI diseases may have a myriad of different systemic problems, but endocrinopathies (eg, hyperthyroidism), metabolic diseases (eg, renal or liver failure), inflammatory diseases of the liver or pancreas, cardiovascular diseases (eg, heartworm disease), central nervous system (CNS) disorders (eg, vestibular or inflammatory CNS diseases), and neoplasia (eg, mast cell tumors, other cancers affecting visceral organs outside the GI tract) are most common.1-6

This wide spectrum of potential causes of vomiting in cats increases the difficulty of making a definitive diagnosis. Nevertheless, it is important to carefully consider each of the potential differentials to prevent the problem from progressing to create further problems. This article provides an overview of the process of making a diagnosis of some of the more common causes of vomiting in cats and discusses the best approaches to their treatment. Because it is an important factor, the role of diet in both diagnosis and treatment of vomiting is also discussed.

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GI function testing includes that of feline pancreatic lipase immunoreactivity, feline trypsin-like immunoreactivity, cobalamin, and folate. These tests are important for assessing pancreatic function but also give an indication of small intestinal health, as cobalamin and folate are important indicators of intestinal dysbiosis or disease. If primary GI disease is considered likely based on physical examination, history, or normal laboratory results, then imaging (eg, radiographs, abdominal ultrasound) is indicated either to make a definitive diagnosis or identify abnormalities that require further diagnostic steps. In some cats, more invasive tests (eg, gastroduodenoscopy, exploratory laparotomy) may be required to obtain biopsy material or remove the problem (obstruction).

The decision to pursue endoscopy versus exploratory surgery depends on availability of necessary equipment and expertise as well as the likelihood that endoscopy can be a useful
diagnostic or treatment tool (eg, an endoscope will not reach the mid or distal jejunum).

Among gastric diseases to consider as causes of vomiting are parasitic infestation (eg, with *Physaloptera* or *Ollanus* spp), bacterial infections (eg, with *Helicobacter* spp), neoplastic diseases (eg, lymphoma, adenocarcinoma, leiomyosarcoma), inflammatory diseases (eg, ulcers, inflammatory bowel disease [IBD]), obstructive disorders (eg, hairballs, foreign bodies, masses), and diet-related causes (ie, intolerance, hypersensitivity). Specific diagnosis of individual causes may require additional procedures (eg, histopathologic evidence of spiral organisms deep in gastric glands associated with gastritis) to rule them in or out.

**Small Intestinal Disease**

Small intestinal disease in cats is a common cause of vomiting associated with the prevalence of inflammatory disease; however, true idiopathic IBD must be distinguished from the simple presence of inflammatory infiltrates in the small bowel, as a variety of dietary, infectious, and parasitic agents can cause either inflammation in the small bowel or dysbiosis, the latter of which causes inflammation.

Dietary sensitivity and intolerance are also important causes of vomiting in cats and should trigger appropriate dietary trials to rule them out. This process may be easier said than done, as finding a commercially available food without the offending substance (ie, intolerance) or antigen (hypersensitivity) and that the cat will readily consume is a challenge. In most cases of small intestinal disease affecting the intestinal wall, with the exception of adverse reactions to food, obtaining a definitive diagnosis will require biopsy—either via endoscopy or exploratory surgery.

**Adverse Reactions/Sensitivity to Food**

Food intolerance, food allergy (hypersensitivity), food poisoning, food idiosyncrasy, and pharmacologic reactions to foods all fall under the category of food sensitivity (or adverse reactions to food). \(^7\) Discussion here is limited to the first two conditions.

Food intolerance, a nonimmunologic, abnormal physiologic response to a food, nutrient, or food additive, is the most common cause of food sensitivity in cats. Food allergy, or hypersensitivity, is characterized by adverse reactions to a food or food additive (typically protein) with a proven immunologic basis. Both allergy to and intolerance of food can result in vomiting, diarrhea, or a combination of signs, depending on the effects: food allergy is more commonly associated with vomiting and dermatologic signs, whereas intolerances of food can present with vomiting or diarrhea but do not produce dermatologic signs.

**Dietary Elimination Trial**

The diagnosis of both food hypersensitivity and intolerance is based on results of a dietary elimination trial. The major difference between the diagnostic processes of these two types of adverse food reactions is the length of time on the diet that is required to achieve a response and the need to identify a novel protein source. Cats with food hypersensitivity require 8 to 12 weeks on a novel antigen (eg, protein) elimination diet before an improvement will be seen. Alternatively, in cats with food intolerance, resolution of signs usually occurs within days (7–14 days is typical) of a diet change in which the offending substance is removed, unless other factors influence the response.

A variety of commercially available and homemade elimination formulations can be used, as can those using hydrolyzed proteins. Many different brands fall under the category of “highly digestible,” but the key is to remember that they are not all alike. Thus, when one diet from this category is not accepted by the cat, is ineffective, or seems to make the problem worse, you cannot assume that all diets in this category will fail. Highly
If one type of highly digestible diet has been fed for at least 2 weeks with minimal response, it is entirely reasonable to try either another comparable diet from a different source or an entirely different dietary strategy. Digestible diets from different pet food manufacturers have a variety of formulations (Table 2), including different protein and carbohydrate sources, different levels of fat, and various additives designed to promote intestinal health (e.g., fructooligosaccharides, maltooligosaccharides, omega-3 fatty acids, antioxidant vitamins, soluble fiber).

If one type of highly digestible diet has been fed for at least 2 weeks with minimal response, it is entirely reasonable to try either another comparable diet from a different source or an entirely different dietary strategy (e.g., high protein/low carbohydrate, novel antigen, hydrolyzed protein). Thus, a dietary trial consisting of novel meat-source proteins or hydrolyzed foods may not be adequate to remove the offending items from the diet. For example, if the problem is being created by presence or type of carbohydrate in the food, feeding a diet high in protein (>40% metabolizable energy [ME]) and low in carbohydrates (<10% ME) that is highly digestible (>85% digestibility of protein) will resolve the problem.

In some cats, however, the only way to remove the source and confirm this problem is by feeding a homemade diet that consists of a meat source (e.g., cooked chicken thigh with the fat included) and a vitamin/mineral supplement but no added carbohydrate or other ingredients. This diet can be fed for up to 2 to 3 weeks, but a complete and balanced food should be formulated by a nutritionist if the diet must be fed longer.

The key feature that separates food intolerance from an allergy is that once the offending agent is removed from the diet, the vomiting (or other GI signs) will resolve quickly. Another key point is that in dietary intolerance the offending substance may be difficult to identify using typical commercial foods, thus a food trial using a homemade diet can be quite helpful.

Nevertheless, dietary management is a process of trial and error. No single diet or diet family will benefit all cats in all situations.

### Inflammatory or Immune-Mediated Causes of Vomiting

IBD, a commonly diagnosed condition of adult cats, is likely due to multiple causes but ultimately culminates from a combination of genetic susceptibility, intestinal microbial dysbiosis, and persistent inflammation of the gut wall, resulting in signs of vomiting, diarrhea, weight loss, or combinations of all three.8 Idiopathic IBD is characterized by persistent clinical signs of GI disease occurring with histologic evidence of mucosal inflammation and structural changes of the villous epithelium.

A number of possible causes of intestinal inflammation must be considered in the diagnostic process, and all should be investigated thoroughly or therapeutic trials instituted prior to settling on the diagnosis of idiopathic IBD—a disease requiring long-term therapy with immunosuppressive drugs. In particular, appropriate food trials are an extremely important component of both diagnosis and therapy of cats with suspected IBD (or GI disease in general). In addition, the diagnostic plan for a cat with chronic vomiting should include assessment of thyroid and FeLV/FIV status as well as intestinal vitamin (cobalamin/folate) status.

Serum cobalamin levels in cats commonly decrease with chronic pancreatitis or severe bowel disease; in cats with hypcobalamine-
mia, inappetence or vomiting will not resolve until replacement therapy has been instituted. Cobalamin therapy (250 g/cat SC weekly for 6 weeks, then once per week every other week) in some cats may be lifelong, while in others once the clinical disease resolves the supplementation can be discontinued.

In addition, radiography and ultrasonography are important in detecting the presence of infiltrative diseases, such as feline infectious peritonitis, granulomas, histoplasmosis, or lymphosarcoma. Ultrasonography has been particularly helpful in identifying intestinal wall layer changes and mesenteric lymphadenopathy—two findings that support intestinal inflammation or disease but do not differentiate type. Ultimately, intestinal biopsies, either obtained endoscopically or at exploratory surgery, are essential for both diagnosing IBD and ruling out other specific causes of GI clinical signs.

### Treating IBD

At this time, therapy of IBD in cats continues to include inflammatory suppression and antibiotic therapy, and while evidence to support a specific role for probiotic therapy is lacking, its use to help control dysbiosis or IBD seems to have merit. The most effective therapies for IBD include steroids (prednisolone or methylprednisolone, 1–2 mg/kg q12h PO) or other drugs that interrupt the proinflammatory pathways active in the gut. In cats intolerant to steroids or those in which steroids are no longer effective, immunosuppressive therapy may be necessary. Currently, either chlorambucil or cyclosporine is most frequently chosen.

Antibiotic therapy with metronidazole (5–10 mg/kg q12h PO) or tylosin (5–15 mg/kg q12h PO) has been effective for control of bacteria-associated disease and continues to be recommended for initial therapy of IBD. Whether this action can be attributed to the antibiotic effects of these drugs and their influence on the intestinal microflora or their immune-modulating activities is unknown. Nevertheless, such therapy is often helpful. Caution is advised in using either drug on a continuous or long-term basis but especially metronidazole due to its potential for genotoxicity. If needed, they should be used intermittently, not continuously.

Studies of probiotic therapy in cats have primarily focused on the use of Fortiflora (Purina) in a shelter environment among kittens or young cats with parasitic diseases (giardiasis, cryptosporidiosis, etc) or stress-induced diarrhea. Under these circumstances, probiotic therapy resulted in a faster resolution of diarrhea and more rapid resolution of infection. However, placebo-controlled clinical trials using probiotics in cats with IBD are only in their early stages, so specific recommendations await their findings.

Finally, general agreement exists among gastroenterologists that foods with fewer carbohydrates (a source of intolerance and malabsorption) and based on highly digestible protein sources (primarily meat) are beneficial in cats with IBD, reducing the bacterial changes that can occur when undigested foods remain in the GI tract. These formulations may include so-called hypoallergenic diets but do not necessarily require hypoallergenicity. A scoring system that can be used in monitoring response to treatment of IBD as well as to assist in diagnosis in cats in which IBD is suspected has been published by Albert Jergens et al.8

### Extraintestinal Causes of Vomiting: Feline Pancreatitis & Cholangitis

Feline pancreatitis is difficult to diagnose definitively antemortem, especially in its more common lymphoplasmacytic form, and is associated with vomiting only occasionally or intermittently. This difficulty is partly attributable to lack of both specific clinical signs in cats and a highly sensitive test for diagnosis of the disease.

The clinical signs of pancreatitis in cats can...
be quite different from those in dogs. Acute necrotizing pancreatitis is frequently encountered in obese dogs fed a high-fat diet, while cats are more likely to be underweight and high-fat diets do not appear to be an important predisposing factor. Cats of all ages, sexes, and breeds are affected, although Siamese cats reportedly have the more acute, necrotizing form of pancreatitis more frequently.

The most common form in cats, lymphoplasmacytic pancreatitis, is more insidious, and the clinical signs are vague, with the most common being lethargy (100% of cats in one study), anorexia, and dehydration.11 Vomiting and anterior abdominal pain, which are common clinical signs in dogs with acute pancreatitis, occur in only 35% and 25% of cats, respectively. However, there is strong belief among feline practitioners that pancreatic pain or discomfort may be underreported due to the tendency of cats to hide overt signs. Thus, clinical signs may be quite variable, and this must be taken into consideration with each patient.

Routine evaluation of vomiting cats with suspected pancreatitis or other extra-GI causes of vomiting is similar to that mentioned above: a minimum database, GI function testing, and retroviral testing are always appropriate. Tests for hyperthyroidism, liver function, or other specific tests may be indicated in some cats.

Hematologic findings in cats with pancreatitis are nonspecific but may include nonregenerative anemia, leukocytosis, or leukopenia (less common). In a recent study, cats with pancreatitis consistently had elevated white blood cells (20,300/L) and mild decreases in platelets (mean, 180,000/L). Neutrophils were not degenerate or toxic. Reported changes in the serum biochemistry profile include elevated serum alanine aminotransferase (ALT), elevated serum alkaline phosphatase (ALP), hyperbilirubinemia, hyper- or hypoproteinemia, lipemia, and hyperlipidemia.
cholesterolemia, hyperglycemia, azotemia, and hypokalemia. Common abnormalities in cats with severe pancreatitis were hyperglycemia (180 mg/dL), hyperbilirubinemia (2.5 mg/dL), hypocholesterolemia (130 mg/dL), and hypalbuminemia (1.8 g/dL).

In cats with mild or lymphoplasmacytic pancreatitis, liver enzyme elevations were more common, with gamma-glutamyltransferase, ALP, and ALT being moderately elevated. Hypocalcemia is less commonly observed but, when present, may be a poor prognostic sign seen in cats with severe pancreatitis or multiple-organ dysfunction. Serum lipase may be increased early in acute pancreatitis, but in a recent study, amylase and lipase were found to be of little diagnostic value in distinguishing normal cats from those with pancreatitis. There are no changes in the urinalysis consistently observed or specific for pancreatitis in cats.

The feline trypsin-like immunoreactivity (fTLI) test was developed years ago as the definitive test for diagnosis of exocrine pancreatic insufficiency, and the data and follow-up have confirmed its usefulness in diagnosing this condition. While an increase in fTLI can be found in cats with pancreatitis, a normal value does not rule out pancreatitis, as the leakage of enzymes tends to decrease rapidly following an event and the enzymes are inactivated and scavenged by the body’s peptidases (eg, macroglobulin) within 12 to 24 hours following an acute insult. This test is still quite useful in cats with chronic pancreatitis, however, due to the insidious nature and lack of clinical signs of the disease. Cats may sustain a loss of pancreatic function, indicated by a decreased fTLI. In fact, in a recent unpublished study by the author’s group of 150 cats with exocrine pancreatic insufficiency tested at the Texas A&M GI laboratory, the most common clinical sign was weight loss (not diarrhea or vomiting). Thus, measurement of fTLI is an important aspect of assessment in cats with chronic low-grade inflammation of the pancreas that may not have overt signs of inflammation or illness but have lost significant pancreatic functional capacity.

The test of choice for pancreatic leakage is the radioimmunoassay for feline pancreatic lipase (fPLI); this test has a sensitivity and specificity of nearly 100% in cats with severe pancreatitis (determined by pancreatic biopsy). However, the sensitivity in moderate pancreatitis was found to be 80% and as low as 65% in mild pancreatitis, while the specificity in healthy cats was 75%. Thus, in cats with chronic pancreatitis, it is still necessary to evaluate the combined historical, physical examination, and laboratory data as well as imaging information, along with the fPLI results, when making a diagnosis.

**Imaging Studies**

Imaging studies are frequently used to help identify cats with acute pancreatitis, but in those cats with the more common chronic form, changes on ultrasound imaging are not consistent and can be particularly subject to interpretation and operator expertise. The most common ultrasonographic findings are hypoechoic pancreas, hyperechoic mesentery, mass effect, dilated common bile duct, or normal appearance throughout. In previous research, the sensitivity of ultrasonography for diagnosis of pancreatitis was reportedly 24%. In a recent study, mild pancreatitis was still shown to be difficult to diagnose via abdominal ultrasound imaging, but ultrasound was 80% sensitive and 88% specific in cats with moderate to severe pancreatitis.

The most reliable method for making an accurate diagnosis of pancreatic disease remains direct visualization and histopathology. This approach can be expensive and can increase the risk for complications (during anesthesia/surgery). In cases with focal involvement, which is common with chronic pancreatitis, lesions may be missed. In short, pancreatitis remains a challenging diagnosis and an even more challenging disease to treat once the diagnosis has been confirmed.
Feline Liver Diseases (Cholangitis, Idiopathic Hepatic Lipidosis)

There are four major types of feline liver disease: hepatic lipidosis, cholangiohepatitis complex, infectious hepatitis (e.g., feline infectious peritonitis, toxoplasmosis, fungal/parasitic hepatitis), and neoplastic liver disease (e.g., lymphoma). As with all diseases of the liver, histopathology is required for definitive diagnosis and is the most important step in determining treatment and prognosis. Nevertheless, once a diagnosis has been obtained, the goal for treatment of cats with liver disease is to provide optimal nutritional and pharmacologic support that maximizes liver function; minimizes future liver or biliary duct damage or scarring; controls concurrent clinical signs, such as vomiting; and thus promotes a high quality of life.

Inflammatory, infectious, or metabolic liver disease can present in cats with few external clinical signs other than inappetence, vomiting, or lethargy or can cause severe illness resulting in development of ascites, icterus, hepatoencephalopathy, coagulopathy, and loss of ability to metabolize protein or carbohydrates appropriately. Thus, there is no single set of clinical signs or laboratory abnormalities that can define all liver disease patients. Nevertheless, some important clues can help guide the clinician to making a definitive diagnosis. The most common cause of severe liver disease or failure in the cat is idiopathic hepatic lipidosis, but the most common cause of increased liver enzymes and chronic intermittent clinical signs is cholangitis/cholangiohepatitis. In several recent studies using biopsy results to confirm diagnosis, cats with inflammation of the peribiliary structures consistent with cholangitis also had lymphoplasmacytic infiltrate in the pancreas (66%–75% in separate studies).13,14 Thus, there is growing evidence that these two diseases in cats may be linked: when one occurs, the other follows. At this time, there is no agreement about cause; however, there is some evidence that bacteria may be an important culprit, as bacterial DNA was found in at least 30% of livers with a neutrophilic inflammatory component.15 Conversely, in another paper, no bacterial DNA was found, but the majority of study cats had the more chronic lymphocytic form of the disease.16 Whether this dichotomy represents two separate diseases or different stages/phases of the same disease (acute progressing to chronic) is unknown, but it suggests that further work to better control and define the origin of intestinal dysbiosis in cats is warranted.

Finally, a number of other important extraGI causes of vomiting also need to be considered, including chronic renal disease, endocrinopathies (e.g., hyperthyroidism, diabetic ketoacidosis), and other systemic diseases (e.g., heartworm disease). A complete discussion of each is not possible, but readers are reminded to consider these possibilities when confronted with vomiting cats for which a definitive diagnosis has not been made.

Nonspecific Therapy of Vomiting

Several antiemetic agents are available for use in cats (Table 4); some are more commonly used in the hospital setting because they are injectable and may require frequent administration. The newest antiemetic drug family, neurokinin (NK) inhibitors, represented by maropitant, are clearly the most effective in cats. In addition to the excellent antinausea effects of maropitant, it also appears to be effective for controlling visceral pain, which may be an essential aspect of therapy in feline chronic pancreatitis. The feline dose is 1 to 2 mg/kg PO or SC q24h for 3 to 5 days, but it may be given longer if needed.

The 5-HT₃ antagonists are effective antiemetic agents for cats as well at doses of 0.5 to 1.0 mg/kg of ondansetron, 0.1 to 0.5 mg/kg of granisetron, or 0.5 to 1.0 mg/kg of dolasetron PO or IV q12–24h. In addition, cats may be treated with chlorpromazine, an α₂-adrenergic antagonist, at 0.2–0.4 mg/kg q8h SC or IM. Dopaminergic antagonists

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such as metoclopramide are less effective in the cat and, because they antagonize dopamine, may potentially reduce pancreatic blood flow. (This effect has not been proven in cats with pancreatitis.) However, metoclopramide is available in an oral preparation that can be used for at-home therapy.

While such nonspecific therapy may be indicated to control vomiting, finding the cause is more important than simply controlling the clinical sign. Thus, antiemetic therapy should be used judiciously in the clinical setting and as an adjunct to therapy for the primary problem.

References


Suggested Reading

Decline in body weight is common in cats older than 11 years of age. Sometimes this loss is readily attributable to apparent disease, but in many cases there are no obvious signs of illness and routine diagnostic approaches fail to reveal evidence of an underlying problem. Energy requirements of older cats apparently do not decline as markedly as they do in dogs and humans, perhaps because physical activity does not decrease as much with age in cats. Indeed, the maintenance energy requirement of older cats may increase rather than decrease. Although cats might be expected to regulate their energy intake to compensate for these changes to maintain body weight, this clearly is not always the case.

It has been recognized for many years that both protein and fat digestibility decrease in many apparently normal cats after 10 years of age. While the cause of the decreases remains unclear, the changes are quite marked in some individuals and in particular can be dramatic with regard to fat digestibility. Often these changes are not readily apparent from...
casual observation of feces and may only be verified if fecal fat content is quantified by appropriate analytic testing. Methods for such testing are rarely available for evaluation of veterinary patients, even at referral centers.

Whatever the explanation for weight loss and decline in nutrient digestibility in older cats, progressive decline in body weight has been reported in the 2 years prior to death from a variety of seemingly unrelated diseases. As cats live increasingly longer lives and receive attentive health care, this weight loss is more frequently recognized. This article reviews what is known about common age-related changes and what may be done to halt or reverse the decline in body weight that is apparently a predictable prelude to death.¹⁻⁴,⁶

**Attributable Weight Loss**

Well-recognized causes of weight loss in old cats include chronic renal disease, diabetes mellitus, hyperthyroidism, inflammatory bowel disease (IBD), exocrine pancreatic insufficiency, and dental problems, to name a few. Most are readily suspected and confirmed based on physical examination and routine laboratory testing. At times, selected additional testing of parameters such as serum thyroxine, serum trypsin-like immunoreactivity, cobalamin and folate, dental radiography (Figure 1), or gastrointestinal (GI) endoscopy and biopsy may be necessary. Despite thorough investigation, however, the underlying cause of even severe weight loss can be remarkably difficult to establish conclusively.

**Unattributed Weight Loss**

Subtle weight loss may not even be noted unless careful records of body weight and condition scores are kept over repeated veterinary examinations. Similarly, moderate increases or decreases in food or water intake will probably go unnoticed by most owners. Even when the most attentive owners provide the best veterinary care for their cats, a substantial proportion of senior cats will experience weight loss, despite apparently otherwise good health and no detectable change in food intake.

Evidence exists to indicate that, in these older cats with no apparent classic diseases to explain the weight loss, there is an age-re-
Evidence exists to indicate that, in older cats with no apparent classic diseases to explain weight loss, there is an age-related decline in food digestibility. There is a significant ($p < .0001$) negative correlation ($r = -0.76$) between age and fat digestibility (Figure 2). The incidence of low fat digestibility increases with age, affecting approximately 10% to 15% of mature cats (8–12 years of age) and 30% of geriatric cats (>12 years of age). In some geriatric cats, fat digestibility was found to be as low as 30%, with large stools (not frank diarrhea) and low body weight as the only clinical signs.

There is a significant ($p < .0001$) negative ($r = -0.66$) correlation between age and protein digestibility as well (Figure 3). Low protein digestibility also seems to affect mature and geriatric cats. Although the incidence of low protein digestibility is not as high as that of fat digestibility, approximately 20% of cats older than 14 years show protein digestibility lower than 77%. The incidence of low fat and protein digestibility tends to occur in the same cats. A marked decline apparently becomes particularly prevalent after around age 10 (Figures 4 and 5).

It is perhaps not surprising that these changes were correlated with several other measures of health or well-being, including serum vitamin E (tocopherol), vitamin B12 (cobalamin), skin thickness, body fat, and body condition score. Overall, while obesity tends to be the predominant body-mass concern in cats between 7 and 12 years of age, in those older than 12 years, obesity is rare and being underweight is a far greater life-threatening risk factor (Table 1 and Figure 6).

**Nutrient Digestibility**

The cause(s) of this decline in nutrient digestibility remains unknown but presumably reflects enteropathy of some type. In some cases, this intestinal dysfunction may overlap with what is commonly loosely classified as (idiopathic) IBD. Some cats may compensate for the loss in digestive function by eating more and therefore exhibit no weight loss. It is important to recognize that many cats show only subtle changes in stool characteristics (slightly larger volumes of stool with a more clay-like consistency), but not frank diarrhea, even when steatorrhea is marked.

Regardless of the precise cause(s), weight loss in otherwise healthy older cats, as well as changes in fecal characteristics, should be investigated, as should malabsorption. Through physical examination, routine CBC, serum biochemistry profile, urinalysis, and fecal examination are all indicated, as are radiographic and ultrasonographic evaluations as appropriate. If nothing specific to explain the weight loss is found, serum thyroxine, fe-
line pancreatic lipase, feline trypsin-like immunoreactivity, and cobalamin/folate levels should all be determined. It is this author’s recommendation that these be determined concurrently, as studies have indicated that approximately 50% of hyperthyroid cats have evidence of concurrent intestinal and/or pancreatic abnormalities, including sometimes severe hypocobalaminemia, at the time of initial diagnosis of the endocrinopathy.7,8

Furthermore, all abnormalities detected should be treated concurrently to optimize clinical response to treatment. Many hyperthyroid cats are appropriately diagnosed and treated, but GI signs, especially weight loss, persist despite return to the euthyroid state. Subsequent evaluation of GI function as outlined above then reveals evidence of enteric disease and cobalamin deficiency. Only when these are also appropriately treated do the cats return to optimal health.

The Diagnostic Process
Determination of fecal fat (by percentage) would be desirable and may be the only way to confirm an intestinal problem in some patients. Fecal fat greater than 20% would be indicative of fat malabsorption. Unfortunately, such a test is not commercially available for pet cats. It has been reported that 100% of cats over 7 years of age with serum tocopherol (vitamin E) less than 5 mg/L also have low fat digestibility and that more than 90% of cats with serum cobalamin less than 100 g/L have low fat digestibility.3 So finding such low serum concentrations of either cobalamin or tocopherol can be the basis of inferring that a cat has low fat (and probably protein) digestibility.3

A new test that may reveal abnormalities in intestinal function is an assay of fecal α₁-proteinase inhibitor by species-specific immunoassay.9 This test is presently available only from the GI Laboratory at Texas A&M University. Abnormal results indicate the presence of an enteropathy-associated increase in enteric loss of protein; this test can detect protein-losing enteropathy that is not sufficiently severe to lower serum albumin (the liver can compensate for enteric protein loss). Chronic enteric protein loss can contribute to gradual depletion of lean body mass.

In the future, assay of enteric inflammatory markers such as fecal calprotectin may prove useful in confirming the presence of enteric disease, but the relationship of inflammation to enteropathy is currently un-
certain. Even histologic examination of intestinal biopsy specimens may not provide evidence of a conclusive diagnosis; lesions may be patchy and interpretation of biopsy findings is inherently subjective. It is also likely that in cats, as in dogs, functional problems in the intestine may not be associated with either inflammation or villous atrophy, but rather with intraluminal microbial changes and biochemical derangements in the enterocytes lining the small intestine that are not revealed by classic histologic evaluation.

**Treatment**

In some cats, despite the most thorough investigation, it is not possible to confirm enteropathy conclusively, and a presumptive diagnosis of idiopathic enteropathy is the best that can be achieved. The approach to management in these instances is essentially the same as for patients with histologically confirmed IBD—that is, dietary change (low-carbohydrate alternative fiber source, novel antigen, or hydrolyzed diet), prebiotic or probiotic supplementation, correction of low serum cobalamin/folate concentrations, supplementation with vitamin E and perhaps other antioxidants, antibiotic treatment with metronidazole or tylosin, and perhaps glucocorticoid therapy or immunomodulation with chlorambucil or cyclosporine. However, in the absence of specific laboratory abnormalities or any overt clinical signs to monitor other than perhaps very slowly progressive weight loss, it is probably premature to recommend particularly aggressive treatment for these patients and a cautious, conservative approach is warranted.

As many of the observations about digestive disturbances in elderly cats are relatively new, appropriate clinical studies evaluating treatment interventions have not been performed. Dietary changes and supplements would certainly be the safest and most easily administered interventions. When specific abnormalities such as hypocobalaminemia are identified, they should be rectified. The effect of dietary changes has to be evaluated on an individual trial-and-error basis, which can be difficult if gradual weight loss is the only clinical sign to evaluate. Observing improvements in the newer GI disease markers, such as fecal α1-proteinase inhibitor, may provide objective evidence of a positive response, but the value of this approach remains to be evaluated.

Careful observation of stool characteristics may provide some evidence of improved digestibility, especially if grossly apparent abnormalities were present at the outset. If there is no apparent response to dietary change after 2 to 4 weeks, an alternative diet...
should be tried. This author prefers to select diet changes based on reduced carbohydrate content (generally associated with increased protein content) and/or different amounts or types of fermentable fiber. Adjusting the fat content of the diet does not appear to be particularly useful in treating feline enteropathies. Unfortunately, definitive studies in geriatric cats with malabsorption have not been done. Treatment needs to be individualized and evaluated on a trial-and-error basis.

With regard to older cats in general, there is some evidence that diet can play a role in maintaining body weight and fat mass—and prolonging life. A control diet (nutritionally complete and balanced adult cat food) supplemented with antioxidants (vitamin E and β-carotene), a blend of n-3 and n-6 fatty acids, and a prebiotic (dried chicory root) was associated with reduced decline in body weight and increased longevity (by more than 1 year) compared with feeding either the control diet alone or the control diet supplemented with antioxidants alone.6 These striking observations illustrate the potential benefit to be gained from dietary and other interventions to address the gastrointestinal changes that appear to be so common in aging cats.

References