Diagnosis of Acute and Chronic Vomiting in Dogs and Cats

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Vomiting is among the most common reasons that dogs and cats are presented for evaluation. Because there are a multitude of causes of vomiting, ranging from simple to complex, this can be a challenging problem for clinicians to accurately diagnose and manage. The problem also causes significant concern for pet owners, especially when there is an onset of frequent severe vomiting or when the occurrence becomes more chronic and intermittent without adequate control. However, by following a systematic approach beginning with an accurate history, a thorough physical exam, and appropriate baseline testing (Stage 1), then performing tests more specific for certain conditions or organ systems (e.g., bile acids assay, leptospirosis serology, baseline cortisol or ACTH stimulation, ultrasonography) (Stage 2), and finally where indicated performing advanced procedures for more thorough examination and biopsy or definitive therapy (endoscopy, exploratory laparotomy), most cases can be diagnosed successfully and managed judiciously. Vomiting does not constitute a diagnosis in itself. It is emphasized that vomiting is simply a clinical sign of any of a number of disorders that can involve any organ system in the body. In fact, one diagnostic registry service listed over 400 potential causes of vomiting in dogs! These notes summarize diagnostic approach and various treatment options for managing dogs and cats with vomiting.

Vomiting refers to a forceful ejection of gastric and occasionally proximal small intestinal contents through the mouth. The vomiting act involves three stages: nausea, retching, and vomiting. Serious consequences of vomiting include volume and electrolyte depletion, acid-base imbalance, and aspiration pneumonia.

It is essential that the clinician make a clear differentiation between regurgitation and vomiting at the outset. Regurgitation is defined as passive, retrograde movement of ingested material, usually before it has reached the stomach. Failure to recognize the difference between regurgitation and vomiting often leads to misdiagnosis. Regurgitation may occur immediately after uptake of food or fluids or may be delayed for several hours or more.

A Detailed, Accurate History is ESSENTIAL

One of the most important early considerations is to determine if any toxins or foreign objects may have been ingested. Some compounds can cause life threatening sequelae. The earlier a toxicity is identified, the greater the chance for successful management. Currently, xylitol toxicity is being recognized more frequently, and sago palm plants, which can cause severe hepatotoxicity in dogs and cats, are found in more homes and yards than in previous years. Cocoa mulch toxicity (theobromine) is also occasionally seen. Many animals that have ingested toxins are presented with vomiting as a prominent sign.

History and Clinical Assessment: Clinical Features of Vomiting

Because of the wide variety of disorders and stimuli that can cause it, vomiting may present the clinician with a major diagnostic challenge. A complete historical review with emphasis on all body systems is essential for determining a realistic and effective initial work-up plan and treatment protocol. All too often concentration on only the gastrointestinal tract leads to an incorrect diagnosis and inappropriate treatment. Consideration of the following features is useful in assessing and diagnosing a patient with vomiting:

1. duration of signs
2. signalment and past pertinent history
(3) environment and diet
(4) systems review (e.g., history of PU/PD, coughing and sneezing, dysuria or dyschezia, etc.)
(5) time relation to eating (vomiting of undigested or partially digested food more than 8-10 hours after eating often indicates a gastric motility disorder [more common] or gastric outlet obstruction [less common])
(6) content of the vomitus (food, clear fluid, bile, blood, material with fecal odor), and
(7) type and frequency of vomiting (projectile?, chronic intermittent?, cyclic?, morning vomiting only?).

**Most Common Causes of Acute or Chronic Vomiting in Dogs**

**First need to Rule-Out:**

**Dietary/ingestive problem** (always investigate for any potential environmental materials that the patient may have been chewing on (plants [toxins], debris carpet, etc)
- Indiscretion (e.g., table scraps, sudden diet change, garbage ingestion; toxins, foreign body, ingesting plants in home or yard)
- Food adverse reaction (dietary sensitivity)
- True food allergy

**Parasites**
- Intestinal (including *Giardia*)
- Gastric (*Physaloptera*)

**Drug related problems**
- NSAIDS must always be considered
- Other drugs (e.g., cardiac glycosides, antibiotics, chemotherapeutic agents)
- *Any* drug can potentially cause vomiting, always ask about any supplements that are being given to a pet

**Metabolic disorders**
- Renal disease
- Liver disease
- Electrolyte abnormalities
- Addison’s disease (some are glucocorticoid and mineralocorticoid deficient and will demonstrate typical electrolyte abnormalities; others are only glucocorticoid deficient and require ACTH stim for diagnosis (JAVMA April 15, 2007, p. 1190-1194)

**Rule-Outs for Chronic Vomiting, Once the Causes Listed Above are Ruled Out:**

**Main Categories:**

- **Motility Disorders**
  - Gastric hypomotility (an underappreciated disorder)
- **Inflammatory Disorders**
  - Chronic gastritis (with or without *Helicobacter*)
  - Inflammatory bowel disease
- **Obstructive Disorders**
  - Foreign body not already diagnosed (including cases with a partial small bowel obstruction that has eluded early diagnosis)
  - Hypertrophic gastropathy (uncommon)
- Neoplasia
Most Common Causes of Chronic Vomiting in Cats

Dietary problem
- Food adverse reaction (dietary sensitivity), up to 25% of cases

IBD
Hyperthyroidism
Liver disease
Renal disease
GI lymphoma (intestinal is more common)
Chronic pancreatitis
Heartworm disease

Intermittent Chronic Vomiting

Chronic intermittent vomiting is a common presenting complaint in veterinary medicine. Often there is no specific time relation to eating, the content of the vomitus varies, and the occurrence of vomiting may be very cyclic in nature. Depending on the disorder, other signs such as diarrhea, lethargy, inappetence, and salivation (nausea) may occur as well. When presented with this pattern of clinical signs, the clinician should strongly consider chronic gastritis, inflammatory bowel disease, irritable bowel syndrome, and gastric motility disorders as leading differential diagnoses. A detailed work-up including gastric and intestinal biopsies is often required for definitive diagnosis in these cases. It is important to note that chronic intermittent vomiting is a common clinical sign of inflammatory bowel disease in both dogs and cats.

Vomiting from systemic or metabolic causes may be an acute or chronic sign and generally there is no direct correlation with eating and no predictable vomitus content.

Diagnostic Plan

If reasonable concern is established based on the history (e.g., patient is inappetent, ingested a toxin, is vomiting frequently) or physical assessment (e.g., patient is listless, dehydrated, in pain), then a minimum data base of CBC, complete biochemical profile (or specific tests for evaluation of liver, kidney, pancreas, electrolytes), complete urinalysis (pre-treatment urine specific gravity extremely important for diagnosis of renal failure), and fecal examination is essential. The best way to screen for GI parasites on a single fecal sample is to run both a centrifugal flotation test and a Giardia antigen test. If only a single zinc sulfate centrifugal flotation is run, 25-30% of Giardia cases will be missed. T4 and both a heartworm antibody test and heartworm antigen test are considered routine baseline tests for vomiting cats (approximately 40% of cats with adult heartworms will have vomiting as a clinical manifestation of the disease). Survey abdominal radiographs are indicated if thorough abdominal palpation is not possible or suggests an abnormality (e.g., foreign body, pancreatitis, pyometra). Some institutions now routinely order 3 view abdomen films on patients presented for vomiting (both laterals and a VD). Unfortunately these tests are often not done early enough. Even if baseline results are unremarkable they are more than justified because they help to rule out serious problems at the outset (e.g., vomiting due to renal failure, diabetes mellitus, liver disease). Alternatively, any abnormalities provide direction for initial treatment and further diagnostics.

The decision for performing more in-depth diagnostic tests is based on ongoing clinical signs, response to therapy, and initial test results. These tests include baseline cortisol or ACTH stimulation to confirm hypoadrenocorticism in a patient with an abnormal Na:K ratio or to investigate for this disorder if electrolytes are normal, complete barium series or BIPS study (for gastric or intestinal foreign body, gastric hypomotility, gastric outflow obstruction, partial or complete intestinal obstruction), cPLI* or
**fPLI*** (canine and feline lipase immunoreactivity, respectively, for diagnosis of pancreatitis in dogs and cats), and **serum bile acids assay** (to assess for significant hepatic disease). **Barium swallow with fluoroscopy** is often necessary for diagnosis of hiatal hernia disorders and gastroesophageal reflux disease. **Serum gastrin levels** are run if a gastrinoma (Zollinger-Ellison Syndrome) is suspected.

**Pancreatitis:** Pancreatitis continues to be a challenging disorder to accurately diagnose, short of thorough direct examination and biopsy. Assays for amylase and lipase are of very limited value, especially in cats. In general, the following can be stated regarding the various diagnostic tests for pancreatitis:

### Value of the Various Diagnostic Tests for Pancreatitis

**Amylase/Lipase**
- of value as a screening test in dogs only
- need to be 3x or > above normal reference range in order to suggest pancreatitis
- normal does not rule-out pancreatitis

**Abdominal Ultrasound**
- highly specific, but not very sensitive, especially in cats

**Serum PLI**
- highly sensitive for pancreatitis

**Pancreatic Lipase Immunoreactivity (cPLI and fPLI)**
- Exocrine Pancreatic Insufficiency (EPI)
  - cPLI is reliably significantly decreased
  - cPLI is specific for EPI
- Chronic Renal Failure
  - Increased, but usually still within reference range
- Dogs with Biopsy Proven Pancreatitis
  - cPLI sensitivity is > 80%
  - currently recommended cutoff value for *dogs* is > 200 ug/L
  - results are also promising for cats

**Negative contrast gastrography.**
An excellent technique to quickly evaluate the stomach for presence of a nonradiopaque foreign body. Technique:
- Gastric tube, tranquilize as needed
  (definitely tranq cats)
- Dogs: 8-10 ml/lb air or stop if the animal shows discomfort
- Cats: 5 ml/lb air
- Remove tube, take rads immediately
  (left lateral, VD first)
- Can also use 60 ml carbonated beverage (e.g., Mountain Dew)

**BIPS are barium impregnated polyethylene spheres.** Traditionally, veterinarians have relied on barium liquid as the contrast agent of choice for gastrointestinal studies. However, recognized limitations of barium liquid have led to the development of barium-impregnated solid radiopaque markers for the diagnosis of motility disorders and bowel obstructions. Barium liquid contrast studies are of limited value in detecting hypomotility. Radiopaque markers can be used to investigate a number of common
gastroenteric problems. These spheres have been specifically validated for use in dogs and cats and are the only radiopaque markers with which there is extensive clinical experience in veterinary medicine. BIPS are manufactured in New Zealand and are now available in many countries. Information on availability of this product, including instructions on use and interpretation of radiographic studies, can be found at (www.medid.com; 800-262-2399).

**Ultrasonography** can be useful in the diagnostic work-up of a number of disorders that can cause vomiting. Among the problems that may be detected with ultrasonography are certain disorders of the liver (e.g., inflammatory disease, abscessation, cirrhosis, neoplasia, vascular problems), gall bladder (cholecystitis, choleliths, gallbladder mucocele), GI foreign bodies, intestinal and gastric wall thickening, intestinal masses, intussusception, kidney disorders, and others. Needle aspirations and/or biopsies can be done at many sites under ultrasound guidance.

One of the most reliable and cost efficient diagnostic tools currently available for evaluation of vomiting is **flexible GI endoscopy**. Endoscopy allows for direct gastric and duodenal examination, mucosal biopsy from these areas, and in many cases gastric foreign body retrieval. Endoscopy is considerably more reliable than barium series for diagnosis of gastric erosions, chronic gastritis, gastric neoplasia, and inflammatory bowel disease (a common cause of chronic intermittent vomiting in dogs and cats). It is stressed that biopsy samples should always be obtained from stomach and whenever possible small intestine regardless of gross mucosal appearance. Normal gastric biopsies may support gastric motility abnormalities, psychogenic vomiting, irritable bowel syndrome, or may be noncontributory (i.e., look elsewhere for diagnosis). Many dogs with vomiting due to inflammatory bowel disease have no abnormalities on gastric examination or biopsy. If only gastric biopsies are obtained, the diagnosis may be missed.

**Abdominal exploratory** is indicated for a variety of problems including foreign body removal, intussusception, gastric mucosal hypertrophy syndromes, procurement of biopsies, and for resection of neoplasia.

**fPLI** is available at Texas A&M University. Serum samples can either be sent directly to the GI Laboratory at Texas A&M University, or they can be forwarded to Texas A&M by a commercial laboratory.

**The address is:**
GI Lab at Texas A&M University  
College of Veterinary Medicine  
TAMU 4474  
College Station, TX 77843-4474  
979-862-2861  
www.cvm.tamu.edu/gilab
Diagnosis of Vomiting

Stage 1—Baseline Assessment
- History and physical examination
- Conservative vs. more aggressive diagnostic plan based on patient’s condition and clinician’s concern

Conservative Approach
- Fecal examination
- Selected diagnostics
- Specific/symptomatic therapy

Serious or Systemic Clinical Signs
- Complete blood count
- Complete biochemical profile
- Urinalysis
- Fecal examination
- Parvovirus test if indicated
- Survey abdominal radiographs
- T4 (cats)
- Heartworm antibody and antigen test (cats)
- Appropriate specific/supportive therapy

Stage 2—Further assessment (if vomiting persists or initial tests indicate further investigation should be performed promptly):

- Special Blood Tests
  - Corticotropin stimulation
  - cPLI or fPLI (pancreatitis)
  - Leptospirosis serology and/or lepto PCR
  - Bile acids assay (to assess liver function)
  - Coagulation tests (consider in patients with hematemesis/melena)

- Contrast Radiography
  - Barium contrast
  - Air contrast gastrogram (to further assess for gastric foreign body)
  - BIPS (barium-impregnated polyethylene spheres; with food to assess GI motility)

- Ultrasonography
  - Evidence of GI or non-GI disease
  - Aspirates or biopsy
  - Abdominocentesis

- Nuclear Scintigraphy
  - Transcolonic portal angiography for detection of portosystemic anomaly
  - GI motility study
Stage 3—Invasive Procedures

- **Flexible GI endoscopy** (minimally invasive)
  - Examination, biopsy, foreign body retrieval
- **Laparoscopy**
  - Biopsies (e.g., liver, pancreas)
  - Aspirates (e.g., gall bladder, lymph nodes, mass lesion)
  - Intestinal biopsy
- **Surgical intervention**
  - Therapeutic or exploratory with multiple biopsies

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a. GI parasites, including *Giardia*, should always be considered in dogs with acute or intermittent vomiting. Best baseline testing on a single fecal sample includes centrifugal flotation and *Giardia* antigen test.

b. Endoscopy is a diagnostic or therapeutic tool that can be used in Stage 1, Stage 2, or Stage 3, depending on the clinical situation.

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References

Drug Therapy for Vomiting in Dogs and Cats

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Pharmacologic Control of Acute Vomiting

Initial nonspecific management of vomiting includes NPO (in minor cases a 4-12 hour period of nothing per os may be all that is required), fluid support, and antiemetics. Initial feeding includes small portions of a low fat, single source protein diet starting 6-12 hours after vomiting has ceased. Drugs used to control vomiting will be discussed here.

The most effective antiemetics are those that act at both the vomiting center and the chemoreceptor trigger zone. Vomiting is a protective reflex and when it occurs only occasionally treatment is not generally required. However, patients that continue to vomit should be given antiemetics to help reduce fluid loss, pain and discomfort.

For many years I strongly favored chlorpromazine (Thorazine), a phenothiazine drug, as the first choice for pharmacologic control of vomiting in most cases. The HT-3 receptor antagonists ondansetron (Zofran) and dolasetron (Anzemet) have also been effective antiemetic drugs for a variety of causes of vomiting. Metoclopramide (Reglan) is a reasonably good central antiemetic drug for dogs but not for cats. Maropitant (Cerenia) is a superior broad spectrum antiemetic drug and is now recognized as an excellent first choice for control of vomiting in dogs. Studies and clinical experience have now also shown maropitant to be an effective and safe antiemetic drug for cats. While it is labeled only for dogs, clinical experience has shown it is safe to use the drug in cats as well. In addition to antiemetic effect, maropitant also provides visceral analgesic effect. Maropitant is also the first choice for prevention of motion sickness vomiting in both dogs and cats.

Metoclopramide (Reglan) is a gastric prokinetic drug that also has central antiemetic effect. Metoclopramide increases gastric and proximal small intestinal motility and emptying without causing acid secretion, decreases enterogastric reflux, and provides inhibition of the chemoreceptor trigger zone. The central antiemetic effect is mediated through antagonism of dopaminergic D2 receptors in the chemoreceptor trigger zone of the medulla to inhibit vomiting induced by drugs, toxins, metabolic disease, and acid-base imbalances. Metoclopramide is a less effective central antiemetic drug in cats than in dogs because serotonin receptors, rather than dopaminergic receptors, predominate in the CTZ of cats. For vomiting in cats, I generally usually use metoclopramide only if a prokinetic effect is desired. Chlorpromazine, dolasetron, ondansetron, or maropitant should be used as a first or second choice to control acute frequent vomiting in cats. Parvovirus can cause gastric hypomotility and therefore the promotility effects of metoclopramide may prove beneficial. However, maropitant, dolasetron, or ondansetron are more effective drugs than metoclopramide for managing vomiting caused by parvovirus. Further, maropitant also helps provide visceral analgesia and is the best single drug choice in parvo cases.

The recommended injectable dose of metoclopramide is 0.2 to 0.5 mg/kg IM or SC given TID to QID as needed. Metoclopramide can also be given IV as a constant rate infusion (1 - 2 mg/kg over 24 hours). Metoclopramide should not be used if gastric outlet obstruction or GI perforation is suspected, or in patients with a seizure disorder.
**Metoclopramide - Clinical Applications for Chronic Vomiting**

Several clinical applications for use of metoclopramide in dogs with chronic vomiting have been identified. These include gastric motility disorders, gastroesophageal reflux disease (GERD), primary or adjunctive therapy for antral and pyloric mucosal hypertrophy, and as treatment for nausea and vomiting caused by various other disorders. While cisapride is a superior prokinetic drug, metoclopramide is an effective drug and is often the first choice for prokinetic effect, with cisapride used as a second choice if metoclopramide is not effective. Other drugs that are sometimes used for prokinesis are low dose erythromycin and the H2-receptor blocker ranitidine (Zantac).

Gastric motility disorders have been recognized with increased frequency in veterinary medicine, but are still overlooked. Gastric stasis, characterized by abdominal discomfort, periodic bloating, borborygmus, nausea and vomiting may be associated with a number of clinical states that include inflammatory disorders (e.g., chronic gastritis, IBD), gastric ulcers, gastroesophageal reflux, infiltrative lesions (e.g., neoplasia), and chronic gastric dilatation. Metabolic disturbances that may cause gastric stasis include hypokalemia, hypercalcemia, acidosis, anemia, and hepatic encephalopathy. Short-term continued vomiting that is observed in some cases after apparent recovery from viral enteritis may be due to abnormal gastric motility. Transient (3 to 14 days) gastric hypomotility may also occur after gastric or abdominal surgery. Motility disorders with no organic cause may be best classified as idiopathic. For any of the disorders listed, the primary cause should be treated, and metoclopramide may be a valuable short-term adjunct to therapy in these cases, along with feeding low fat foods in divided amounts. Metoclopramide alternatively may be used as the primary treatment on a long-term basis for idiopathic hypomotility disorders. Metoclopramide has also been useful in treatment of dogs that have chronic vomiting characterized by episodes occurring routinely in the early morning and containing bilious fluid.

In general, patients less than 4.5 kg (10 lb) receive 2.5 mg per dose), 4.5 to 18 kg (11-40 lb) 5 mg per dose, and greater than 18 kg (40 lb) 10 mg per dose. Metoclopramide is given 30 to 45 minutes before meals and again at bedtime. Animals that require chronic medication may need only 1 to 2 doses daily. Because of its short half-life, the drug is not effective when given by intravenous or intramuscular bolus injection for purposes other than when only one treatment would be administered (i.e., to aid in evacuating the stomach if an anesthetic procedure in a non-fasted patient becomes necessary, pre-radiologic contrast study). Subcutaneous administration into fat may be of benefit when oral therapy is contraindicated and an intravenous line is not available.

Metoclopramide is less effective as a promotility drug than cisapride (see later discussion). While many animals with gastric hypomotility respond well to metoclopramide, some have a less than desired response. If a patient with a suspected gastric hypomotility disorder has an inadequate response to metoclopramide, cisapride should be tried next.

**Side Effects**

Some adverse effects may occur if metoclopramide is given in the usual therapeutic doses. Clients should be apprised of these before the medication is prescribed. These effects are uncommon in animals, and somewhat more common in humans.

Motor restlessness and hyperactivity may occur; and when observed, these signs usually begin 20 to 30 minutes after a dose and last 4 to 5 hours. The reaction can range from mild to quite dramatic. Alternatively, drowsiness and depression occasionally occur. Side effects are infrequent in cats, but clients have reported disorientation, frenzied behavior, and hiding tendencies associated with the
medication. Hospitalized animals may chew excessively at catheter sites or be more aggressive toward hospital staff. Sometimes these effects are subtle and nursing staff need to be observant. These side effects are reversible (diphenhydramine [Benadryl 2.2 mg/kg IV] or discontinuing the drug) but generally do not subside when lower doses are given. Unless side effects are infrequent, the use of metoclopramide should be discontinued if adverse reactions are seen. Cisapride does NOT cause these same type of adverse reactions. Metoclopramide crosses the blood brain barrier, cisapride does not.

In general, metoclopramide should not be given to epileptic patients. Other contraindications include evidence of significant mechanical obstruction, simultaneous use of anticholinergic agents (antagonism of metoclopramide’s effects), and pheochromocytoma.

**Ondansetron - Clinical Applications for Acute Vomiting**

Ondansetron (Zofran) is a potent antiemetic drug that has proven to be effective in both humans and animals for control of severe vomiting. It has been used in human cancer patients undergoing cisplatin therapy, a drug that frequently causes nausea and severe vomiting, with very good results. Ondansetron acts as a selective antagonist of serotonin S3 receptors (a principal mediator of the emetic reflex). S3 receptors are found primarily in the CTZ, on vagal nerve terminals, and in the gut in enteric neurons. The principal site of action of ondansetron is in the area postrema, but it also has some peripheral gastric prokinetic activity.

In my experience, ondansetron has produced very good results in either controlling or at least significantly decreasing the frequency of vomiting in dogs and cats with frequent or severe vomiting, including in dogs with severe parvovirus enteritis, in pancreatitis patients, and cats with hepatic lipidosis. The recommended dose is 0.5 to 1 mg/kg IV given as a slow push every 6 to 12 hours (based on patient response). Frequently dogs that appear quite distressed due to nausea and vomiting look much more relaxed and comfortable within 15 minutes of receiving ondansetron. There are no reports of any significant side effects such as diarrhea, sedation, or extrapyramidal signs in human and animal trials. While Zofran was quite expensive for many years, it came off patent in 2007 and is now more affordable for use at any small animal hospital. *Currently, however, my top antiemetic drug of choice is maropitant (Cerenia), because it is a highly effective antiemetic drug but also because it provides visceral analgesic effects as well.* Animals with significant liver disease may be best managed with ondansetron or dolasetron, as maropitant should be used with caution in animals with significant hepatic dysfunction (although it is not contraindicated – some clinicians have used maropitant successfully and safely in animals with liver disease).

**Dolasetron**

Dolasetron (Anzemet) is also a 5-HT3 receptor antagonist antiemetic drug, with action similar to ondansetron. It is a slightly less expensive alternative to ondansetron and only needs to be administered once daily. Indications are the same as for ondansetron, namely, for control of frequent vomiting that is poorly responsive to lesser expensive front-line antiemetic drugs. The dose is 0.5-1 mg/kg IV once daily. Dolasetron is generally well tolerated in animals.

**A NEWER ANTIEMETIC DRUG FOR DOGS**

Most drugs used to control vomiting in animals have been developed for use in humans. There has been a need for a broad-spectrum antiemetic drug for use in animals that is effective in a variety of situations, has a rapid onset of action, is safe and affordable, and is available in both injectable and oral preparations. **Maropitant citrate (Cerenia)** is a newer broad-spectrum antiemetic drug that is indicated for the treatment of acute vomiting in dogs. Maropitant is a neurokinin receptor antagonist that blocks
the pharmacologic action of the neuropeptide substance P in the central nervous system. Substance P is found in significant concentrations in the nuclei comprising the emetic center and is considered a key neurotransmitter involved in emesis. By inhibiting the binding of substance P within the emetic center, maropitant provides broad-spectrum effectiveness against both neural and humoral causes of vomiting. Clinical trials and recent clinical experience, since August 2007 when the drug was released for use in the U.S., have shown maropitant to be very effective for control of a variety of causes of acute vomiting in dogs. It is administered as a once-daily injection (0.45 mg/lb [1 mg/kg] SC for dogs), which is a significant advantage over many other antiemetic drugs, and has a rapid onset of action. Maropitant is also available in tablet form for outpatient use, which makes it a very attractive choice for use in small animal practice. It is the drug of choice for dogs with motion sickness.

**CAUTION:** Use at a reduced dose for animals with significant hepatic dysfunction, OR select an alternative antiemetic for animals with liver disease – e.g., ondansetron or dolasetron.

**The issue of stinging on injection:** Information from clinical experience and studies indicates that there is less likelihood for stinging to occur with maropitant injections when the product is kept refrigerated. The current guidance is that the solution should be kept refrigerated and drawn up and injected right away at refrigerated temp.

**CATS:** Studies have now been done using maropitant in cats and some clinicians in general practice have been using it since 2008. In May 2012 Cerenia was approved for use in cats and also in puppies as young as 8 weeks of age.

**Recommended dose of maropitant for cats:**
- **Injectable:** 0.5-1 mg/kg SC or IV (give SLOWLY over 60-90 seconds if administering IV)
- **Oral:** (1 to 2 mg/kg). This is the starting dose recommended for prevention of motion sickness in cats as well; i.e., somewhat lower than the canine dose for motion sickness.

**How long can Cerenia be used on a consecutive days schedule?**
The label states that Cerenia should not be given for more than 5 consecutive days (injectable or oral at the anti-emesis dose) and for 2 days at the motion sickness prevention dose. However, experience has shown that in some patients Cerenia has been used safely and effectively on a longer term basis (anecdotal reports, e.g., patients with neoplasia or renal disease that were experiencing ongoing nausea, vomiting, and inappetence). Many of these patients have a much better quality of life while on Cerenia, as they have less nausea and vomiting and a much better appetite. There are cats that have been treated with a daily oral dose for months to several years. Use of Cerenia in this fashion is being investigated further.

A study was presented at the Veterinary Cancer Society (VCS) meeting in San Diego Oct. 29-November 1, 2010, and then subsequently at the ACVIM Forum in Denver in June 2011: **Pharmacokinetics of maropitant citrate dosed orally to dogs at 2 mg/kg and 8 mg/kg once daily for 14 consecutive days.** Two groups of eight healthy beagle dogs were administered maropitant citrate at 2 or 8 mg/kg orally once daily for 14 days. Concentrations of maropitant and its metabolite were measured in plasma using a LC-MS/MS assay. Pharmacokinetic parameters were estimated using non-compartmental pharmacokinetic techniques and a modeling approach was used to estimate steady-state.

Results: The model estimate for the number of doses required to reach 90% of steady-state was 4.30 for 2 mg/kg and 8.09 for 8 mg/kg. Four dogs experienced a single dose of vomiting.
Conclusions: Dosing maropitant citrate beyond the label duration was well tolerated by healthy dogs. During the 14 days of dosing there was accumulation, however, steady-state was reached after approximately 4 doses for daily 2 mg/kg dosing and 8 doses for daily 8 mg/kg oral dosing.

Use of Oral Maropitant (Cerenia)

- Confident there is no GI foreign body (i.e., do not use ongoing antiemetic therapy if there could be a foreign body lodged in the GI tract)
- Prevent vomiting during cyclosporine, azithromycin, or other drug induction period (use for 3-5 days in conjunction with the start of a drug that might cause vomiting)
- Vomiting flare-ups in IBD patients (or other chronic disorders)
- Pancreatitis, parvovirus, etc for a few days after vomiting is fairly well controlled with injectable maropitant. Excellent control of nausea may help improve appetite and earlier food intake
- Prevention of vomiting in chemotherapy patients
- Prevention of motion (“car”) sickness
- Renal disease patients – and perhaps chronic use (these patients may benefit tremendously and we have observed many patients that eat better, do not vomit or exhibit nausea, and feel better overall. Studies are ongoing).

Cisapride

Cisapride is a potent GI prokinetic drug and is superior in action to metoclopramide. It is no longer on the market for use in humans, as of 2000, because of an association with fatal arrhythmias. There are no reports of similar complications existing in dogs and cats, however, and cisapride continues to be readily available to veterinarians through compounding pharmacies.

Cisapride has broader promotility effects than metoclopramide (e.g., cisapride has demonstrated excellent efficacy in management of colonic inertia and small intestinal ileus). In contrast to metoclopramide, which has central effect at the CRTZ in addition to its peripheral effects, cisapride has no known direct antiemetic properties. Another contrast is that metoclopramide’s prokinetic effect is most significantly on the stomach. It is NOT a reasonable choice for treatment of small intestinal ileus.

The most relevant uses of cisapride in animal patients include treatment of gastroparesis, especially in patients that experience significant side effects from metoclopramide (e.g., hyperactivity and other dystonic reactions) or where metoclopramide is not sufficiently effective, idiopathic constipation, gastroesophageal reflux disease (if H2-receptor antagonists or proton pump inhibitors and dietary management alone are not effective), and postoperative ileus.

Cisapride is extremely well tolerated by animal patients. I have used cisapride in dogs and cats that have experienced neurologic side effects from metoclopramide. I have observed no adverse reactions to cisapride in any of these patients, even in those whose side effects to metoclopramide included very bizarre behavior changes. The suggested dose of cisapride is similar to what has been recommended for metoclopramide (see earlier discussion).
Introduction
Pancreatitis is a common disorder of dogs, but due to challenges in establishing a definitive diagnosis, the true incidence of pancreatitis seen in clinical practice is not known. Mild cases of pancreatitis that do not show “classical” signs such as acute vomiting and abdominal pain can be very difficult to diagnose. Conversely, pancreatitis is just one of many causes of vomiting and clinicians are challenged daily to try to determine a specific cause in patients presented with vomiting and other clinical signs. Most dogs have acute pancreatitis and most cats have chronic pancreatitis. Clinical presentation and diagnostic criteria differ between species and type of pancreatitis. Acute pancreatitis is potentially reversible but can also be fatal while chronic pancreatitis generally has irreversible changes but is rarely fatal.

Acute Pancreatitis in the Dog
There is confusion and controversy regarding pathogenesis, diagnosis, and treatment of acute pancreatitis in the dog. The spectrum of clinical disease can range from mild signs to those which are fulminant and frequently fatal. It is the development of multisystemic abnormalities that separates mild from severe, potentially fatal pancreatitis. Pancreatitis can be broadly categorized as acute, recurrent acute, or chronic. Medical management is the main form of treatment in most cases. Surgical intervention in diagnosis and management of pancreatitis is not often undertaken and is generally reserved for complex cases of pancreatitis (i.e., acute necrotizing pancreatitis, pancreatic abscess, pancreatic pseudocyst, and generalized peritonitis secondary to pancreatitis).

Etiology
The etiology of pancreatitis is generally unknown. Factors that influence development of pancreatitis include high fat diet, obesity, hyperlipoproteinemia, drugs (e.g., thiazides, furosemide, tetracycline, L-Asparaginase, azathioprine, corticosteroids), duodenal reflux into pancreatic ducts, pancreatic duct obstruction (e.g., parasites, calculi, neoplasia, inflammation, surgery), hypercalcemia, trauma, and pancreatic ischemia (e.g., shock, GDV).

Risk Factors
Risk factors identified in patients with acute pancreatitis include breed (Yorkshire and Silky terrier, toy poodle, miniature Schnauzer, nonsporting breeds), overweight body condition, small breed size, prior gastrointestinal disease, ingestion of garbage and table scraps, diabetes mellitus, hyperadrenocorticism, hypothyroidism and a history of surgery within two weeks prior to development of pancreatitis.

Diagnosis
Acute pancreatitis is one of the most difficult diseases to diagnose. There is no one definitive diagnostic test for pancreatitis, except for histopathology. Biopsy procedures, however, are not commonly done in dogs with suspected acute pancreatitis. Clinical diagnosis is based on a combination of history, physical
examination, and compatible clinicopathologic and imaging findings. The clinician’s index of suspicion is important and keeping an open mind to various possibilities is essential (i.e., avoid “tunnel vision”), since multiple organs can be involved concurrently. When vomiting is associated with systemic signs or is persistent the clinician must differentiate metabolic, polysystemic, toxic, and infectious causes from abdominal causes. Pancreatitis can be “diagnosed” when it is not actually present and easily missed when it is present. Most patients with suspected pancreatitis are managed based on the patient’s condition (mild vs. severe signs) and the various test results and closely monitoring response to therapy.

**Laboratory Findings**

Laboratory findings in dogs with pancreatitis are quite variable and to some extent parallel the severity of the clinical disease and may be representative of multiple organ system involvement in patients with severe pancreatitis. Laboratory results might include leukocytosis, azotemia (prerenal and renal), increases in ALT, AST and ALP, icterus, hyperglycemia, hypokalemia, acid base changes, DIC, and increases in amylase, lipase, concentration of trypsin-like immunoreactivity (cTLI), and pancreatic lipase immunoreactivity (cPLI).

Hematologic findings are quite variable, ranging from mild neutrophilia and slightly increased hematocrit (dehydration) to marked leukocytosis with a left shift, leukopenia with a degenerative left shift, and anemia. However, some dogs with even moderate to severe pancreatitis can have a normal leukogram. Platelet numbers should be assessed. If there is thrombocytopenia, tests for DIC should be performed (one stage prothrombin time (OSPT), activated partial thromboplastin time (APTT), fibrin degradation products (FDP or D-Dimer), and antithrombin III.

Urinalysis allows azotemia to be characterized as prerenal or renal and provides key information for ruling-in or out other disorders (e.g., diabetes mellitus [glucosuria or ketonuria], pyelonephritis which can cause vomiting and abdominal pain [absence of white cell casts or bacteria helps rule-out]).

Serum amylase and lipase activities are insensitive and nonspecific for pancreatitis. Specificity for both tests is only around 50%. Amylase and lipase are found in the oral cavity, GI tract, pancreas, and liver. Dogs with gastritis or intestinal foreign bodies can have a significantly elevated lipase but no gross evidence of pancreatitis. Lipase is produced by the gastric mucosa which explains why it can be increased in disorders of gastric inflammation. Increases in amylase and lipase can be seen in renal disease as well (decreased clearance). Significantly increased amylase or lipase can certainly suggest the possibility of pancreatitis, but, some dogs with even severe pancreatitis have demonstrated normal levels. All things considered, amylase and lipase assessment are not very useful in the diagnosis of pancreatitis.

Clinical factors that help support a diagnosis of pancreatitis include high index of suspicion, acute or chronic vomiting, weakness, abdominal pain, dehydration, diarrhea, fever and shock. There may be a history of recent dietary indiscretion or drug administration. There is no apparent sex predilection. Middle-age to older dogs (greater than 5 years) that are overweight are at higher risk.

Currently, the combination of a quantitated cPLI assay and ultrasonography are considered to provide the most meaningful noninvasive diagnostic information in the clinical setting for determination of whether or not pancreatitis is present. The immunoreactive canine pancreatic lipase assay (cPLI) is the most sensitive assay currently available. Use of the immunoassay allows for the specific measurement of lipase originating from the exocrine pancreas. The sensitivity for serum cPLI concentration is over 85%. However, the specificity is around 75%, meaning that around one-fourth of animals without clinical
Pancreatitis may have a positive PLI assay. Test interpretation is as follows: If the cPLI is > 200 ug/L pancreatitis should be included in the differential diagnosis and the diagnosis is confirmed through other diagnostics. If the cPLI is normal the patient does not likely have pancreatitis and the clinician should continue to look for another disease. If pancreatitis is unlikely, it is not warranted to run a PLI as false positives are possible. cPLI can be used for diagnosing pancreatitis in dogs with renal failure. A study has shown that, while cPLI is elevated in dogs with renal failure compared with healthy dog levels, it is usually still within the reference range (in the higher end of the reference range), but not above the currently recommended cutoff value for pancreatitis. Also, the longterm oral administration of prednisone does not affect cPLI values.

Radiology
The pancreas is shaped like a boomerang. There are three parts: the right lobe, which lies adjacent to the descending duodenum; the body, which lies at the junction between the pylorus and duodenum; and the left lobe, which lies adjacent to the greater curvature of the stomach. The pancreas is not normally seen.

With a diseased pancreas, the duodenum may be displaced ventrally. On the ventrodorsal view, there is usually lateral (right) displacement of the descending duodenum and the pylorus is displaced to the left (widening of the duodenal pyloric angle). The transverse colon as well as ascending colon may be displaced centrally and caudally. Fluid and gas distention of the stomach, duodenum and colon may be present. Localized loss of abdominal detail (ground-glass appearance) may occur with inflammation of the pancreas. The most common change radiographically on survey films is actually no change at all.

Changes that may occur and be visualized relative to pancreatic disease and an upper GI series include fixed position and shape to the duodenum; widened proximal duodenal flexure (the angle between the pylorus and duodenum); and thickening and rigidity of the duodenum, pylorus, and greater curvature of the stomach. Gastric outflow obstruction and duodenal distention (ileus) may also be visualized.

Ultrasonography
Ultrasonography is the imaging method of choice for evaluation of the pancreas in small animals. It can provide information about the size, shape, and contour of the pancreas and may suggest the presence of inflammation, abscess formation, or neoplasia. Ideally, patients should be fasted before abdominal ultrasonography to minimize interference from GI gas.

There are several limitations to pancreatic ultrasonography:

- The normal pancreas is not always seen as a discrete structure; thus, it is actually the pancreatic area, and not the organ itself, that must be examined.
- Ultrasonography lacks specificity. For the most part, ultrasonographic findings do not allow differentiation between inflammatory and neoplastic processes.
- The proximity of the pancreas to gas in the stomach, colon, and duodenum may prevent complete and accurate evaluation of the pancreatic region.

Despite these disadvantages, ultrasonography can provide valuable diagnostic information in most animals with inflammatory or neoplastic diseases of the pancreas if it is done properly and with patience. The healthy pancreas is difficult to image as a distinct organ. Therefore, familiarity with the anatomy of adjacent structures is crucial to successful evaluation of the pancreatic area.
The left lobe of the pancreas is dorsocaudal to the stomach and dorsocranial to the transverse colon. Its distal aspect can be visualized cranial to the left kidney and medial to the spleen. The pancreatic body lies caudal to the pylorus. It is ventral to the portal vein and the caudate process of the liver and craniomedial to the right kidney. The right lobe of the pancreas is found dorsomedial to the descending duodenum, ventral to the right kidney, and ventrolateral to the portal vein. Both the cranial and caudal pancreaticoduodenal veins are located in the parenchyma of the right lobe and run parallel to the descending duodenum.

Normally, pancreatic parenchyma has a homogeneous echotexture. The pancreaticoduodenal vein may be apparent in the right lobe. The left lobe of the healthy pancreas occasionally is seen in the triangular region defined by the spleen, stomach, and left kidney. Gas in the adjacent stomach and transverse colon makes imaging of all but the most distal portion of the left lobe difficult.

**Ultrasonography Findings in Pancreatitis**

Ultrasonography has proven to be a reliable tool for identifying changes associated with pancreatic inflammation and is currently considered the imaging method of choice for evaluating pancreatitis and pancreatic neoplasia.

Ultrasonography provides several distinct advantages in the diagnostic evaluation of pancreatitis:

- It can identify abnormalities in animals with pancreatitis. In many cases, it also provides information about the severity of inflammation.
- It is noninvasive and can be repeated frequently, providing a means of following disease progression and/or resolution.
- It allows evaluation of peripancreatic structures, such as the biliary system, duodenum, and stomach, which are often secondarily involved in acute pancreatitis.
- It is an important tool for identifying complications of pancreatitis, such as biliary obstruction, abscess formation, and pseudocyst formation.

The ultrasonographic findings that characterize pancreatitis represent changes in either the pancreas itself or in peripancreatic structures. The most common ultrasonographic abnormality noted in animals with pancreatitis is a hypoechoic mass dorsomedial to the descending duodenum and caudal to the stomach. This mass represents the inflamed pancreas, and although its overall echogenicity is usually decreased, it may sometimes appear inhomogeneous.

The peripancreatic mesentery and associated fat are often hyperechoic but may have variable echogenicity. The edges of the pancreas are distinct if the inflammation is mild but become poorly defined when severe pancreatitis is present, probably as a result of the edema, necrosis, and hemorrhage that accompany severe pancreatic inflammation. The overall pancreatic image tends to become better defined with more distinct edges as inflammation subsides. Improved resolution of the pancreatic margins may be partially related to saponification of surrounding fat. The ultrasonographic changes associated with chronic pancreatitis are often less severe than those associated with acute pancreatitis, although it is difficult to differentiate one condition from another based on ultrasonography alone.

Changes in peripancreatic structures also contribute to the ultrasonographic diagnosis of pancreatitis. Free peritoneal fluid secondary to focal peritonitis may be apparent in the pancreatic region. The descending duodenum typically becomes dilated and fluid-filled, with thickened walls and no apparent peristalsis. With severe duodenitis, the duodenal wall may have a corrugated appearance.
Potential complications of pancreatitis include pseudocyst or phlegmon formation, abscess formation, and biliary obstruction. Pancreatic phlegmons are edematous masses of indurated pancreas and adjacent tissue with varying degrees of necrosis that develop within several days of the onset of acute pancreatitis. They may resolve spontaneously or may cause persistent fever and abdominal pain. Pancreatic abscesses result from secondary infection of necrotic pancreatic tissue or of a phlegmon. Ultrasonographically, pancreatic phlegmons and abscesses appear as pancreatic masses of mixed echogenicity and variable size. Gas in a pancreatic mass, identified as an echogenic interface with reverberation, suggests abscess formation.

Pancreatic pseudocysts appear ultrasonographically as primarily anechoic masses but they may contain some internal echoes. They cause mild acoustic enhancement of distal structures. Unfortunately, ultrasonography cannot usually differentiate between pancreatic phlegmons, abscesses, or pseudocysts. Extrahepatic biliary obstruction is another complication of acute pancreatitis that may necessitate surgery.

**Cytology**

Fine needle aspiration of suspected areas of pancreatitis and suppurative inflammation may help support the diagnosis.

Abdominocentesis may be helpful if effusion is present. Suppurative inflammation is the typical finding, but it is rarely septic. In addition, abdominal fluid analysis combined with measurement of abdominal fluid lipase concentration is helpful. Abdominal fluid lipase concentration higher than serum lipase concentration supports the diagnosis of pancreatitis in many cases.

**Histopathology**

Biopsy provides the definitive diagnosis. Surgery or laparoscopy is generally required to obtain a diagnostic biopsy. Pancreatic biopsy techniques are generally safe, given careful tissue handling. The primary consideration in obtaining biopsy samples is whether or not a patient with suspected acute pancreatitis is a safe anesthetic risk and whether or not the step of obtaining tissue samples from a patient will add significantly contributory information to patient management to justify any risks and also costs related to performing a biopsy procedure. Most patients that undergo pancreatic biopsy are examined during the course of a laparoscopic or surgical exploratory procedure in which various areas of the abdomen are being examined and biopsied (e.g., liver, intestines).

Although acute pancreatitis is not generally considered a surgical condition patients progressing to a more severe necrotizing pancreatitis with pancreatic abscess and peritonitis may be candidates for exploratory laparotomy.

**Medical Management**

Initial treatment of pancreatitis should be supportive and is tailored for the individual patient, taking into consideration any abnormalities detected on physical examination and testing. Basic therapy involves correction of fluid and electrolyte imbalance, control of nausea and vomiting, pain management, nutritional considerations (early feeding is the goal), and the control of secondary complications.

Management considerations for severe and often life-threatening acute pancreatitis include pancreatic rest in the form of fasting for one to three days for vomiting patients (try to minimize the fasting period), fluid and electrolyte therapy and in some cases colloid administration, and antibiotics for severe cases or
whenever there is evidence of sepsis or concurrent liver disease (antibiotics are not indicated for all cases of pancreatitis). Plasma or whole blood may be indicated in some cases. Antiemetics are given to control vomiting and decrease fluid loss and enhance patient comfort (i.e., control nausea and hopefully allow the patient to rest more and eat earlier). Maropitant (Cerenia) given at 1 mg/kg once daily SC or IV (slowly over a 60-90 second period) is a highly effective antiemetic drug that also provides visceral analgesia, making it a very attractive antiemetic drug to use in patients that have visceral pain. Use of opioid analgesics should be strongly considered in the patient with pancreatitis even if there is no outward evidence of abdominal pain (e.g., buprenorphone for mild pain; and morphine, hydromorphone, or fentanyl for moderate to severe pain). Constant rate infusion of pure opioid drugs is an ideal way to more effectively control pain consistently hour by hour. Lidocaine infusions can also be administered when additional pain control is needed. Careful attention to detail on pain control is absolutely essential and too often inadequate therapy is administered in this area.

Why is Early Feeding Important?
Nutritional support of critically ill patients has long been considered a supportive measure of low priority. Recent advances in both human and veterinary medicine have demonstrated that nutritional support is an important therapeutic modality and can aid in the management of many diseases. In diseased states, the inflammatory response triggers alterations in cytokines and hormone concentrations and shifts metabolism toward a catabolic state. With a lack of food intake, the predominant energy source is derived from accelerated proteolysis, which in itself is an energy-consuming process. Thus, critically ill animals may actually preserve fat deposits in the face of lean muscle tissue loss. The goal of nutritional support in these catabolic patients is to feed the catabolism with exogenous sources of protein and fat thereby sparing endogenous protein which is critical to recovery.

Malnutrition in veterinary patients is thought to increase morbidity and mortality, but this has not been statistically quantified. However, nearly every body system is affected by negative energy balance. In the GI tract transit times increase, absorptive capabilities decrease, and there is an increased risk of bacterial translocation. In the kidneys, excretion of urinary calcium and phosphorus increases, ability to excrete acid decreases, gluconeogenesis increases and glomerular filtration rate decreases. Malnutrition has been documented to decrease humoral immunity and barrier function (skin and mucosal surfaces), inflammatory response, leukocyte motility and bactericidal activity. Patients are at risk for pulmonary complications as a result of decreased response to hypoxia, decreased lung elasticity, and secretin production, altered permeability and decreased tidal volume. Cardiovascular complications include increased incidence of arrhythmias and decreased weight of the heart muscle. Protein calorie malnutrition may also alter the normal or expected metabolism of certain drugs, which may increase or decrease their therapeutic effect even when given at recommended dosages.

Feeding Dogs with Pancreatitis
Critical illnesses associated with gut barrier dysfunction include severe acute pancreatitis, inflammatory and non-inflammatory bowel disease, severe burn injury, multisystem trauma and high risk surgery. Gut barrier dysfunction can exacerbate critical illnesses by leading to bacteremia, endotoxemia, systemic inflammatory response syndrome and multiple organ dysfunctions. The nutritional management of these disorders has traditionally included an initial period of starvation, ranging from 3 to 7 days. However, the most important stimulus for intestinal mucosal growth, repair, and integrity is the presence of nutrients within the gut lumen. The absence of luminal nutrients leads to marked small intestinal mucosal atrophy and suppressed crypt cell proliferation, marked reductions in gut-associated lymphoid tissue cell mass and function, increased intestinal permeability to bacteria and toxins, and
enhanced pro-inflammatory cytokine generation and acute-phase responses. For pancreatitis the recommendation for starvation was based on the belief that “strict pancreatic rest” prevents stimulation of exocrine pancreatic secretion, thus protecting against autodigestion. Recently, this recommendation has come into question. Studies in dogs, rodents and man have demonstrated that exocrine pancreatic excretion is already inhibited by the inflammation associated with pancreatitis and feeding has no impact on exocrine pancreatic secretion. A systematic review of human literature found that patients with acute pancreatitis receiving enteral nutrition have fewer episodes of death, systemic infections, multiple organ failure and operative interventions. This data suggests that enteral nutrition (EN) should be considered the standard of care for patients with acute pancreatitis requiring nutritional support.

Recent studies support the recommendation that one of the management priorities in treating acute pancreatitis should be to feed early and enterally. Prolonged fasting leads to immunosuppression, decreased wound healing and increased bacterial translocation, sepsis and decreased survival. Ideally, canine patients should not be held NPO for more than 48 to 72 hours including the time they were anorectic prior to presentation. Once vomiting is adequately controlled, feeding should be instituted. Enteral feeding improves enterocyte health and immune function. Documented benefits of maintaining a healthy gut barrier function include reduced mucosal permeability, reduced incidence of bacteremia, endotoxemia and septic morbidity, attenuation of the acute phase response and reduced incidence of multiple organ failures, reduced catabolism and preservation of a positive nitrogen balance and perhaps most importantly improved clinical outcomes. Early enteral nutrition is superior to both starvation and total parenteral nutrition in critical illnesses associated with gut barrier dysfunction.

One recent study comparing enteral and parenteral nutrition in dogs with acute pancreatitis documented a significantly greater number of vomiting or regurgitation episodes in dogs receiving parenteral nutrition (PN) versus enteral nutrition. Additionally dogs receiving enteral nutrition did not demonstrate any noticeable postprandial pain. There were more catheter-related complications in the PN group. The authors concluded early EN delivered proximal to the pylorus is well tolerated in dogs with severe pancreatitis and resulted in fewer complications than PN.

Depending on the situation, enteral feeding can be done either per os or via nasoesophageal or esophagostomy tube (see below for tube placement procedure details). Currently, prepyloric feeding via esophagostomy tube seems to be well tolerated and this route is certainly easier than placing a jejunostomy tube. Elemental diets or polymeric diets can be fed via tube. Of the liquid diets, Vanilla Ensure is specifically preferred in canine pancreatitis patients because it is lower in fat compared to other commonly used liquid diets (e.g., Clinicare, chocolate Ensure). Vanilla Ensure is not designed for longterm feeding but it is fine for the initial feeding stage in pancreatitis. When beginning to feed solid food the diet should be a carbohydrate-rich and low-fat food given as small frequent meals. Continued fat restriction (longterm maintenance feeding) is usually recommended for dogs that have had more than one bout of pancreatitis. For dogs with a single bout of pancreatitis, a low fat diet should be few for the first month or two and then if desired the patient can usually be returned to its regular diet if so desired.

Nasoesophageal tube placement
Nasoesophageal intubation is an easy, effective, and efficient means of providing enteral nutritional support. The availability of small bore, soft polyvinyl and silastic feeding tubes (i.e., 3.5 and 5 French 36 inch tubes, Argyl or National Catheter Company) and low viscosity, nutritionally complete liquid diet formulations, and patient tolerance of tube placement has made nasoesophageal tube placement a
popular avenue for feeding malnourished patients. Nasoesophageal tube placement is indicated in any patient with protein-calorie malnutrition that will not undergo oral, pharyngeal, esophageal, gastric, or biliary tract surgery.

**Technique:** Local nasal anesthesia, sedation, or light general anesthesia may be necessary for placement of a nasoesophageal/ nasogastric tube in dogs and cats. In the majority of cases, topical anesthetic or light sedation is all that is necessary for proper tube placement.

**Anesthesia for dogs:** Place 0.5-1 ml of 0.5% proparacaine hydrochloride into the nasal cavity and tilt the head upwards for several seconds to allow adequate dwell time. Repeat application of local anesthetic before attempting to pass the nasoesophageal tube. If the patient does not tolerate passage of the tube, sedation or light general anesthesia may be required.

**Tube size:** Select an appropriate size feeding tube
- Dogs - 2 to 15 kg  5 French X 91 cm
- Dogs - >15 kg  8 French X 91 cm

Estimate the length of tube to be placed in the esophagus or stomach by placing the tube from the nasal planum along the side of the patient to the 7th or 8th intercostal space (i.e., to ensure mid-esophageal placement). It is our recommendation that the feeding tube not pass through the lower esophageal sphincter, as this may result in sphincter incompetence and esophageal reflux of hydrochloric acid and other gastric content, potentially causing esophagitis. Place a tape marker on the tube once the appropriate measurement has been taken. Lubricate the tip of the tube with 5% lidocaine viscous prior to passage. Hold the patient’s head in a normal functional position (i.e., avoid hyperflexion or hyperextension).

**Tube placement:** Identify the prominent alar fold, and direct the tube from a ventrolateral location in the external nares, to a caudoventral and medial direction as it enters the nasal cavity. When the tube is introduced 2 - 3 cm inside the nostril, feel it contact the median septum at the floor of the nasal cavity. At this moment, push the external nares dorsally to facilitate opening the ventral meatus, elevate the proximal end of the tube, and continue to advance the tube into the oropharynx and esophagus.

**Confirming esophageal placement:** Confirm esophageal placement by injecting 3 to 5 ml of sterile saline through the tube and eliciting a cough or placing 6 - 12 ml of air and auscultating for borborygmus at the xiphoid. Placement can also be confirmed by taking an x-ray of the chest. If the patient requires general anesthesia, visually confirm tube placement in the esophagus.

**Securing the tube to the patient:** In the dog, the tube is secured to the lateral aspect of the nose and dorsal nasal midline with an encircling suture and Chinese finger trap or cyanoacrylate glue or both depending upon the patient’s level of activity. An Elizabethan collar should be used immediately postoperatively and until it is determined that the patient will tolerate the presence of the tube.

**Tube management:** Place a column of water in the tube and cap it when not in use; this prevents intake of air, reflux of esophageal contents, and occlusion of the tube by diet. Three and 5 French feeding tubes come with appropriate size caps. Nasoesophageal/ nasogastric tubes can be left in place for several weeks, are well tolerated, easily removed, the patient can drink and swallow around the tube, and repeated orogastric intubation is prevented.
**Esophagostomy Tube Placement**

**Indications:** Esophagostomy tube feeding is indicated in anorexic patients with disorders of the oral cavity or pharynx, or anorexic patients with a functional gastrointestinal tract distal to the esophagus.

**Contraindications:** Esophagostomy tube placement is contraindicated in patients with a primary or secondary esophageal disorder (e.g., esophageal stricture, after esophageal foreign body removal or esophageal surgery, esophagitis, megaesophagus) and patients with a history of vomiting.

**Advantages:** Advantages of esophagostomy tube feeding include ease of tube placement, tubes are well tolerated by the patient, large bore feeding tubes can be used allowing use of blenderized diets, tube care and feeding is easily performed by the client, patients can eat and drink around the tube, and tube removal can be performed any time after placement. Esophageal tube placement eliminates local pharyngeal irritation, coughing, laryngospasm, or aspiration occasionally associated with pharyngostomy tubes.

**Disadvantage:** The major disadvantage of use of an esophagostomy tube is the need for general anesthesia and endotracheal intubation during placement.

**Placement Technique:** Provide general anesthesia. Place the patient in right lateral recumbency with the left side uppermost. The tube can be placed on either the right or left side of the midcervical region, however, the esophagus lies slightly left of midline making left sided placement more desirable. Aseptically prepare the lateral midcervical area from the angle of the mandible to the thoracic inlet. Slightly extend the neck and hold the mouth open with a mouth speculum.

Pre-measure and mark a 20 to 24 French feeding tube from the level of the mid-cervical region (i.e., exit point of feeding tube) to the level of the seventh or eighth intercostal space; ensuring mid- to caudal esophageal placement. Make certain the tube does not cross the lower esophageal sphincter (LES) as this may cause sphincter incompetence, gastric reflux of acid, esophagitis and subsequent vomiting or regurgitation. Prior to tube placement, enlarge the two lateral openings of the feeding tube to encourage smoother flow of blended diets.

**Eld Esophagostomy Tube Placement Technique**
The following technique requires the use of an Eld feeding tube placement device. Place the oblique tip of the instrument shaft through the oral cavity and into the esophagus to the level of the mid cervical region (i.e., equal distance between the angle of the mandible and thoracic inlet) and palpate the tip as it bulges the cervical skin. Make a small skin incision over the device tip. Activate the spring loaded instrument blade until it penetrates esophageal wall, cervical musculature, subcutaneous tissue and is visible through the skin incision. Carefully enlarge the incision in the subcutaneous tissue, cervical musculature and esophageal wall with the tip of a #15 scalpel blade to allow penetration of the instrument shaft. Place a 2-0 Nylon suture through the side holes of the feeding tube and through the hole in the instrument blade. Tighten the suture until the tip of the instrument blade and feeding tube tip are in close apposition. Retract the instrument blade into the instrument shaft so the feeding tube tip just enters the instrument shaft (i.e., deactivating the instrument blade. Place sterile water-soluble lubricant on the tube and instrument shaft. Retract the instrument and pull the feeding tube into the oral cavity to its predetermined measurement. Remove the 2-0 Nylon suture to free the feeding tube from the instrument. Place a stylet through one of the side holes of the feeding tube and against its tip (do NOT use a stylet when placing an E-tube in cats). Lubricate the feeding tube and advance it into the esophagus until the entire oral portion of the tube disappears. Gently retract the stylet from the oral
cavity being careful to ensure its release from the feeding tube. If you encounter resistance and cannot pass the feeding tube into the esophagus you may have engaged the endotracheal tube. If this happens remove the feeding tube and replace it under direct visualization. Secure the tube to the cervical skin with a Chinese finger-trap suture of #1 Novafil.

**Curved Carmalt Hemostat Technique**
A curved Carmalt hemostat can be used to place an esophagostomy feeding tube. The curved Carmalt forceps is placed into the patient’s oral cavity with the curve of the hemostat directed toward the cervical region. The Carmalt is directed to a point equidistant between the ramus of the mandible and point of the shoulder midway between the dorsal and ventral aspect of the neck. The hemostat is pushed laterally so as to make a ‘buldge’ in the cervical region at the desired exit point described above. A scalpel blade is used to incise over the tip of the Carmalt until the tip protrudes through the skin. The tip of the feeding tube is then grasped with the Carmalt hemostat and the tube is exited out through the oral cavity. The tube is pulled out until the flanged end of the tube just comes in contact with the cervical skin. The tip of the tube is then turned back on itself, grasped with the Carmalt forceps, and redirected into the oral cavity of the dog. The tube should remain in the jaws of the Carmalt hemostat until the tip of the tube is beyond the cervical exit point of the tube. The feeding tube is then released from the Carmalt and pushed into the esophagus until the tube is in the mid-esophagus (i.e., 7 or 8th intercostals space). The tube is secured using a Chinese finger-trap friction suture.

Regardless of technique used, the exit point of the tube can be left exposed or bandaged. A column of water is placed in the tube and the exposed end capped with a 3 cc syringe; this prevents intake of air, reflux of esophageal contents, and occlusion of the tube by diet. Most patients tolerate the tube without the need of an Elizabethan collar.

Esophagostomy tubes can be removed immediately after placement or left in place for several weeks to months. Care of the tube exit site may require periodic cleansing with an antiseptic solution. Tube removal is performed by cutting the finger- trap suture and gently pulling the tube. No further exit wound care is necessary; the hole seals in one or two days and heals by 7 - 10 days.

**Complications:** Complications associated with esophagostomy tube placement include early removal by the patient or vomiting the tube. No significant long-term complications have been reported (e.g., esophagitis, esophageal stricture, esophageal diverticulum, or subcutaneous cervical cellulitis). Reflux esophagitis can occur from improper tube placement (i.e., through the lower esophageal sphincter) or esophageal irritation from the tube itself. Mid-esophageal placement of silicone rubber tubes greatly reduces the incidence of esophageal injury and eliminates reflux esophagitis.

**Other Potential Therapies**
Hyperbaric oxygen therapy (HBOT) can also be very helpful in patients with severe pancreatitis (shown to be beneficial in both humans and animals). Physiological effects include:

- Oxygen delivered to the alveoli under increased atmospheric pressure results in large increases in the amount dissolved in plasma
- Increase in neovascularization
- Enhancement of WBC oxidative killing and antibacterial effects
- Inhibition of neutrophil adherence to microvascular endothelia resulting in SUPPRESSION of the deleterious cascade of events that follows in ischemia-reperfusion injury
- Modification of cytokine effects (antiinflammatory)
Inhibition of free radical formation
- Down regulation of intercellular adhesion molecule (ICAM-1) expression

A 2012 review article on the pathophysiology of pancreatitis by Caroline Mansfield in the Journal of Veterinary Internal Medicine implicates perpetuation of inflammation in pancreatitis by the adhesion of leukocytes to endothelial walls via expression of ICAM-1 and selectins mediated by IL-8. In addition, a disturbance in pancreatic microcirculation with ensuing ischemia is implicated as a major factor in the ongoing cycle of inflammation associated with pancreatitis. For veterinarians who have access on a referral basis to a hospital with a hyperbaric chamber HBOT is an exciting modality that can be used in addition to all of the other high priority therapeutic modalities already discussed.

Unproven therapy should be considered only after careful evaluation of the individual case and may include corticosteroids, somatostatin, a hormone that decreases pancreatic secretion, and low dose dopamine, which was found to preserve vascular permeability during experimental pancreatitis in cats and may be a beneficial adjunctive therapy in the management of clinical pancreatitis. Antioxidants may be of benefit in the acute management of pancreatitis; vitamin E is a potent membrane antioxidant and SAMe replaces glutathione stores that may have some benefit in pancreatitis, peritoneal lavage removes inflammatory products in the peritoneal cavity before they are absorbed, and pancreatic enzyme supplementation has been reported to decrease the pain that accompanies chronic pancreatitis in humans by the feedback inhibition by endogenous pancreatic enzyme secretion. It is not known if enzymes are helpful in the acute cases but such supplementation may have some benefit in early nutrition of patients with acute pancreatitis.

**Surgical Management of Pancreatitis**

Surgery is rarely indicated for pancreatitis. However, there are situations where surgery may be necessary. Indications may include pancreatic abscess, septic suppurative peritonitis secondary to severe necrotizing pancreatitis, pancreatic pseudocyst, jejunostomy feeding tube placement, and open peritoneal lavage and drainage. Surgery of the pancreas is discussed in current surgery textbooks.

**Conclusion**

Acute pancreatitis can vary in severity of signs and often results in multiple organ system involvement. Despite extensive literature on pathogenesis of pancreatitis and its complications, there have been few notable advances made in its medical and surgical management. It is possible that future research on modification of enzymatic disturbances will result in an effective treatment for acute pancreatitis. Surgical treatment of pancreatitis remains a controversial topic and is generally reserved for patients with severe necrotizing pancreatitis with septic peritonitis or pancreatitis associated with pancreatic mass.

**References**


Acute and Chronic Diarrhea in Dogs and Cats: 
Giardia, Clostridium perfringens Enterotoxiosis, 
Trichromonas foetus, and Cryptosporidiosis

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Introduction
These seminar notes will focus on the diagnosis and management of important and sometimes challenging to diagnose causes of diarrhea in dogs and cats, with particular emphasis on Giardia, Clostridium perfringens enterotoxiosis, cryptosporidiosis, and Tritrichomonas foetus. These disorders should be investigated early in the course of diarrhea, whether it is persistent or intermittent, along with evaluation for dietary causes of GI signs (including both dietary indiscretion and adverse reactions to specific foods), nematode parasites, bacterial and viral causes, and acute idiopathic colitis. This group of disorders constitutes a thorough differential list for animals with acute & intermittent diarrhea (Table 1).

The challenge to veterinarians is in making an accurate diagnosis, so that the most indicated therapy can be instituted as early as possible. This will then lead to the best opportunity for successful control of the medical disorder. It is also important to recognize that some animals may have several disorders at the same time (co-morbidities), so a thorough diagnostic approach is recommended. This is why it is often best to run tests for these disorders at the same time, through use of a “fecal diagnostics panel” that is now available at many commercial laboratories. A single fecal sample is submitted to the lab, and tests for each of these disorders are done at the same time. This provides a prompt and thorough analysis for important clinical disorders of the GI tract. The clinician then has more clear direction on how to proceed with treatment, or other diagnostic tests in the event that none of these disorders is identified.

It is also important to include blood tests for complete blood count, urinalysis, and complete biochemical profile to help evaluate for any major organ abnormalities (e.g., liver, kidneys, hypoproteinemia associated with protein losing enteropathy), especially in cases in which diarrhea does not resolve with the initial therapies and dietary changes. Only animals should have these tests done early in order to establish a minimum data base.

Table 1: Common Causes of Acute Diarrhea in Dogs and Cats

<table>
<thead>
<tr>
<th>Young Animals</th>
<th>Older Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary problems</td>
<td>Dietary problems</td>
</tr>
<tr>
<td>Parasites</td>
<td>Parasites less common but always possible</td>
</tr>
<tr>
<td>- nematodes</td>
<td>- nematodes</td>
</tr>
<tr>
<td>- protozoa (Giardia, Trichomonads)</td>
<td>- protozoa (Giardia, Trichomonads)</td>
</tr>
<tr>
<td>- coccidia (including Cryptosporidium)</td>
<td>- coccidia (including Cryptosporidium)</td>
</tr>
<tr>
<td>Viral and bacterial</td>
<td>Viral causes uncommon in older animals</td>
</tr>
<tr>
<td>Clostridium perfringens enterotoxiosis (CPE)</td>
<td>Acute colitis (fairly common cause of diarrhea in older animals)</td>
</tr>
</tbody>
</table>

Giardia is an important cause of diarrhea, and for some patients other GI signs as well. It is an important pathogen in dogs and cats, as well as humans and other species. Historically, accurate diagnosis of
Giardia has posed a significant challenge to veterinary practitioners, but there are now much more sensitive tests readily available for veterinarians to use on a routine basis. Because of the impact that this organism can have on animals, and also humans because of its zoonotic potential, it is important that veterinarians perform accurate diagnostic testing on animals to determine whether or not an animal is infected with Giardia. These notes will emphasize steps for accurate diagnosis, and also management of giardiasis.

Clostridium perfringens enterotoxiosis is a common cause of intermittent diarrhea in dogs and cats. Veterinary practitioners should test for the enterotoxin whenever faced with a patient that has unexplained diarrhea.

Cryptosporidiosis is now recognized to be a more common disorder in dogs and cats than was previously thought. It can cause significant abnormalities, and it has zoonotic potential. Cryptosporidiosis can be fatal in people that also are immunosuppressed (e.g., on chemotherapy or corticosteroids, carriers of HIV). Therefore, it is incumbent on veterinarians to test for this disorder, as there are important implications to both the patient as well as to humans who may come in contact with an infected animal.

**Early Diagnostic Screening in Animals with Diarrhea**

**Diarrhea – Making the Correct Diagnosis(es)**

<table>
<thead>
<tr>
<th>Acute Diarrhea – DOGS (initial screening)</th>
<th>Acute Diarrhea – CATS (initial screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Direct smear in house (fresh sample (perform by &lt;1hr)</td>
<td>□ Direct smear in house (fresh sample (perform by &lt;1hr)</td>
</tr>
<tr>
<td>□ ZnSO₄ w/centrifugation</td>
<td>□ ZnSO₄ w/centrifugation</td>
</tr>
<tr>
<td>□ Giardia antigen test</td>
<td>□ Giardia antigen test</td>
</tr>
<tr>
<td>□ Parvo test if indicated</td>
<td></td>
</tr>
</tbody>
</table>

**Later if Persistent:**

- □ Repeat all of the above
- □ Cryptosporidium IFA
- □ Clostridium perf enterotoxin assay

**Antech SA 350 Fecal Panel Includes:**

- Giardia Antigen and IFA
- Cryptosporidium IFA
- Clostridium perfringens enterotoxin assay

**Negative results do not make a rule-out. Be persistent, as retesting can be very important.**
Diagnosis and Management of Giardia

Diagnosis
Standard diagnostic tests used in any practice setting should include fresh saline fecal smears and zinc sulfate flotation with centrifugation. Zinc sulfate flotation with centrifugation, rather than gravity flotation alone, is a somewhat more sensitive means of testing for Giardia and other parasites. Trophozoites are more likely to be found in loose stools, while cysts are more often found in semi-formed or formed stools. Performing both zinc sulfate concentration with centrifugation and a Giardia antigen test together constitutes the most accurate means of evaluating a patient for the presence of Giardia. This has been recognized as the “gold standard” in human medicine, and is true also in veterinary medicine.

Direct Saline Smear
Direct smears should be performed on fresh fecal samples as soon as possible after being passed, but definitely within 1 hour. A fresh saline smear is made by mixing a drop of feces with a drop of saline on a glass slide. A coverslip is applied and the preparation is examined immediately under 40x magnification. Trophozoites are pear-shaped and have a characteristic concave ventral disk. They demonstrate rolling/wobbling motion (e.g., like a falling leaf). Adding a drop of Lugol’s solution of iodine on the edge of the coverslip can be done as an optional procedure and this will enhance the morphologic features of the organisms and make them easier to find. The iodine kills the parasite, so motion will no longer be seen if this procedure is used. Differentiation of trichomonads from Giardia is based on a different motion pattern (more forward motion with trichomonads versus rolling motion with Giardia), the absence of a concave disk, a single nucleus, and the presence of an undulating membrane. Identification of Giardia trophozoites is diagnostic, while their absence in fecal samples does not rule out presence of infection.

Zinc Sulfate Concentration with Centrifugation
Many studies have now shown that zinc sulfate concentration with centrifugation is the most reliable test available for demonstration of Giardia cysts in fecal samples. The test can be done in any practice setting, and the technique is described below. Alternatively, because the best accuracy in detection of Giardia is achieved through well trained and experienced lab personnel consistently setting up the assay and studying the microscopic specimens on time, many practices now submit fecal samples for centrifugation assays to a commercial laboratory.

Zinc sulfate centrifugation is also a very effective method for identifying nematode eggs in feces. It is therefore now used as the standard test for screening for intestinal parasites in most academic and many private practices. Studies have shown that approximately 70-75 percent of Giardia positive dogs can be identified on a single zinc sulfate centrifugation test (as opposed to approximately 40 percent of dogs after 3 separate saline smear preparations). Slides should be examined within 10 minutes of preparation because the cysts may begin to shrink. Since animals shed Giardia on an intermittent basis it is recommended that a series of zinc sulfate concentration tests be run over a 3 to 5 day period in order to maximize chances of accurately diagnosing or ruling out Giardia in animals with chronic diarrhea (or, alternatively, an antigen test can be run at the same time to help increase diagnostic efficiency and accuracy – this is what I recommend now as a standard practice). Diagnostic efficiency increases to 95 percent when 3 zinc sulfate examinations are conducted over a 3 to 5 day period. A positive result on any of the tests warrants treatment for Giardia.
Caution: It is not uncommon for plant spores, yeast bodies, and other amorphous debris to be mistaken for Giardia cysts. In fact, Giardia is frequently misdiagnosed – either it is being diagnosed incorrectly, or the wrong tests are being run and animals with Giardia are being missed. Giardia cysts are 11-13 u in size, and the subtle characteristics of the nuclei, axostyles, and median bodies are often more easily observed under 100X oil immersion magnification. Sometimes there are crescent shaped indentations of the cyst wall. Yeast bodies are similar to Giardia in size, shape, and color. Yeast bodies appear to be far more common than Giardia.

Zinc Sulfate Concentration - Summary
- Zinc sulfate is the flotation solution of choice in small animal practices (excellent for detection of Giardia as well as nematodes)
- Zinc sulfate concentration with centrifugation is the best test for identification of Giardia cysts
- Causes less distortion of Giardia cysts than standard salt solution

Giardia Antigen Testing
Other diagnostic tests for Giardia include an enzyme-linked immunosorbent assay (ELISA) test for Giardia antigen in feces, a direct immunofluorescent assay, duodenal aspiration under endoscopic guidance, and the peroral string test. The latter two tests are impractical for routine use in small animal practice, especially when the effectiveness of today’s fecal tests is recognized.

The fecal ELISA test detects Giardia antigen that is produced by dividing trophozoites. The test is very sensitive in humans and reportedly detects 30 percent more cases of Giardia than does zinc sulfate. Studies have now confirmed that this is also an excellent test for use in animals. One advantage of the ELISA test is that, since it detects Giardia specific antigen in the feces, it avoids the problem of intermittent cyst excretion in the feces. This test can be a significant aid in accurate diagnosis of Giardia in any private practice setting, and I highly recommend that veterinarians utilize this test in order to more consistently make an accurate diagnosis of giardiasis in their small animal patients.

Indications for Running Giardia Antigen Test:
- Cases of acute or chronic diarrhea in which zinc sulfate centrifugation tests are negative for parasites
  *Including young dogs with suspected viral or bacterial enteritis – Giardia and other parasitic infections can significantly compromise animals with these conditions. I recommend that all puppies with parvoviral enteritis be screened early for parasites with a combination of zinc sulfate with centrifugation and a Giardia antigen test (both tests day one or two on a single fecal sample)
- Cases in which it is unclear whether Giardia cysts are being seen on flotation tests (e.g., vs. plant spores)
- For evaluation of animals with unexplained weight loss, unthriftiness, abdominal pain
- Acute or chronic vomiting **(some animals with disease related to Giardia have only vomiting as a clinical sign)
- Many hospitals are now using the ZnSO4 with centrifugation and Giardia antigen combination assay as a routine screening test for GI parasites and wellness testing. This is because there are animals that have Giardia but that do not have any GI signs (loose stools, vomiting, etc) at the time of the exam. The addition of the antigen assay significantly improves the diagnostic sensitivity for Giardia. In summary, this approach offers: Better more sensitive diagnostic testing, more convenience to the client (one sample only), and ultimately it is more economical.
Treatment of *Giardia*
For many years the primary treatment for *Giardia* in dogs and cats has involved metronidazole. For dogs in which metronidazole proved ineffective, quinacrine was often used in the past. However, although quinacrine has been shown to be more effective than metronidazole, it frequently causes side effects, including lethargy, anorexia, and vomiting. It was also used in cats. Quinacrine is no longer available, however. More recently it was shown that albendazole (Valbazen) is highly effective in controlling *Giardia*. I recommended albendazole as an effective treatment for *Giardia* from 1993-1997, but experience with albendazole in dogs and cats has shown that it can cause bothersome side effects; including leukopenia, lethargy, and inappetence. Therefore, I have not recommended albendazole for many years. I mention it here because some veterinarians still do use it.

Fenbendazole (Panacur), well known for its effectiveness against a variety of intestinal parasites, also appears to be very effective against *Giardia*. In a controlled trial at Cornell University 6/6 dogs were effectively treated in an initial study. The same dose that is used to treat roundworms, hookworms, whipworms, and the tapeworm *Taenia pisiformis* (50 mg/kg orally once daily for 5 consecutive days [there have been treatment failures occasionally when therapy is given for only 3 days]) is used to treat *Giardia*. If the infection is not cleared on this regimen, a longer course of therapy is used (7 days). Fenbendazole has a proven track record for being very safe and is thought to not have any teratogenic effects. **Fenbendazole is therefore the drug of choice for treatment of *Giardia* in pregnant animals.** This is now also the preferred treatment for *Giardia* in cats.

Drontal Plus (Bayer Animal Health) is also an excellent choice for treatment of *Giardia*. This product includes febantel in addition to praziquantel and pyrantel pamoate. Febantel is the drug component that treats *Giardia*. Febantel is metabolized into fenbendazole and oxyfenbendazole after oral administration. Drontal Plus is administered once daily for 3 to 5 consecutive days for treatment of *Giardia*. Drontal Plus has been approved for use in dogs. Drontal Plus has been administered to cats empirically at a dosage of two small dog tablets per cat (about 50 mg/kg febantel) orally for 5 days with subsequent demonstration of decreased shedding of cysts (Scorza, Radecki, and Lappin).

Metronidazole is still a useful drug for treating *Giardia*, and it has the added advantage of having antibacterial as well as antiinflammatory properties. In situations in which it is unclear whether diarrhea is due to giardiasis, bacterial overgrowth, or mild inflammatory bowel disease, metronidazole is an excellent choice, especially when a client requests empirical therapy rather than definitive diagnostic testing. Metronidazole is only 67-74 percent effective in eliminating *Giardia* from dogs, however, and if a positive diagnosis is made fenbendazole or febantel would also be a reasonable choice. Potential side effects of metronidazole include anorexia, vomiting, and neurologic problems (ataxia, vestibular problems, seizures). In my experience these side effects are not common. They are more likely to occur when the anti-*Giardia* dose is used (25 to 30 mg/kg orally every 12 hours for 5 to 7 days). **The total dose of metronidazole should not exceed 65 mg/kg per day (30 mg/lb per day).** A lower dose (10 to 20 mg/kg every 12 hours) is used in treatment of intestinal bacterial overgrowth and inflammatory bowel disease. Side effects are infrequent at this dose. In the past, if a 5 to 7 day course of metronidazole failed to eliminate *Giardia*, a longer follow-up course (10 to 14 days) was often used. With the availability of fenbendazole and Drontal Plus it is recommended that one of these drugs be used instead in this situation.

Metronidazole neuro toxicity can be resolved more quickly by administering diazepam for several days. This is likely related to modulation of the GABA receptor within the cerebellar and vestibular systems.
In addition to use of pharmacotherapy to eradicate *Giardia*, it is important to consider environmental control so as to minimize chances of reinfection, especially in kennel or cattery situations. Cysts present in a cool environment can remain infective for a long period of time. Cages and runs should be thoroughly cleaned of all solid fecal material. Steam cleaning, or treatment with a quaternary ammonium compound (e.g. A 33) are both very effective measures for killing cysts. Allowing time for thorough drying is important, to desiccate any remaining cysts.

**Bathing:** Steps to prevent reinfection play an important role in resolution of giardiasis in dogs. Dogs may be reinfected with cysts from the hair or the environment, and bathing at the time that drug therapy is concluded, thereby removing cysts that could be licked from the hair coat by the animal, may be a very helpful additional step in decreasing the chances of reinfection. Changing the environment, if possible, can also be beneficial.

**Dietary Therapy and Supplementation:**
In animals that are known to be chronic carriers of *Giardia*, it may be beneficial to supplement the diet with fiber. Increased dietary roughage may make it more difficult for *Giardia* trophozoites to attach to the small intestinal mucosa (use either commercial diets or simply add a fiber source such as Metamucil or pumpkin, for example, to the animal’s standard diet

**Rx for Chronic Giardiasis: Will Probiotics Help?**
- *Lactobacillus johnsonii* has been shown to inhibit *Giardia* proliferation in vitro
  - Due to alterations in pH from production of lactic acid
  - In guinea pigs, in vivo, prophylactic feeding of Lj greatly reduced fecal shedding following experimental inoculation with *G. intestinalis*
- Enterococcus faecium SF68 fed to mice
  - Stimulated increase in anti-*Giardia* intestinal IgA and circulating IgG
  - Increased CD4+ immunocytes
- Reduced shedding and more rapid clearance of *Giardia*?
- Studies are ongoing

**Zoonotic Potential:** Current information indicates that zoonotic potential may exist with some *Giardia* genotypes, but certainly not all. When both animals and humans living in the same environment become infected, a common source of infection rather than direct transmission must also be considered.

**Are most *Giardia* spp. infections shared between animals and man?** The genus *Giardia* contains multiple species of flagellated protozoans that are indistinguishable morphologically. Host specificity was thought to be minimal for *Giardia* spp., but not all small animal isolates cause disease in human beings. There have been varying results concerning cross-infection potential of *Giardia* spp.. Human *Giardia* isolates usually grow in cell culture, animal isolates often do not. Recent genetic analysis has revealed 2 major genotypes in people. Assemblage A (*G. duodenalis*) has been found in infected humans and many other mammals including dogs and cats. Assemblage B (*G. enterica*) has been found in infected humans and dogs, but not cats. It appears that there are specific genotypes of *Giardia* that infect dogs (*G. canis*; Assemblages C and D) and cats (*G. felis*; Assemblage F) but not people. Accordingly, healthy pets are not considered significant human health risks for HIV infected people by the Centers for Disease Control (www.cdc.gov/hiv/pubs/brochure/oi_pets.htm).
Should Giardia Positive But Asymptomatic Animals Be Treated?
The question whether animals that are asymptomatic carriers of *Giardia* should be treated is often asked. *Giardia* cysts have been found in many animals with well-formed feces. *Giardia* is clearly not pathogenic in some animals, while in others it causes significant enteritis. And there may be others that experience intermittent GI upsets that could potentially be related to chronic parasite carriage, and that may benefit in the long term from more effective parasite control. Because the public health considerations must still be considered, I do recommend that all animals with fecal samples that are positive for *Giardia* be treated, using these guidelines:

- Administer Fenbendazole (Panacur) 5 days
- Re-check fecal at 14-28 days, not later – use the zinc sulfate w/centrif assay, NOT the antigen test (we don’t know how long it takes to go negative)
- If positive on O&P, treat once more
  - Fenbendazole again, or febantel (in Drontal PLUS); could also combine with metronidazole for this second round of therapy
- If still not clinical, stop here, don’t re-check again
  - Pet is not clinical and likelihood of transmission of any infectious agent to a human is very low
  - Is the Giardia even a significant problem for the patient?

NOTE: We do not want to overtreat! The antigen test should not be used as a recheck test in the immediate post treatment phase. The idea is to use the best diagnostic approach up front and then to manage the patient judiciously.

Preventing Infection/Premises Control
In controlled environments, the following methods should be used to keep the area as decontaminated as possible:

1. Decontaminate the environment
2. Treat all animals in the environment
3. Bathe at the conclusion of drug therapy to remove cysts from haircoats
4. Prevent reintroduction of infection

In hospital and kennel/cattery situations (controlled environments) moving animals away from contaminated areas so they can be cleaned and decontaminated is very important. Steam cleaning after all fecal material has been removed is very effective. Chemical disinfection can be effectively accomplished using quaternary ammonium (QUAT) – containing disinfectants (e.g. Roccal, Totil), which will inactivate cysts in one minute at room temperature. The area should be allowed to dry completely and if possible left open for a few days. Animals should be bathed with a general cleansing shampoo before being returned. In some situations, e.g., shelters, research facilities, it may also be advisable to bathe the animals a second time, especially around the perianal area, using a quaternary ammonium compound. These can be safely left on the coat for 3 to 5 minutes, before being thoroughly rinsed off (longer exposure can cause irritation). Allow the coat to dry thoroughly before returning the animal to the clean area, and then administer one more course of anti-Giardia therapy, preferably using a different drug than was used during the initial course. Subsequently, any new animals introduced to the kennel or cattery should be tested as a matter of routine, but also bathed and treated as well, regardless of whether the fecal tests are positive or negative for *Giardia*. 
**Tritrichomonas foetus**

*Tritrichomonas foetus* is a recently identified enteric protozoan of cats. It causes chronic large bowel diarrhea (loose stools, presence of blood and mucus, straining to defecate), and is most commonly seen in young cats that have resided in densely populated housing such as catteries and shelters. The diarrhea may be intermittent or persistent. Loose stool may dribble out (lack of control) and the anal area may become edematous. The organism is present in the ileum, cecum, and colon as a trophozoite. The organism does not encyst, so trophozoites are the only recognized stage. Infection in feral cats and healthy cats appears to be uncommon.

Until 2005 no effective treatment had been identified. Unfortunately, some cats with chronic diarrhea and dyschezia were euthanized due to a lack of any therapy that could control the clinical signs. It was exciting news in 2005 when Dr. Jody Gookin and colleagues at North Carolina State University reported that the nitroimidazole drug ronidazole is effective in controlling *T. foetus*. Although the diarrhea eventually resolves over a period of time (months up to one to two years) in untreated cats, ronidazole is the recommended therapy once a diagnosis has been established. It is important that an accurate diagnosis be made so that clients can be counseled appropriately, i.e., they should expect that their cat(s) will continue to have abnormal stools for some period of time. Further, there can be side effects of significant concern related to ronidazole, so this is NOT a drug that should be used empirically in lieu of testing. Also, it is not uncommon for cats to be co-infected with *Giardia* or *Cryptosporidium* or even both, so a thorough evaluation for parasites is important (run a minimum of one zinc sulfate with centrifugation and a *Giardia* antigen test and consider IFA fecal assays to check for *Cryptosporidium*). Accurate and thorough testing is essential and once any causative agents are identified they can be treated appropriately for the benefit of the patient and its owner.

*Tritrichomonas foetus* is commonly mistaken for *Giardia* trophozoites on direct smear exam. All trichomonads possess three to five anterior flagella, an undulating membrane, and a recurrent flagellum attached to the edge of the undulating membrane. All flagella originate from an anterior basal body. An axostyle extends the length of the trichomonad and extends posteriorly. A cyst stage is not known for this genus. Video clips showing both *Giardia* and *Tritrichomonas* trophozoites are available on the North Carolina State University website cited in the reference list below.

Definitive diagnosis can be made in some cases by direct smear of fresh feces in saline and examined at 200 to 400x magnification. Sensitivity is low, however, for diagnosis by direct smear (only 14% in one study), so results can often be false negative. To increase the chance of finding *Tritrichomonas* trophozoites on direct smear, it is recommended that multiple direct smears be done on the same day. Whenever possible, a cat with suggestive signs should be hospitalized for part or all of a day so that each fecal sample that is passed can be examined quickly via direct saline smear.

*Tritrichomonas foetus* can also be grown from feces via incubation at 37 degrees C in Diamond’s medium. A commercially available culture system is also available and is recommended for use in clinical practice (InPouch TF, Biomed Diagnostics Inc., San Jose, CA). The medium in InPouch does not support the growth of Giardia species or *Pentatrichomonas hominis* so presence of organisms is consistent with *T. foetus*. PCR is the most sensitive means for confirming a diagnosis. In one study of 36 cats with *T. foetus* infection, 20/36 were positive on the InPouch TF test and 34/36 were positive on PCR. Details on the PCR assay can be reviewed on the North Carolina State website.
Studies at North Carolina State University in 2005 showed that ronidazole is effective for treatment of *T. foetus*. The original dosage guidance was to administer 30 mg/kg BID for 14 days. **However, a study reported in 2008 provided new guidance: 30 kg/kg once daily is effective and safer, i.e., less likely to cause neurologic adverse events** (RONIDAZOLE PHARMACOKINETICS IN CATS AFTER IV ADMINISTRATION AND ORAL ADMINISTRATION OF AN IMMEDIATE RELEASE CAPSULE AND A COLON-TARGETED DELAYED RELEASE TABLET; Levine, Papich, Gookin et al).

Ronidazole is a nitroimidazole antimicrobial that is not licensed for any use in the U.S. The medication has become more readily available in the United States through compounding pharmacies. The drug has mutagenic properties, so it must be compounded the same way as chemotherapy drugs. We have had some cats experience mild neurological side effects to ronidazole, similar to what can be seen with metronidazole. These resolved upon discontinuation of the drug. It is expected that there will be fewer instances of neurotoxicity with the new schedule of 30 mg/kg on a once daily dosing schedule. It is important that an accurate diagnosis be made so that clients can be counseled appropriately, i.e., they should expect that their cat(s) will continue to have abnormal stools for some period of time until definitive treatment can be administered.

Other recommended steps during therapy include isolating cats to decrease the risk of reinfection and to discard any litter boxes the cat has used, after treatment is completed.

**Follow-up testing:** Dr. Gookin recommends testing by PCR at 1 to 2 weeks and 20+ weeks after treatment is completed. Negative results should be interpreted with caution since PCR cannot prove the absence of infection and prolonged symptomatic carriage of the organism after antimicrobial therapy may be common.

An alternative drug which can be tried is tinidazole. This is also a nitroimidazole antimicrobial. A dose of 15-30 mg/kg SID can be tried. It should be safe and may or may not be effective. Studies have been ongoing, however, and results have not been very impressive.

**References:**

There is an excellent reference section titled **AN OWNERS GUIDE TO DIAGNOSIS AND TREATMENT OF CATS INFECTED WITH TRITRICHOMONAS FOETUS**.

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### Clostridium Perfringens Enterotoxicosis

Over the last 12 years *Clostridium perfringens* enterotoxicosis (CPE) has emerged as a frequently recognized cause of chronic intermittent diarrhea in dogs. Although it is likely a less common cause of diarrhea in cats it is still diagnosed frequently enough that it should be considered in the diagnosis of diarrhea in cats as well. This is not a new disease. Frequent use of the definitive test (enterotoxin assay performed on feces) for this disorder has revealed that CPE is seen relatively commonly in clinical
practice and that CPE is a disorder that should be considered in any dog or cat with intermittent or chronic persistent diarrhea.

*Clostridium perfringens* is a normal vegetative enteric organism. Simply identifying *C. perfringens* on a fecal culture is meaningless. The pathogenesis of CPE is through an enterotoxin that is produced after certain strains of *C. perfringens* sporulate. The toxin damages epithelial cells of the distal ileum and colon. Inciting factors that promote sporulation are not clearly understood but may include stress, diet changes, concurrent disease, or inherent immune status.

The most common clinical signs are chronic intermittent or persistent diarrhea. In some animals acute diarrhea is the primary sign. In fact, some of the cases of hemorrhagic gastroenteritis (HGE syndrome), characterized by acute bloody diarrhea and an increased packed cell volume that most practitioners have seen over the years, may have been due to CPE. Many animals exhibit signs of large bowel diarrhea, but small bowel signs may be seen as well. In some cases signs may be seen for only a day or two at a time, with persistent recurrences on a weekly, monthly, or on a less frequent basis. Stressful events or diet changes may incite flare-ups of clinical signs. In other cases *C. perfringens* enterotoxicosis is one of several problems that an animal may have concurrently and diarrhea may be persistent.

**Diagnosis**
CPE must be considered whenever more than one animal in the environment has diarrhea (e.g., household, kennel, cattery). Transmission from animal to animal can occur. A presumptive diagnosis may be suggested on fecal cytology in which more than 3-4 spores per high power oil immersion field are observed (the spores have a safety pin appearance and are larger than most bacteria). However, **definitive diagnosis** is by identification of enterotoxin which is currently done via a fecal assay. Clinicians should be aware that simply seeing spores on fecal cytology does not establish a definitive diagnosis (see JAVMA February 1, 1999). Stool is submitted to the lab for enterotoxin analysis. Fecal samples that will be shipped off from the hospital directly to a laboratory should be sent on ice via overnight express. If a courier service will be picking up samples for transport to the laboratory it is sufficient to keep the sample refrigerated until pick-up. The courier service will keep the sample properly chilled during transport. The minimum amount of stool that should be submitted is the size of a pea. Typically I submit samples in a red top tube, without serum separator. In animals with intermittent diarrhea the chances of a positive toxin finding are greater when abnormal rather than a normal stool is examined. A negative result does not definitively rule-out CPE.

**Treatment**
Several antibacterial drugs are effective in controlling CPE. Acute cases often respond well to amoxicillin (22 mg/kg BID) or metronidazole (10-20 mg/kg BID) for 7-28 days. Many clinicians have likely treated CPE with these medications empirically without knowing what they were treating. Chronic cases tend to respond best to tylosin powder. The recommended dose is: Animals greater than 23 kg ¾ tsp BID, 12 to 23 kg 1/8 tsp BID, 5 to 12 kg 1/12 tsp BID, and less than 4.5 kg 1/16 tsp BID (a “pinch”). Cats definitely do not accept the powder well at all, even when it is mixed in very tasty foods. It is best to have the powder reconstituted to capsule form for administration to cats. The medication is very safe. Some animals require treatment for several to many months (3 to 12 months or more). Over time the dose may in some cases be successfully reduced to SID and then every other day dosage (after several months or more on a BID schedule).
Dietary fiber supplementation may also help control CPE. Probable mechanisms include decreased \( C. \ perfringens \) fecal concentration, lower colonic pH, which prevents sporulation, and increased concentrations of SCFA. Some patients may respond well to dietary fiber supplementation alone.

Follow-up testing at 3-6 months can be done to determine if toxin persists. Once daily to every other day tylosin in conjunction with dietary fiber supplementation are used in chronic cases.

**Cryptosporidiosis**

Infection with *Cryptosporidium* is much more common than most small animal practitioners recognize. Currently it is recommended that all dogs and cats with diarrhea, whether acute or chronic, be screened for *Cryptosporidium* in addition to testing for nematode and protozoan parasites. In 2004 the American Association of Feline Practitioners adopted a position statement recommending that all kittens and adult cats with diarrhea be screened for *Cryptosporidium*. It is recommended that the same policy be followed with dogs (given that the cause is not simple diarrhea related to an acute upset due to sudden change in diet or dietary sensitivity).

*Cryptosporidium* spp. are coccidians that reside in the gastrointestinal tract. Infection can be associated with diarrhea in both immunocompetent and immunodeficient hosts. In the past, most of the cases of mammalian cryptosporidiosis were attributed to *C. parvum*. However, molecular studies have demonstrated that cats are usually infected with the host-specific *C. felis*, dogs are infected with *C. canis*, and people are infected with *C. parvum* or *C. hominus* (Scorza and Lappin). In a recent study at Colorado State University, they documented the presence of *Cryptosporidium* spp. DNA in diarrhea from 24.3% of the 292 animals tested (180 cats, 112 dogs) (Scorza and Lappin). This highlights the importance of testing dogs and cats for cryptosporidiosis. PCR is much more sensitive than the tests that are used most commonly at this time (acid fast staining of fecal smears or IFA). In this same series with 24.3% positive on PCR, only 2.7% were positive on IFA.

All dogs and cats infected with *Giardia* or *Cryptosporidium* species should be considered potentially zoonotic, even though the number of cases in which humans are infected through contact with pets is probably not high. Infection in humans is sometimes fatal in the presence of severe immunosuppression. Acute symptoms may include diarrhea, abdominal pain, vomiting, fever, and listless behavior. Infection can also be subclinical in dogs and cats. Chronic unresponsive diarrhea has been associated with cryptosporidiosis in cats with serious underlying disease as well as in dogs.

Because *Cryptosporidium* oocysts are quite small (as little as one-tenth the size of common *Isospora* oocysts) and are usually present in the feces in small numbers, they are very difficult to detect on routine fecal flotation and microscopy. The best tests currently available for routine testing for *Cryptosporidium* are fecal IFA and acid fast staining of fecal smears; however, they lack sensitivity. These tests are readily available at commercial laboratories (acid fast staining can also be done in house). PCR is a much more sensitive test but is labor intensive, expensive and is only available at a limited number of laboratories. Antigen tests for detecting *C. parvum* in human species are not sensitive for use in dogs and cats. In time there will be more sensitive tests readily available.
**Treatment**

The following treatment regimens may be used for cryptosporidiosis:

### Canine

- **Azithromycin** 5-10 mg/kg, BID orally, for 14-28 days

### Feline

- **Azithromycin** 7-15 mg/kg, BID, orally for 14-28 days

### Paromomycin

- 150 mg/kg, SID orally, for 5 days

### Tylosin

- 15 mg/kg, BID orally, for 21-28 days

### References

8. Scorza AV and Lappin MR. An update on three important protozoan parasitic infections of cats: cryptosporidiosis, giardiasis, and tritrichomoniasis. Supplement to Veterinary Medicine, March 2006; 18-32.
Introduction
Inflammatory bowel disease (IBD) is not a specific diagnosis; rather it is a histological description of a syndrome resulting from a host hypersensitivity response to antigenic stimuli. In IBD there is an increase in the inflammatory cell population in the intestinal mucosa. The predominant inflammatory component can be lymphocytic-plasmacytic (most common type), eosinophilic, neutrophilic, or granulomatous. Primary causes of intestinal inflammation that should be considered include parasites, bacteria (specific agents or bacterial overgrowth), fungal disorders (e.g., Histoplasma, pythiosis), immune-mediated diseases, and food sensitivities. Many cases of IBD are likely idiopathic in nature. A definitive diagnosis can be made only by intestinal biopsy.

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

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

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

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

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

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

Testing for parasites in dogs with diarrhea is best accomplished using zinc sulfate flotation with centrifugation. This is an excellent test medium for detection of nematode parasites as well as *Giardia*. *Zinc sulfate flotation with centrifugation* is superior to flotation with sodium nitrate, or flotation with zinc sulfate without centrifugation. Testing for *Giardia*-specific antigen in feces is also an excellent means of diagnosing giardiasis. A fecal assay for *Clostridium perfringens* enterotoxin should also be done.

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

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

**Intestinal Biopsy Techniques**

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

Clinicians need to make sure they are taking an adequate number of endoscopic biopsy samples for accurate diagnosis. It is recommended that clinicians take 8 to 12 biopsy samples from the upper small intestine so that the pathologist will have enough tissue to work with. Also, it is recommended that both upper and lower GI endoscopy be done in dogs with chronic diarrhea. In this way biopsies from the ileum can be obtained by passing the endoscope along the full length of the colon and through the ileocolic orifice and into the ileum. If the ileum cannot be entered, it may be possible to obtain at least blind biopsies of the ileum by passing the endoscopic biopsy instrument through the ileocolic orifice with the endoscope tip positioned at the ileocolic sphincter area. Colon biopsies are always obtained as well during colonoscopy in order to evaluate for inflammation in the colon.

**Surgical Biopsy:** In cases where exploratory surgery is done to obtain intestinal biopsies, three full thickness samples are usually obtained (one each from duodenum, jejunum, and ileum). If there is any
lymph node enlargement a biopsy should be obtained, and during exploratory surgeries the liver is also biopsied as a matter of routine.

**Treatment of Inflammatory Bowel Disease**

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

**Drug Therapy**

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

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

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

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

When a patient is either poorly responsive to corticosteroids when used as outlined above, or if there is poor tolerance, the next best options are to try either budesonide or cyclosporine. Cyclosporine is described further below. Budesonide is a newer corticosteroid for use in humans. Budesonide is a glucocorticoid that also represents an alternative for management of IBD in dogs, especially in severe cases that have proven to be refractory to prednisone, metronidazole, azathioprine, and dietary
management; or that are intolerant of the corticosteroids discussed above. Budesonide undergoes high first pass metabolism in the liver and 90% is converted into metabolites with low corticosteroid activity. It has minimal systemic availability. The potential for typical corticosteroid side effects is significantly reduced as a result of decreased bioavailability and the resulting limited systemic exposure, which makes this a particularly attractive drug for use in humans and animals that are poorly tolerant of other corticosteroids. Budesonide also has a high receptor-binding affinity in the mucosa. It has been referred to as a “locally acting” corticosteroid.

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

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

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

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

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

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

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

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

The anti-inflammatory effect of cyA in human IBD is believed to be due to suppression of activated T cells infiltrating the mucosa, thereby decreasing the amount of proinflammatory cytokines, and ultimately, the clinical signs of disease. The cyA dose used in the study of 14 dogs was 5 mg/kg SID. The sole therapy was cyA. There were transient adverse effects observed in 5 dogs, most of which occurred in the first 1 to 2 weeks of therapy, after which time they abated. Adverse reactions included vomiting and inappetence (4/14 dogs), and gingival ulceration and alopecia followed by hypertrichosis in 1 dog. A lag phase of 7 to 10 days has been seen in humans before there are obvious signs of clinical improvement, and a similar finding was observed in the dogs in the study reported here.

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

**Duration of Pharmacotherapy**

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

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

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

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

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Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is not a specific diagnosis; rather it is a histological description of a syndrome resulting from a host hypersensitivity response to antigenic stimuli. In IBD there is an increase in the inflammatory cell population in the intestinal mucosa. The predominant inflammatory component in cats with IBD can be lymphocytic-plasmacytic (most common type), eosinophilic, or neutrophilic. Changes in mucosal architecture and cell morphology should also be noted (crypt lesions including abscesses, villus atrophy or fusion, edema, epithelial erosions or ulceration, fibrosis). The etiology of IBD is poorly understood. Primary causes of initiation and perpetuation of intestinal inflammation that should be considered include parasites, bacteria (specific agents including normal luminal bacteria or bacterial overgrowth), immune-mediated diseases, and food sensitivities. Many cases of IBD are likely idiopathic in nature.

Treatment of IBD

It is important that the clinician formulate a treatment plan based on a correlation of clinical course, laboratory and gross findings, and histologic findings (considering both cellular infiltrate and morphology) rather than relying on histologic changes alone. Since food sensitivities can be a cause of IBD, dietary trials are an essential part of both the diagnostic and therapeutic strategy, utilizing hydrolyzed protein diets and novel protein diets and treating each patient as an individual (i.e., there can be variable responses to specific diets varying from patient to patient). Regarding pharmacotherapy, while corticosteroids have long been considered the cornerstone of treatment for idiopathic inflammatory bowel disorders, antimicrobial agents may play a role as well. Bacteria have been implicated in the pathogenesis of IBD.

Guidelines for corticosteroids in cats with IBD are as follows. Mild to moderate cases of IBD often respond to prednisolone (preferred over prednisone in cats) at a starting dose of 1 to 2.2 mg/kg divided twice daily for two to four weeks followed by a gradual decline in 50% increments at two week intervals. Cats with inflammatory changes graded as mild usually respond quite well to the lower dose and alternate day or every third day treatment can often be achieved by two to three months. Occasionally treatment can be discontinued altogether by three to six months.

If biopsies reveal disease that is moderate to severe a prednisolone dose of 2 to 4 mg/kg divided twice daily is used in cats for the first 2 to 8 weeks or until clinical signs resolve. This dose of corticosteroid is usually well tolerated in cats. In some cases a dose of 1 to 2 mg/kg per day may be necessary long term (months to years) to maintain clinical remission. Use of combination drug therapy may also be required at the outset to control clinical signs and prevent progression of the disease (e.g., metronidazole or tylosin plus prednisolone). Cats with hypoproteinemia and histologic changes graded as severe often respond quite well when an aggressive therapeutic course is undertaken.

Budesonide is a glucocorticoid that represents an alternative for management of IBD in dogs and cats, especially in severe cases that have proven to be refractory to prednisolone, metronidazole, azathioprine, chlorambucil, tylosin, and dietary management; or that are intolerant of the corticosteroids discussed above. Budesonide is one of a group of novel corticosteroids that have been in development for use in humans in an attempt to make available alternative preparations that will help limit toxicity associated with corticosteroid use.
Budesonide undergoes high first pass metabolism in the liver and 90% is converted into metabolites with low corticosteroid activity. It has minimal systemic availability. The potential for typical corticosteroid side effects is significantly reduced as a result of decreased bioavailability and the resulting limited systemic exposure, which makes this a particularly attractive drug for use in humans and animals that are poorly tolerant of other corticosteroids. Budesonide also has a high receptor-binding affinity in the mucosa. It has been referred to as a “locally acting” corticosteroid.

Therapeutic results with budesonide have been promising in humans with Crohn’s disease, collagenous colitis and lymphocytic colitis, ulcerative colitis, either when administered as a retention enema or in oral form, and primary biliary cirrhosis. Budesonide has been used by some veterinary clinicians in recent years to treat IBD in dogs and cats. Dose recommendations vary. In humans, a range of 6 mg to 9 mg per day has been used during initial therapy. In general, budesonide is administered to cats at 1 mg administered once per day (this dose level is prepared at a compounding pharmacy). Budesonide can be used in combination with other drugs. Since cats tolerate corticosteroids very well, there is little indication to use budesonide as initial therapy for IBD. However, this may be a very attractive option for use in diabetic cats that also have IBD, or in patients where conventional therapies have not been sufficiently effective.

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

When combination therapy is indicated metronidazole is usually the first choice to be used in conjunction with prednisolone. Metronidazole’s mechanism of action includes an antiprotozoal effect, inhibition of cell-mediated immune responses, and anaerobic antibacterial activity. A dosage of 10 to 20 mg/kg two times daily is used for IBD. Ideally, at least several months of metronidazole therapy is given once it is started. In some cats with severe disease long term consecutive use or one to two month cycles of treatment may be required. Side effects to metronidazole at this low dose are uncommon in cats. Occasionally nausea or vomiting may be seen.

If a client is unable to successfully administer oral medications, methylprednisolone acetate (Depo-Medrol) can be used as sole treatment for cats with mild to moderate IBD or as adjunctive therapy when oral prednisolone and/or metronidazole are used as the primary treatment and flare-ups of clinical signs occur. Consistent control of clinical signs in cats with moderate to severe IBD is more difficult to maintain when methylprednisolone acetate is used alone, however. It is recommended that sole use of methylprednisolone acetate be reserved for situations in which the owner is unable to consistently administer tablet or liquid prednisolone preparations. Initially 20 mg is given subcutaneously or intramuscularly and is repeated at 2-week intervals for 2 to 3 doses. Injections are then given every 2 to 4 weeks or as needed for control.

If remission cannot be maintained with use of corticosteroids and metronidazole then chlorambucil (Leukeran) should be used. Azathioprine was used more in the past but it has been largely supplanted now by chlorambucil. Chlorambucil is an alkylating agent. Alkylating agents alter DNA synthesis and inhibit rapidly proliferating cells. Chlorambucil is administered initially at 0.1 to 0.2 mg/kg/day in conjunction with prednisolone at 2.2 mg/kg/day. The small pill size of chlorambucil (2 mg) allows for easy dosing. Most cats receive one-half tablet (1 mg) per day. Various dosage schedules for cats have
been published. An alternate schedule is 0.15 to 0.3 mg/kg every 72 hours. Toxicities are uncommon in cats but may include anorexia, vomiting, and diarrhea, but these problems generally resolve rapidly when chlorambucil is reduced from daily to every other day administration. Bone marrow suppression is possible but uncommon, and is mild and rapidly reversible when it does occur. Once the desired clinical response is achieved, chlorambucil is gradually tapered over several months while prednisolone is continued as the primary maintenance drug.

Cyclosporine is another immunosuppressive drug that can be used in management of IBD. Cyclosporin inactivates calcineurin phosphorylase in T cells, preventing transcription of interleukin-2 (IL-2) as well as other cytokines. Cyclosporin inhibits activation of T cells, natural killer cells, and Langerhans (i.e., antigen-presenting) cells. Suppression of the Th1 or Th2 response induces antigen tolerance. The dose is 5 mk/kg once daily. Once sufficient response is achieved the dosage interval can be reduced to administration of a full dose every 48 hours and subsequently even further, on an individual patient basis.

**Cobalamin therapy in cats:** Significant tissue level cobalamin deficiency is present in some animals with GI disease. This is usually secondary to reduced cobalamin absorptive capacity. It is essential that all cats with any form of GI disease (including involvement of liver, stomach, pancreas, intestines) have a serum cobalamin level run to determine if the patient is hypocobalaminemic. Response to therapy will be limited if low cobalamin levels are not resolved. The reference range for cobalamin in cats is 290-1500 ng/L. Therapy is given if the value is less than 500 ng/L (i.e., in the low part of the reference interval; don’t wait until the level drops below the low end point of the reference range).

Therapy involves administering injectable cobalamin at the following schedule for cats: 250 ug subcutaneously once a week for 6 weeks, then every 2 weeks for the next 6 doses, then dose monthly. Most generic cobalamin preparations contain 1 mg/ml (1000 ug/ml). It is important to note that multi-vitamin and B-complex injectable formulations contain significantly lower concentrations of cobalamin and they also cause pain when injected. Therefore, it is recommended that these preparations not be used for cobalamin supplementation. Unless the intestinal disease is totally resolved, long-term and perhaps lifelong supplementation with cobalamin may be necessary. The frequency of injections on a long-term basis is determined by regular measurement of serum cobalamin concentration.

Because dietary allergens may play a role in the cause if IBD, specific dietary therapy may be beneficial. Often, moderate to severe degrees of IBD are either temporarily responsive or only minimally responsive to careful dietary manipulations. However, long term control of IBD with as minimal a drug administration schedule as possible may be aided by specific dietary management. This should be started as soon as a diagnosis is made and continued as drug therapy is decreased later. Feed elimination (novel protein) or hydrolyzed protein diets. Chicken, duck, lamb, fish, or venison based diets are often tried initially. Elimination diets have been found to be very beneficial in cats.

**Poor responses to treatment** of cats with IBD usually result from:

1. Inadequate initial or long-term maintenance corticosteroid dosage in cats with more severe forms of IBD (moderate to severe disease).
2. Failure to use ancillary medications (metronidazole, chlorambucil, cyclosprinetylosin) in cases where disease is moderate to severe.
3. Failure to recognize and treat a concurrent condition (e.g., gastric hypomotility disorder that may either be secondary to IBD or idiopathic in nature, hyperthyroidism, parasitism [e.g.,
4. Treatment for only small intestinal inflammatory disease when colitis is present as well. Some cats with concurrent IBD and colitis may show minimal or no clinical signs of colitis.
5. Failure to recognize and treat low body cobalamin levels (measure serum cobalamin).
6. Failure to identify an effective diet.
7. Poor client compliance

What If Biopsies are Not Definitive for Either IBD or Small Cell Lymphoma?
It can be difficult to definitively differentiate benign IBD from small cell intestinal lymphoma, even when full thickness intestinal biopsies are obtained. If the biopsies were obtained via endoscopy, one option is to proceed to exploratory laparotomy to obtain full thickness samples. However, this is not practical in some cases and involves a more invasive procedure and more expense. Further, there is no guarantee that the differentiation can be made even when full thickness samples are obtained. Another option that is employed more commonly now is to perform special tests to help differentiate benign IBD from low-grade, small cell lymphocytic malignant lymphoma. Specific immunohistochemical techniques can be done to identify populations of malignant B and T lymphocytes (i.e., phenotyping) and molecular (PCR) testing is done for clonality. Clients should be given the option of ordering these additional tests if the pathologist indicates on the initial histopathology interpretation that the differentiation can’t be made definitively between IBD and lymphoma. If the client declines to have the additional tests performed, the clinician then needs to decide whether or not to just go ahead and treat for the disease that poses greater concern, i.e., lymphoma. Low grade small cell lymphoma is often treated with the combination of prednisolone and chlorambucil (see later discussion on treatment details in the next section).

Treatment of Intestinal Lymphoma in Cats
Lymphoma is the most common feline neoplasm. It is also the most common form of gastrointestinal neoplasia in cats. Gastrointestinal lymphoma is often referred to as either well differentiated (low grade or lymphocytic), poorly differentiated (high grade, lymphoblastic, or immunoblastic), and intermediate (or mixed). Endoscopy has been shown to be a very useful modality for diagnosis of intestinal lymphoma in cats, especially when multiple biopsies are obtained using proper technique and instruments that can procure adequate size tissue samples. Immunohistochemical stains are beneficial for differentiating IBD from intestinal lymphoma in cases where it is difficult for the pathologist to distinguish between the two. Full thickness intestinal biopsies may be required in a very limited number of cases in order to establish the correct diagnosis.

Many cats respond favorably to treatment for intestinal lymphoma, especially with the low grade or chronic lymphocytic type. Clinical signs can be very similar to cats with IBD. Therefore, it is strongly recommended that cats with chronic GI signs undergo a biopsy procedure as early as possible, so that the correct diagnosis can be established and the best course of therapy be made available for each individual cat. Biopsies should be obtained from both the upper and lower (ileum) small bowel.

Multi-agent chemotherapy is recommended for all cats with GI lymphoma. Surgery is done only if there is an isolated mass that is causing some degree of luminal obstruction. Survival times in excess of 12 to 18 months are not unusual. In some cats the response is somewhat shorter (three to six months). The prognosis for longer survival time is much better if the diagnosis is made before clinical signs become chronic and debilitation results.
One study has reported excellent results in cats with small cell lymphoma using a protocol of prednisone (10 mg PO per cat per day) and chlorambucil (Leukeran) at a dosage of 15 mg/m2 PO, once every day for 4 days, repeated every 3 weeks (Note: prednisolone is used routinely at this time, rather than prednisone, in cats). Sixty-nine percent of the cats with lymphocytic lymphoma treated with this regimen achieved a complete remission. The median disease free interval for cats that achieved complete remission was 20.5 months (range, 5.8-49 months). The median survival for all cats with lymphocytic lymphoma treated with chemotherapy was 17 months (range, 0.33-50 months).

Cyclophosphamide (Cytoxan) was used for rescue in some of the cats that were entered in this protocol (225 mg/m2, PO, every 3 weeks).

Lymphoblastic lymphoma is treated more aggressively and various protocols are published in the oncology textbooks. For clinicians inexperienced in administering chemotherapy, or who have not treated many cats with intestinal lymphoma, it is recommended that a veterinary oncologist or internist be consulted for guidance on protocol selection and ongoing management. Many cats with intestinal lymphoma can be managed successfully for some period of time!
Large Intestinal Disease in Dogs

History
Large bowel disorders are common in dogs. These disorders can usually be managed very successfully. It is useful in any patient with diarrhea to begin by attempting to differentiate between primarily small bowel and large bowel diarrhea, based on presenting signs and characteristics of the stool. Tests and treatment often vary for small and large intestinal disorders, making this initial characterization very important. Because large bowel - type problems occur so commonly, I often begin by asking questions relative to this area of the intestinal tract when presented with a patient with diarrhea. Specifically, the presence or absence of mucus, fresh blood, straining, and any change in frequency of defecation are discussed.

Small bowel diarrhea is often characterized by an increased frequency of defecation with evacuation of larger than normal amounts of soft stool. Dyschezia and tenesmus are not characteristics of a small bowel disorder and are apparent only if a large bowel disorder is present as well (this is an important historical point, indicating probable diffuse intestinal involvement). Urgency may be present in acute small bowel disorders or in those associated with cramping. Generally, rapid evacuation of a large volume of watery diarrhea ensues (as opposed to large bowel problems in which only a small volume is passed). Presence of undigested food indicates malabsorption, which is generally due to either EPI or rapid bowel transit time.

The presence of weight loss and inappetence in conjunction with chronic diarrhea suggests a significant small intestinal disorder (e.g., inflammatory bowel disease, lymphangiectasia, histoplasmosis, neoplasia), and their presence should hasten the clinician’s efforts toward making a definitive diagnosis. The combination of chronic diarrhea, weight loss, and increased appetite in cats suggests hyperthyroidism, inflammatory bowel disease, EPI (rare in cats), and occasionally lymphosarcoma (some cats with GI lymphoma actually have an increased rather than decreased appetite). This combination of signs in dogs is most consistent with EPI. Characteristics of diarrhea in animals with EPI include voluminous soft consistency stools that are often rancid in nature. Coprophagy is an ancillary sign that frequently occurs in dogs with EPI. Weight loss and inappetence rarely occur in dogs and cats with intestinal disorders limited to the large bowel.

Physical Examination
Along with the history, physical findings help direct the clinician regarding what specific tests, if any, should be done and how quickly a work-up should be expedited. Particular attention is paid to the animal’s attitude, hydration, and posture. Abnormal posture (e.g., arched back) may indicate abdominal pain that can be associated with acute or chronic disorders. Body weight and overall physical stature should be noted. The act of defecation, especially if there is a history of dyschezia or tenesmus, should be observed by the clinician whenever possible.

Careful abdominal palpation is done to examine for thickened bowel (inflammatory or neoplastic infiltration), intussusception, presence of a mass that could be causing partial intestinal obstruction with resultant diarrhea, and lymphadenopathy (benign or neoplastic). The caudal dorsal abdominal region should be palpated in dogs with signs of large bowel diarrhea in order to see if there is evidence of
discomfort. A rectal examination is always done in dogs with diarrhea, of any type, to examine for increased mucosal sensitivity, presence of narrowing (e.g., infiltrative disease, stricture), foreign body, or mass effect and to obtain a fresh stool sample for gross examination.

**Diagnosis**
In mild cases a diagnosis is often established based on **fecal parasite examination** (e.g., whipworms, hookworms, coccidia, and *Giardia*); **positive response to empirical treatment for difficult-to-diagnose parasite problems** (*Giardia* and whipworms); **response to dietary trials** (fiber augmented diet, elimination diets); or **response to empirical treatment for acute colitis**. Diagnostic tests for chronic large bowel diarrhea principally involve:

1. **Fecal cytology** to look for inflammatory cells (specifically neutrophils), which suggest bacterial or primary inflammatory disease. The finding of *Clostridium* spores is not meaningful, as they can be found in increased numbers in normal fecal specimens as well as diarrheic samples, and studies have shown there is no correlation between presence of spores and the presence or absence of *Clostridium* enterotoxin.
2. **Fecal culture** if history or fecal cytology suggests the possibility that bacterial infectious disease exists (*Campylobacter, Salmonella*). Fecal cultures are not commonly indicated in small animal patients.
3. **Enterotoxin assay** on stool to confirm a diagnosis of *C. perfringens* enterotoxicosis (test of choice for CPE).
4. **Colon biopsy** via colonoscopy (preferred technique) or surgery (see later discussion).

**Colonoscopy**
**Complete colonoscopy** with examination of the rectum, descending, transverse, and ascending colon, cecum, and ileocolic orifice area is preferred. Although examination and biopsy of the descending colon with a rigid colonoscope is commonly diagnostic in animals with large bowel diarrhea, such problems as occult trichuriasis in which whipworms may be grossly evident in the cecum but not in the descending colon, ileocolic or cecocolic intussusception, typhlitis, or neoplasia that is localized in the transverse or ascending colon may be missed unless a complete examination of the colon is done with a flexible endoscope. Another advantage of using a flexible endoscope is that ileoscopy may be accomplished in after complete colonoscopy. Biopsy samples should always be obtained during colonoscopy, regardless of gross appearance.

The primary **indications** for performing colonoscopy are for chronic recurrent large intestinal ñ type diarrhea, suspected chronic small intestinal disease in patients in which both upper and lower small intestinal biopsies are desired (both duodenum and ileum), and for evaluation of dyschezia, hematochezia without abnormal stool consistency, and for evaluation of a mass or possible intussusception (cecolic or ileocolic).

**Management of Large Intestinal Diarrhea**
Treatment of large intestinal diarrhea frequently involves dietary manipulation, specific anthelmintic therapy for parasite infections, antibacterial drugs or antifungal agents for infectious disorders, and antinflammatory therapy for large intestinal inflammatory bowel disease (sulfasalazine and metronidazole are the most common drugs used to control inflammation of the large intestine in dogs). Symptomatic therapy for acute non-complicated diarrhea includes bowel rest and dietary manipulation, and in some cases probiotics. The treatment for *Clostridium perfringens* enterotoxicosis is variable. Some patients respond to dietary fiber alone. Others need both antibiotics (amoxicillin or metronidazole...
for mid short-term cases, and tylosin for more chronic, recurrent type cases) and dietary fiber supplementation. If pharmacotherapy is deemed necessary for acute large intestinal diarrhea, metronidazole is often the most indicated drug and is frequently used for 5 to 7 days on an empirical basis. It is emphasized that some animals with chronic diarrhea may have several disorders at the same time (e.g., inflammatory disease, *Clostridium perfringens* enterotoxemia, and small intestinal bacterial overgrowth). A thorough work-up will lead to diagnosis of each disorder, with subsequent development of a comprehensive treatment plan. The likelihood of more rapid resolution of symptoms is much greater when each existing problem is properly treated.

Sulfasalazine (Azulfidine) is a drug that is commonly used for colitis in dogs. It is used somewhat less commonly in cats, primarily because corticosteroids are very effective in controlling colitis in cats, whereas corticosteroids are rarely effective in dogs with colitis (unless the disorder is primarily eosinophilic colitis, which is very uncommon in my experience). Sulfasalazine is a combination of 5-aminosalicylic acid (ASA) and sulfapyridine tied together by an azo bond that prevents significant absorption of the drug before it reaches the colon. Once in the colon, where the bacterial count is considerably higher than the small intestine, bacteria split the bond and release the 5-ASA for its local effect. Olsalazine (Dipentum), Asacol, and Pentasa are drugs that contain only 5-ASA combined by an AZO bond. These drugs can reach the colon in higher concentration than Azulfidine. They are more expensive, however, and dosage preparations are limited. I still use Azulfidine in most dogs in which use of a 5-ASA containing drug is desired.

The starting dose of Azulfidine in dogs is generally 10-15 mg/lb TID. In more chronic or severe cases a dose of 15-25 mg/lb TID is recommended. The dose should not exceed a total of 5 grams per day. Side effects are uncommon, but may include keratoconjunctivitis sicca (KCS), allergic dermatitis, nausea and vomiting, and cholestatic jaundice. In my experience, KCS occurs quite uncommonly in dogs on sulfasalazine. I do, however, routinely take the precaution of doing a Schirmer tear test on middle age to older dogs before instituting sulfasalazine. Duration of therapy is quite variable. In mild colitis cases, 7-14 days of therapy with sulfasalazine may be sufficient, while in others several months may be required. In some dogs with chronic unrelenting colitis sulfasalazine may be needed for months to years. In these cases the lowest possible frequency is used. For example, the dose may be gradually reduced to a BID and then SID schedule, and in some cases a single dose given every other day may be effective on a long-term basis.

Sulfasalazine works well in combination with metronidazole. If clinical signs suggest significant patient discomfort and/or biopsies reveal moderate to severe large intestinal disease I will frequently administer both drugs in combination.

Metronidazole has both an antibacterial and antiinflammatory effect. It is useful in treatment of both small and large intestinal inflammation. Metronidazole’s mechanism of action includes an antiprotozoal effect, inhibition of cell-mediated responses, and anaerobic antibacterial activity. Metronidazole is administered at 5 to 10 mg/lb two times daily. Also, I have successfully managed some canine patients with mild to moderate lymphocytic-plasmacytic colitis on a long-term basis with metronidazole.

**Histiocytic Ulcerative Colitis of Boxer Dogs**

Histiocytic ulcerative colitis (HUC) is a severe inflammatory disease of the large intestine that affects young Boxer dogs (and occasional dogs from a few other breeds), between 6 months to 4 years of age. Other affected breeds may include mastiff, Alaskan malamute, Doberman pinscher, and French bulldogs.
Historically, this was known as a debilitating disease for which there was no curative therapy. Multimodal therapy was typically employed and the goal was to minimize clinical signs. It was uncommon for signs to completely come under control even when multiple drugs were used to control the typical large bowel diarrhea and dyschezia associated with the disease. The usual result after months to several years of therapy was euthanasia due to the effects of chronic wasting disease. The good news is that there is now curative therapy through use of antimicrobials (specifically enrofloxacin). This represents one of the great, serendipitous findings (in 2002) in identifying a cause and new therapy for successfully managing and curing dogs with a severe GI disease!

HUC of dogs has features similar, but not identical to, several diseases in humans, including Crohn’s disease, ulcerative colitis, and Whipple’s disease. Investigations in recent years have been conducted by Dr. Kenny Simpson and colleagues at Cornell, using a combination of culture-independent molecular techniques (16srDNA sequencing and fluorescence in situ hybridization) to examine the mucosa-associated bacterial flora of colonic biopsies from healthy dogs, dogs with lymphoplasmacytic colitis, and boxer dogs with HUC. The findings strongly suggest that HUC is a consequence of mucosal colonization by luminal E. coli in a susceptible individual (i.e., an undefined breed-specific abnormality in boxer dogs). HUC is considered to be a breed-specific, immune-mediated disease of unknown etiology.

It is very important that dogs that may have HUC be correctly identified. This requires colonoscopy with mucosal biopsies and evaluation by a veterinary pathologist using special stains to identify the accumulation of large numbers of periodic acid-Schiff (PAS)-positive macrophages. Histologic features typically include loss of colonic epithelium and goblet cells.

Not all boxer dogs with signs of large bowel diarrhea have HUC. It is best to do colonoscopy with biopsy on any potentially affected dog so that whatever the animal’s problem is can be correctly characterized and the best treatment and monitoring course can be followed.

Treatment with enrofloxacin alone or in combination with metronidazole and/or amoxicillin has generally lead to resolution of clinical signs within 2 weeks. Most dogs are currently treated with enrofloxacin alone. It is recommended that enrofloxacin be continued for a full 8-12 weeks before it is discontinued. If there is a relapse of signs, enrofloxacin is reinstituted. If it turns out that longer term therapy will be required, enrofloxacin can be administered at 68 mg orally once every 24 to 72 hours. After a period of months it may be possible to discontinue therapy. Many dogs respond quite favorably to the initial 8 to 12 week course. Alternative antibiotics that could be considered are chloramphenicol and azithromycin.

References:
Management of Constipation, Obstipation, and Megacolon in Cats

Introduction
Constipation is a fairly common problem seen in middle aged to older cats. It can become severe (obstipation) and be debilitating; causing discomfort, lethargy, and inappetence. Fortunately, with attentive oversight and medical management many cats can be managed successfully for their normal life expectancy. Mild constipation resolves spontaneously or is treated on an outpatient basis by dietary adjustment and oral laxatives. Severe constipation is treated initially by complete evacuation of impacted feces from the colon followed by a management course tailored to the needs of each specific cat. For most cats with chronic constipation management will include either single or combination therapy including stool softeners, prokinetic drugs to stimulate colonic propulsive activity, and dietary fiber given in moderation (i.e., type and amount can make a difference). Recently, a new therapeutic food has been shown to be quite effective for increasing frequency of defecation and many cats have improved significantly, while concurrently facilitating lower ancillary medication requirements. In cases that are refractory to all attempts at medical management, surgical removal of the colon can be performed (colectomy) and when in the care of an experienced surgeon and with excellent post-operative management, most cats do quite well.

Definitions
Constipation: Infrequent or difficult evacuation of dry, hard feces. This may be acute or chronic in nature and in general less than one stool is passed every other day.
Obstipation: A severe form of constipation. Feces are hard and dry and the animal is no longer able to defecate. Intractable or refractory constipation. Medical intervention is required.
Megacolon: A state beyond constipation whereby fecal material is not passed and there is generalized colonic dysfunction with radiographic evidence of colonic dilatation and fecal impaction. Abnormalities in smooth muscle function have been identified as a cause of megacolon. Different forms of megacolon have been identified depending on the cause; including dilated (end-stage of idiopathic colonic dysfunction) and hypertrophic (result of obstructive disease, e.g., pelvic injury with narrowing of the canal, colonic stricture, tumor, foreign body).

Clinical Presentation
Constipation, obstipation, and megacolon can occur in cats of any age, sex, or breed, but middle aged male cats are the group most commonly affected. In a recent clinical review of cases in Canada males outnumbered females 3.4:1, the average age was 8 years, and the average weight was 8 kg. In another series 70% of the cases were male cats, the mean age of affected cats was 5.8 years, and breeds represented were domestic shorthair (46%), domestic longhair (15%), and Siamese (12%). Affected cats are usually presented for reduced frequency or absence of defecation for a period of time ranging from days to weeks to months. Some cats are observed making frequent attempts to defecate and little or no fecal material is evacuated. Some cats have painful defecation. Others may actually sit in the litter box for prolonged periods without assuming a defecation posture. Any feces that are passed are dry and hardened. There may occasionally be hematochezia due to the irritant effect of hardened feces on the colonic mucosa, and sometimes diarrhea can be intermittently present as well. Other signs may include anorexia, lethargy, vomiting, dehydration, and weight loss.

Diagnosis
The diagnosis is established through the history and physical examination. Diagnostic tests may help determine a cause.
**History:** The history should determine duration of constipation, how frequently the cat is attempting to defecate or visit the litter box, and information on diet. Dietary information is particularly important as diets low in fiber or high in nondigestible material such as hair, bones, or other foreign material can contribute to constipation. Water consumption should also be discussed. Good hydration status is essential for normal defecation. Environmental factors should also be considered. These include lifestyle (a sedentary lifestyle with lack of exercise, which could be the cat’s norm or possibly related to arthritis, an especially important point to consider in older cats), any change in environment (e.g., recent boarding), and factors related to the litterbox (i.e., easy to reach location or not, easy to enter and exit [low walls vs. walls that may be too high for a particular cat], and whether or not the litterbox is cleaned frequently enough and fresh litter provided are all important factors to consider in gaining a complete perspective. Any recent or current medication administration should also be reviewed (e.g., narcotics, bismuth compounds, diuretics, sucralfate, mood modifier drugs, etc) as some drugs could contribute to prolonged fecal retention. Any past trauma should also be notes (e.g., pelvic fractures with potential for narrowing of the pelvic canal).

**Physical Exam:** Abdominal palpation readily reveals presence of a large amount of very hard fecal material in the colon. Cats are often at least mildly dehydrated at the time of presentation. Palpation along bony structures may identify discomfort that can be associated with osteoarthritis. Thorough rectal palpation is important and is performed under sedation or general anesthesia, prior to any attempts to administer enemas or perform manual debulking. Rectal examination may detect a narrow pelvic canal in cats with pelvic fracture malunion or other unusual causes such as a foreign body, rectal diverticulum, stricture, or mass. Any matting of perineal hair in longer-haired cats should be noted, as pseudocoprastasis can be a causative factor.

**Diagnostic Tests:** It is important to perform a thorough diagnostic evaluation at the time of initial presentation for constipation or obtipation. Testing may reveal an underlying cause. While most cases are idiopathic, the baseline assessment is still very important so that a more complete understanding of the cat’s overall health status can be established. Baseline evaluation should include CBC, complete biochemical profile, T4, urinalysis, and survey abdominal radiographs. Blood tests will identify metabolic causes of constipation (e.g., hyperparathyroidism, hypothyroidism, hypokalemia, hypercalcemia), where there may be interference with colonic smooth muscle function. In cats with chronic GI disease it is always a good idea to include a serum cobalamin test as well. If the cobalamin is in the low normal or subnormal range, supplementation is provided. Most cats with constipation/obstipation do not require advanced diagnostics, however, in some cases ultrasound, contrast radiography (barium enema) or colonoscopy may be indicated to further examine for any specific causes of disease.

**Immediate Treatment of Cats Presented with Acute Constipation, Obstipation, and Megacolon**

The first step is to address dehydration and any electrolyte abnormalities (pay close attention to potassium). Anesthesia should not be administered for manual deobstipation until a baseline assessment is completed and fluid therapy instituted (route and volume depends on the patient’s condition) and the patient is appropriately stabilized. If manual debulking is planned it may help during this interim time period to administer a few enemas consisting of warm water and K-Y lube just to begin the fecal softening process. It is not expected that early enemas without concurrent manual breakdown of the fecal mass will produce any fecal evacuation. In obstipated cats *either* manual debulking under anesthesia is required or alternatively oral lavage solutions can be administered via slow trickle through a nasoesophageal tube and in these patients enemas are often not necessary.
The manual debulking process includes administration of enemas with concurrent means of manually breaking down the fecal mass. Usually the most difficult part is to break down and remove the large hard mass closest to the anus. Once this first large segment is removed the remainder of the fecal mass usually doesn’t pose as much difficulty. IMPORTANT: Use a well cuffed endotracheal tube, because cats will sometimes vomit during the deobstipation process.

Often just warm water (5-10 ml/kg per enema) with some basic lubricant added is the enema solution administered. Other solutions can include warm isotonic saline (5-10 ml/kg), dioctyl sodium sulfosuccinate (DSS; 5-10 ml/cat), mineral oil (5-10 ml/cat), or lactulose (5-10 ml/cat). Caution: DO NOT combine DSS with mineral oil as there is risk of systemic absorption of mineral oil resulting from action of the docusate, and mineral oil coats the feces, reducing the emollient effect of the docusate. Also, DO NOT use sodium phosphate (Fleet Children’s Enema) enemas in cats because they can cause dangerous hypernatremia, hyperosmolality, hyperphosphatemia, and hypocalcemia. Soapy solutions should also be avoided as these can be irritating and hexachlorophene can be neurotoxic.

Other solutions such as pediatric glycerin suppositories (irritant and osmotic effect) and bisacodyl suppositories (promote colonic contractions) should be reserved for simple cases of constipation. Administer the enemas with a well-lubricated 10-12 French rubber catheter or feeding tube that is gently inserted into the colon. It may help to infuse solution while the tube is being advanced, once it is passed far enough in to prevent solution from just flowing right back out as soon as it is infused. Administer the solution slowly, as too rapid administration may cause vomiting or even perforation. Manual breakdown of hard impacted fecal masses is best accomplished by abdominal palpation and manipulation. The manipulation should be done as gently as possible so as to minimize trauma to the colon. Rectal palpation may help. In some cases it is necessary to use a sponge forceps instrument passed rectally. Once again, caution is advised so that mucosal trauma is minimized, and this is especially important in cases of a devitalized colon. These procedures are expected to take time and patience is essential. In particularly severe cases it may be best to do the complete deobstipation over the course of several days in order to avoid prolonged anesthesia times and hypothermia, which are dangerous for debilitated cats.

An alternative approach that has worked quite well in some settings is to administer polyethylene glycol 3350 (GoLytely[Braintree Laboratories], Colyte [Schwarz Pharma]) via nasoesophageal tube at rates between 6 to 10 ml/kg/hr to aid removal of fecal impaction. The median total dose in a group of cats treated with the NE tube protocol was 80 ml/kg (range 40-156 ml/kg). The median time to significant defecation in obstipated cats was 8 hours (range 5 to 25 hours) (Carr, 2010). With this approach cats may not need any enemas.

**Longterm Management and Prevention of Recurrent Constipation and Obstipation**

Once the colon has been completely evacuated, a treatment regimen is instituted to prevent or at least minimize further occurrences of constipation or obstipation. For many cats, this initially includes prokinetic and laxative therapy, and dietary management. While minor cases of constipation can often be managed with dietary therapy alone (fiber supplementation), moderate to severe cases require combination therapy, at least at the outset.

**Colonic Prokinetic Therapy**

The 5-HT4 serotonergic agonists (cisapride, prucalopride, tegaserod, mosapride) stimulate motility from the gastroesophageal sphincter to the descending colon with relatively few side effects in animals. Metoclopramide does not have any significant effect on intestinal motility and is of no benefit in
managing constipation in cats or any other species. The H2-receptor blocker drugs ranitidine (Zantac) and nizatidine (Axid) may have some beneficial effect in increasing colonic motility. Over the last 20 years cisapride has by far been the most used drug for colonic prokinetic effect in cats and it has been remarkably effective in management of chronic constipation.

Cisapride is a benzamide derivative that enhances colonic propulsive motility by stimulating colonic smooth muscle, increasing the physiologic release of acetylcholine from post-ganglionic nerve endings of the myenteric plexus, and acting as a 5-HT4-serotonergic agonist. The initial recommended starting dose is 1 mg/kg orally every 8 to 12 hours, administered 30 minutes before food. In general, cats weighing 4.5 kg (10 pounds) or less receive 2.5 mg per dose initially, and for cats weighing more than 4.5 kg the starting dose is 5 mg per dose. The dose can be gradually increased if necessary over time. Treatment failures are often related to giving too low a dose of cisapride (e.g., 2.5 mg per dose for a 6.3 kg [14 lb] cat). It is better to be a little more aggressive at the outset and the dose can always be lowered over time. Some cats with milder disease may respond well to cisapride or stool softeners given alone or in combination with special dietary therapy.

Over time some cats with megacolon will become refractory to the initial effective dose. In this case the cisapride can be gradually and safely increased, e.g., cats receiving 5 mg every 8 hours are increased to 7.5 mg for 2 or 3 of the daily doses, then later all 3 doses are at 7.5 mg, cats receiving 7.5 mg per dose are increased sequentially to 10 mg, etc. If doses higher than 10 mg every 8 hours are required, strong consideration should be given to recommending colectomy. It is also important of course in the refractory cats to ensure optimum therapy with stool softeners and dietary management. Note that recently the Royal Canin Feline Fiber Response diet came on the market (latter part of 2010 in the United States, and earlier in Europe and Canada) and this diet has been quite effective in management of chronic constipation in cats. In many cats medication requirements are lowered when this particular food is fed. The diet is discussed further along in the dietary therapy section of these notes.

Despite the fact that cisapride was removed for the market for use in humans in 2000, due to concerns about cardiac arrhythmias possibly occurring in some individuals, it has been remarkably safe in animals and it has seen frequent use in veterinary medicine and available through compounders. It has been for many years the most effective therapy for constipation in cats. However, in mid 2012 the supplies of raw product became limited and could potentially be gone entirely at some point. If cisapride will no longer be available, we will be turning to other prokinetic drugs, and these potentially may include prucalopride or mosapride.

Ranitidine (Zantac) and nizatidine (Axid) are H2-receptor antagonists that also stimulate GI and colonic motility at standard doses (recommended doses for cats are: 3 mg/kg orally every 12 hours, nizatidine 2 to 4 mg/kg orally every 12 to 24 hours). They increase acetylcholine by inhibiting synaptic acetylcholinesterase. However, these drugs are not as potent as cisapride as promotility agents and their use is likely limited to milder cases of constipation in cats.

**Laxative Therapy**

Laxatives promote evacuation of the bowel through inter-related effects on both intestinal mucosal fluid transport and colonic motility. They are classified by their properties and mechanisms of actions as (1) bulk forming, (2) lubricant, (3) emollient, (4) osmotic, and (5) stimulant. Use of the oral laxatives often needs to be individualized by adjusting the dose until the desired frequency of defecation and fecal consistency are obtained. There are myriad products available for management of constipation. The stool softeners used most frequently in cats are the osmotic laxatives lactulose (Cephulac, Chronulac) and MiraLax (polyethylene glycol 3350), and fiber (bulk forming).
Lactulose is one of the most effective laxatives in the osmotic group and is usually the first product prescribed for cats. Osmotic laxatives consist of poorly absorbed disaccharides (such as lactulose), ions (such as magnesium hydroxide and magnesium citrate), or inert osmotic agents (polyethylene glycol) that osmotically retain water in the colon and thereby help soften or liquefy feces. Lactulose is started at 0.5 to 1 ml/kg given every 8 to 12 hours and then adjusted to effect. It is a safe and effective “all purpose” laxative for short or long-term use. If the dosage is too high, abdominal discomfort, flatulence, and diarrhea may occur. This problems resolve when the dose is reduced. Some cats will tolerate lactulose for a while, but then they drool or have other untoward effects that may be bothersome to the owner.

If lactulose is not well tolerated one of the polyethylene glycol products such as MiraLax can be tried. MiraLax has been well tolerated. The starting dose is ¼ tsp powder mixed in the food twice daily and it can be increased if necessary.

Dietary Management
While fiber can be very beneficial to cats with mild constipation, feeding too much fiber to cats with megacolon can be detrimental (too much bulk is created for a weakened colon to evacuate). In recent years megacolon cats were more commonly fed a highly digestible, low fiber diet (often a wet food) for this reason, and they were primarily managed with cisapride and either lactulose or MiraLax (stool softeners). In late 2010 a new diet was introduced in the United States from Royal Canin – the Feline Gastrointestinal Fiber Response diet. This dietary formulation has become a very effective therapeutic option for cats with chronic constipation and megacolon. The diet was available earlier in Europe and reports were presented at ECVM in 2010 and AAVN in 2011. The fiber content is 11.5% psyllium fiber, compared to other high fiber diets which often contain in excess of 20% fiber on an as fed basis. The specific fiber content supports healthy digestive transit and eases defecation. This is a dry formulation and clinical experience has shown excellent palatability and most cats have readily embraced this food. It can be fed to other cats in the same household that are unaffected by constipation problems. Some cats with chronic constipation have actually been able to come off prokinetic and stool softener medications altogether, while others that still require medication may do quite well on less frequent dosing.

References