Vermont Veterinary Medical Association

# 2016
# WINTER MEETING

Saturday February 13, 2016
Burlington Hilton Hotel

**Todd R. Tams, DVM, DACVIM**
Chief Medical Officer, Veterinary Centers of America
Los Angeles, CA
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## UPDATES IN CLINICAL GASTROENTEROLOGY OF DOGS AND CATS

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# HOLD THE DATES!

## VVMA SUMMER MEETING

Friday, June 24, 2016
Burlington Hilton Hotel
6 CE Credit Hours

**Small Animal Neurology:** Alexander de Lahunta, DVM
**One Health: A Community Approach to Shared Bacteria – MRSA and Beyond:** Meghan Davis, DVM, Ph.D., MPH
**Large Animal:** Bovine topic TBD

## VVMA SPAY/NEUTER MEETING AND WET LAB

Saturday and Sunday
October 8-9, 2016
Capital Plaza Hotel, Montpelier
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**Stay tuned for more information.**

**Thanks for being a member!**
**We are pleased to welcome the following members who joined since our 2015 Summer Meeting:**

Elizabeth Brock, Northwest Veterinary Assoc.
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***To be the preeminent authority on veterinary medicine and animal well-being in Vermont***

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Vermont Veterinary Medical Association

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For questions or more information on the VVMA, contact Executive Director Kathy Finnie

Vermont Veterinary Medical Association

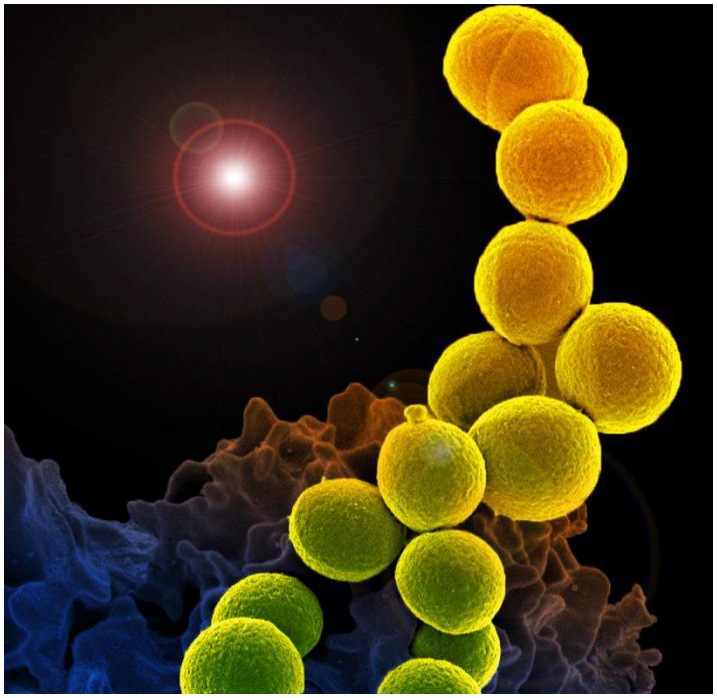
with Vermont Department of Health & UVM Medical Center

# A Community Approach to Shared Bacteria: MRSA and Beyond

**Friday, June 24, 2016**

**9:00 – 4:30**

**Burlington Hilton Hotel**



National Institute of Allergy and Infectious Diseases (NIAID)

**Meghan Davis, PhD, MPH, DVM**

*Assistant Professor of Environmental Health Sciences*

*Johns Hopkins Bloomberg School of Public Health*

Dr. Davis will discuss microbial sharing between animals and people and the role of the environment as a reservoir. She will also consider allergies and asthma and their relationship to microbiome and the hygiene hypothesis.

Open to veterinarians, physicians, and allied health professionals.

Online registration available spring 2016 www.vtvets.org

Vermont Veterinary VVMA Medical Association

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# Esophageal Disorders in Dogs

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA

**Megaesophagus** is one of the most common causes of regurgitation in dogs. Megaesophagus refers to a specific syndrome characterized by a dilated hypoperistaltic esophagus and should be differentiated from other causes of esophageal dilation (e.g., foreign body, vascular ring anomaly, mucosal stricture, neoplasia) which may or may not be characterized by abnormal peristalsis. Significant complications of regurgitation include aspiration pneumonia and chronic wasting disease.

**Esophagitis** occurs more commonly than is usually recognized in clinical practice. This seminar will emphasize diagnosis and management of esophageal hypomotility and esophagitis in dogs and cats.

Regurgitation refers to a passive, retrograde movement of ingested material to a level proximal to the upper esophageal sphincter. Usually this occurs before ingested material reaches the stomach. The term reflux refers to movement of gastric or duodenal contents into the esophagus without associated eructation or vomiting. This process may or may not produce symptoms.

Regurgitation is usually a clinical sign of an esophageal disorder. The esophagus is a tremendously dilatable muscular tube that acts via a series of well-coordinated peristaltic contractions to move ingesta from the mouth to the stomach. Regurgitation in most cases results from abnormal esophageal peristalsis, esophageal obstruction, or asynchronous function of the gastroesophageal junction.

### *Diagnostic Procedures*

It is essential that the clinician make a clear differentiation between regurgitation and vomiting at the outset. Failure to recognize the difference between regurgitation and vomiting often leads to inappropriate testing (i.e., tests most useful for diagnosis of abdominal disorders are generally performed), misdiagnosis, and the use of ineffective treatment protocols. Therefore, the first diagnostic step is to obtain an accurate history. This is best accomplished by a clinician who maintains a high index of suspicion regarding the possible occurrence of regurgitation and who subsequently asks clear questions of the client about their pet's clinical signs.

Thoracic radiography for survey evaluation of the esophagus is the most important screening procedure in the diagnosis of a regurgitation disorder. Radiographs are evaluated for evidence of esophageal dilation and the presence of a foreign body or thoracic mass. Remember that transient dilation may occasionally occur and can be related to aerophagia, anxiety, dyspnea, anesthesia, and vomiting. Knowledge of the history is important in differentiation of potentially transient causes from those that are more long-standing. If survey radiographs fail to provide a definitive diagnosis, a barium esophagram (with fluoroscopy if available) should be performed. A liquid barium suspension (10 to 20 ml prior to each exposure) is best for evaluating for esophageal dilation. A mixture of food and barium is superior for evaluating

esophageal motility because in some patients with slightly to moderately decreased contractility peristalsis may be adequate for liquid but clearly unable to propel solids aborally in a normal manner.

A baseline CBC and biochemical profile should be run in all patients with megaesophagus to look for evidence of underlying problems. Specific tests to evaluate for systemic disorders such as hypoadrenocorticism (ACTH stimulation), CK (polymyositis), and serum lead levels are done if the history and/or physical examination indicate that these primary disorders may exist. Myasthenia gravis should be considered in any patient with megaesophagus. The test of choice is an acetylcholine receptor antibody titer. Acetylcholine receptor antibody titers are run at the Comparative Neuromuscular Laboratory in La Jolla, CA (Dr. Diane Shelton). Contact the laboratory for forms and sample submission instructions.

The address is:
**Comparative Neuromuscular Laboratory**
9500 Gilman Drive
Basic Science Building, Rm. 2095
University of California, San Diego
La Jolla, CA 92093-0709
**Phone:** (858)534-1537 **Fax:** (858)534-0391
**Web:** http://vetneuromuscular.ucsd.edu/
**Email:** musclelab@ucsd.edu

If radiographs reveal any suggestion of esophageal stricture, foreign body, mass, or diverticulum, endoscopy provides the most rapid and cost effective method of making a definitive diagnosis.

### *General Management Principles for Megaesophagus*

The main objectives of treatment for regurgitation disorders are to remove the initiating cause as early as possible, minimize chances for aspiration of esophageal content, and maximize nutrient intake to the GI tract. In most cases, idiopathic megaesophagus is incurable, and treatment involves an individually tailored feeding regimen with the patient eating in an elevated position. Esophageal foreign bodies and intraluminal strictures can often be managed successfully with endoscopic techniques and bougienage or balloon dilation respectively. Medical management is indicated for such secondary causes of esophageal dilation as myasthenia gravis, hypoadrenocorticism, systemic lupus erythematosis, polymyositis, and esophagitis.

Megaesophagus patients are best fed with the upper body in a fully upright position. This is best accomplished by positioning the dog in a special high chair (see information below about Bailey chairs). It is important that proper positioning be clearly demonstrated to the client so that there is no misunderstanding. Whenever possible the elevated position should be maintained for a full 10 minutes after ingestion of food is completed. Various props to aid in the elevation process have been used successfully, including ladders, stairs, ramps, tables, and chairs. Since the esophagus is virtually never completely empty in a megaesophagus patient it is often helpful to hold the animal in an elevated position for 5 to 10 minutes at a time sometime between meals and at bedtime (I ask all of my clients to at least do the bedtime

elevation in an effort to empty the esophagus as much as possible prior to an expected period of prolonged recumbency).

Megaesophagus patients are ideally fed 2 to 4 times daily. This depends, of course, on the caregiver's time constraints. I have had the best success feeding soft moist to solid (chopped) canned food consistency. I only recommend trying gruels if the semi-moist consistency is not well tolerated. Some patients do well when fed a series of "meatballs" fashioned from canned food. Others can tolerate dry food fairly well. A key point is that each patient is an individual and clients should be instructed to experiment with various food consistencies in order to determine the best approach for their own pet.

Many patients with idiopathic megaesophagus can be managed successfully for months to years. I have known many dedicated owners who have managed to find the time required to care for their pets. As a result of this experience I try to offer as much encouragement as possible at the time of diagnosis. The most worrisome complications that can occur are aspiration pneumonia and significant weight loss. The prognosis is guarded to poor in patients that suffer recurrent episodes of pneumonia.

An option in cases where frequent regurgitation remains an ongoing problem with or without aspiration events is to place a gastric feeding tube (e.g., percutaneous endoscopy-guided gastrostomy tube [PEG]). All food and water can then be administered through the feeding tube (some patients have been maintained for as long as 3 or more years in this way). Periodic tube replacement will be necessary. Low profile feeding tubes often work best for long term tube feeding. This method of management has been highly successful for some dogs that continue to regurgitate frequently despite excellent efforts to manage them with an elevated feeding program.

**Special Feeding Chairs**

**Bailey Chair:** There is a lot of information available on the internet about a special feeding chair that was designed by Donna and Joe Koch, the owners of a dog named "Bailey." "Bailey" had been diagnosed with megaesophagus. The dog sits in a totally upright ("begging") position to eat, drink, or take medication and gravity aids transit of anything ingested to the stomach. Use key words "Bailey Chair" for an internet search and information on how to acquire or build a Bailey chair (also see support group information below).

**Custom Bailey chairs: www.BaileyChairs4Dogs.com**

**Megaesophagus Client Information and Support Group**

**www.caninemegaesophagus.org**

Provides information on the causes of congenital and idiopathic *canine megaesophagus*, the clinical signs, risk factors and accompanying disorders, with lots of feeding tips.

A Support Group for owners of dogs that have, had or may have megaesophagus, was established at Yahoo Groups in 2002 by Dave Kay and Katy Weeks, in memory of their Golden Retriever, Rusty. Members of the group can provide suggestions and ideas for feeding and care of dogs with megaesophagus. A veterinarian monitors the group as an advisor and offers suggestions for members to discuss with their veterinarians. The group is at: http://groups.yahoo.com/group/megaesophagus/ and requires membership.

## Esophagitis

**Inflammatory diseases of the esophagus occur more commonly than they are recognized.** Inflammatory changes can range from mild mucosal inflammation that may or may not be grossly evident, to moderate to severe ulceration and transmural involvement. Any disorder that causes acute or chronic frequent vomiting has the potential for causing esophagitis. This especially includes causes of severe vomiting, such as intestinal foreign bodies, gastric foreign bodies, acute pancreatitis, parvovirus enteritis, and gastrinoma. Dogs with parvovirus enteritis that are debilitated and recumbent are especially at risk. Vomited fluid that is retained in the esophagus is not cleared adequately in weak and recumbent patients. As a result the esophageal mucosa is bathed with gastric acid and activated enzymes that will cause mucosal injury.

Other causes of esophagitis include esophageal foreign bodies, chemical and thermal injuries, injury from lodged medication (doxycycline capsules in cats can become lodged and cause esophagitis and even stricture formation), gastroesophageal reflux, and anesthesia related reflux.

### *Diagnosis of Esophagitis*

The clinical signs of esophagitis vary considerably, depending on the degree of inflammation present. The clinician must maintain a high index of suspicion because in many cases only subtle clinical signs may be evident. With mild esophagitis there may be increased swallowing motions, salivation, and inappetence. In more severe cases there may be gulping, regurgitation, dysphagia due to pain, total anorexia, and signs that suggest esophageal pain, such as reluctance to move, standing with the head extended, reluctance to lie down, and trembling. Heartburn pain in humans can be quite intense, and it is suspected that a similar situation exists in animals. Esophageal hemorrhage may occur in severe cases. Signs such as increased attempts at swallowing, salivation, and regurgitation, and inappetence that occur within 1 to 4 days of an anesthetic procedure strongly suggest reflux esophagitis. Chronic reflux esophagitis occurs most commonly in patients with hiatal hernia disorders.

Radiographic survey and contrast studies are often normal in patients with mild to moderate esophagitis. Survey films may show increased esophageal density in moderate to severe esophagitis. There may also be various degrees of esophageal dilation, since esophageal inflammation may inhibit motility. Persistent contrast in the thoracic esophagus or esophageal dilation, or both, suggest the possibility of gastroesophageal reflux.

A definitive diagnosis of esophagitis is most often made by endoscopic visualization of the esophageal mucosa. Variable degrees of mucosal erythema or isolated patches of eroded mucosa may be seen. However, as also occurs in humans, some animals with esophagitis do not have gross esophageal abnormalities, and in these cases symptom patterns in conjunction with positive response to therapy are the key components to a presumptive diagnosis.

### Treatment of Esophagitis

It is important to note that, although the esophagus is physically a very tough and resilient structure, once it is injured it does not always heal very quickly. For inflammatory disorders

fairly aggressive combination drug therapy is often required. Treatment may include dietary modification, proton pump inhibitors (PPIs), H2-receptor antagonists, GI promotility agents, anti-inflammatory drugs, and mucosal protectant therapy. Single or combination drug therapy may be required, depending on factors that include whether treatment is designed mostly for prevention, duration or severity of mucosal injury, and clinical signs. Most affected dogs and cats are managed with either an H2-receptor antagonist or a PPI (e.g., omeprazole). Additionally, high-protein and low-fat diets, a prokinetic drug, and cytoprotective medication are indicated in some cases.

Mild reflux esophagitis is often asymptomatic and generally resolves without therapy. If clinical signs suggestive of reflux esophagitis occur within several days of an anesthetic procedure, treatment should be instituted, regardless of whether endoscopy is available for definitive diagnosis. Treatment in this situation usually includes an H2-receptor antagonist or a PPI, and a prokinetic drug (metoclopramide or cisapride). The duration of therapy will typically be 7 to 14 days. A longer duration will be required if clinical signs persist.

H2-receptor antagonists are used to decrease gastric acid production, thereby decreasing acid volume available for reflux. H2-recptor antagonists also reduce the volume of gastric acid that is produced. There is no adverse effect on resting or stimulated LES pressure levels. Ranitidine (2.2 mg/kg [dog], 3 mg/kg [cat] orally every 12 hours), or famotidine (Pepcid, 1 to 1.2 mg/kg orally every 24 hours, or every 12 hours if there is severe esophagitis) is generally used for 2 to 3 weeks in dogs and cats with acute reflux esophagitis. I have strongly preferred to use famotidine (Pepcid) because of its long dosage interval and the fact that it is associated with fewer side effects. Further, studies have shown that famotidine is the most effective H2-blocker drug for dogs and cats. It should also be understood that none of the H2-receptor antagonists are highly effective in dogs and cats (i.e., okay to use in mild cases of esophagitis, but patients should be observed carefully for signs of adequate response). Another H2-receptor antagonist that can be tried is nizatidine (Axid). The dosage is 2.5 to 5 mg/kg orally every 24 hours. Ranitidine and nizatidine also have a mild gastric prokinetic effect. Long-term therapy should be used in hiatal hernia patients with chronic reflux esophagitis if corrective surgery either is not performed or is unsuccessful.

PPIs are drugs that much more significantly inhibit gastric acid secretion in response to all modes of stimulation. This class of drug is used when esophagitis is moderate to severe, as H2-receptor antagonists are not as effective in reducing acid levels. PPIs include omeprazole (Prilosec), lansoprazole (Prevacid), esomeprazole (Nexium), pantoprazole (Protonix), and rabeprazole (Aciphex). Omeprazole is the PPI that has been used most frequently in animal patients. PPIs decrease acid secretion by inhibiting H+, K+ ATPase (commonly called the proton pump), thereby blocking the final, common step in the secretion of gastric acid. PPIs control both basal and meal-stimulated acid secretion. Therefore, the acid suppression achieved by a PPI is more complete and longer lasting than can be attained with an H2-receptor antagonist. The currently recommended dosage for omeprazole is 1.5-2.5 mg/kg orally (this dose is based on studies published in 2012), once to twice daily, administered 30-45 minutes prior to feeding. It may be best to administer twice daily as a matter of routine for the first 7 to 10 days, and BID for longer periods in more severe cases. Maximal acid reduction is not achieved until 2 to 5 days after oral administration is begun; therefore,

famotidine is often administered concurrently during the first 5 days to ensure some level of acid reduction as early as possible.

**Moderate to Severe Esophagitis – IV PPI Protocol**
The PPI drug pantoprazole is currently available in an injectable preparation. Lansoprazole was available in an IV formulation at one time but this is not currently available. In situations where the patient is NPO or where more rapid effective blood levels are needed, pantoprazole is administered IV.

**Pantoprazole (Protonix) IV, 40 mg/vial** Marketed by: Wyeth(R) Pharmaceuticals Inc.

**Dose:** 0.7-0.8 mg/kg q24 hours (but it can be dosed at q22 hours to get 2 doses out of 1 bottle as it's $$)

**Administration:** The Protonix should be reconstituted with 10mL of 0.9% NaCl and then further diluted with 100mL of 0.9%NaCl, LRS or 5%Dextrose.

**Final concentration** = 0.4 mg/mL

Give over 15-20 minutes

***Esophagitis Associated with Frequent Vomiting***
Clinicians are especially cautioned to be more attentive to patients that might have esophagitis secondary to frequent or severe vomiting (e.g., caused by GI foreign bodies, parvoviral enteritis, acute pancreatitis, or renal failure). Esophagitis can easily develop in these situations, and it no doubt adds significantly to the discomfort that the patient is already experiencing. In these cases, both sucralfate and an H2-receptor antagonist are used to treat esophagitis. I use famotidine (Pepcid) injectable at 0.5 mg/kg IV BID. An antiemetic drug such as maropitant (Cerenia) is injected to help decrease the frequency of vomiting. We are also using Cerenia much more frequently now PRE-OP to help decrease the frequency of vomiting post-op. Studies have shown that Cerenia is very effective in reducing the incidence of perioperative vomiting and animals often return to feeding earlier and eat a greater volume of food if they received Cerenia before surgery.

Sucralfate is given orally, in suspension form so as to better coat the esophagus, usually 30 to 60 minutes after antiemetic therapy has been administered. The duration of therapy in patients with reflux esophagitis depends on the cause and degree of inflammation. For moderate to severe esophagitis, 4 to 8 weeks of therapy or more may be required to achieve full healing of the esophagus. For esophagitis related to frequent or severe vomiting, treatment is usually administered 5 to 7 days, and only longer if clinical signs or endoscopic findings warrant.

## Diagnosis of Acute and Chronic Vomiting in Dogs and Cats

Todd R. Tams, DVM, DAVCIM
Chief Medical Officer
VCA

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 (sensitivity on lipase depends on which specific test is being done)
- 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
- ****new lipase assay from Antech (2 DGGR) approximates sensitivity of PLI for diagnosis of pancreatitis**
- Antech has discontinued the somewhat less sensitive 1,2-diglyceride assay as of October 4, 2015. The new assay is 2 DGGR and is on every biochemical profile for dogs and cats (where lipase is normally included)

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[a]
Selected diagnostics
Specific/symptomatic therapy

**Serious or Systemic Clinical Signs**

Complete blood count
Complete biochemical profile
Urinalysis
Fecal examination[a]
Parvovirus test if indicated
Survey abdominal radiographs (3 views)
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 baseline or ACTH stimulation
  - —cPLI or fPLI (pancreatitis)
  - —Leptospirosis serology and/or lepto PCR
  - —Bile acids assay (to asses 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**[b] (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

[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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# Drug Therapy for Vomiting in Dogs and Cats

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA

## 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 and cats. 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, borborhygmus, 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: We generally advise that Cerenia be used at a reduced dose (50%) 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. In practice a sting can still be expected in some patients even when the product is kept refrigerated.

**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.

**Note: On January 14, 2016, Zoetis announced a new label claim for IV use of Cerenia.** In two separate bioequivalence studies conducted in 2015 by Zoetis in dogs and cats, when delivered intravenously, CERENIA reached concentration and absorption levels as quickly as with subcutaneous injection. Additionally, two separate safety studies in dogs and cats

indicated no related effects on survival or clinical findings, and there were no reports of pain on intravenous injection.

**Consider Using Cerenia More Routinely Administered Pre-Operatively**

Some practices have now instituted the practice of including an injection of Cerenia administered routinely in the pre-operative period. I am a strong proponent. Reasons for doing this include:

- Help prevent post-op vomiting and nausea and decrease chances of aspiration
- Adjunctive visceral analgesia
- Improved patient comfort in the post-op period
- Earlier return to eating, with improved appetite and volume of food consumption

In this setting, Cerenia can be administered anytime in the pre-op period. If morphine or hydromorphone are going to be given as part of the pre-anesthesia sedation and preemptive analgesia plan, and the clinician desires to *prevent* vomiting secondary to these emetogenic drugs, Cerenia is administered 45 minutes prior to the emetogenic drugs. In one study when Cerenia was administered 45 minutes prior to morphine at 0.5 mg/kg, 0/15 dogs vomited, while 15/16 dogs who received saline instead of Cerenia vomited at least once (and 4 of the dogs vomited 4 times). We have seen excellent post anesthesia recovery periods in dogs that have undergone a variety of procedures, including OVH/neuter as well as prolonged anesthesia for dental procedures, major abdominal procedures, etc. We are also using Cerenia more routinely prior to performing endoscopic procedures.

The uniform response is that most patients recover more smoothly, more quietly and are presumably more comfortable overall. Clients of course are very happy when their pet eats earlier than would be otherwise expected. This has represented a gratifying advance in patient care in many ways - - helping our patients be more comfortable is always good.

**How long can Cerenia be used on a consecutive days schedule?**

The original label guidance stated 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.

Further, in 2015 the label was changed, based on studies that evaluated the effect of maropitant when given at various doses for longer periods of time. Cerenia has a high safety profile and a longer duration of use, based on each patient's individual needs, is now well accepted.

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 original label duration of 5 days 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 ledged 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).

# Acute and Chronic Diarrhea in Dogs and Cats

## Giardia, *Clostridium perfringens* Enterotoxicosis, *Tritrichomonas foetus*, and Cryptosporidiosis

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA
Los Angeles, California

**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* enterotoxicosis, 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 and 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 is 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**

| **Young Animals** | **Older Animals** |
|---|---|
| **Dietary** problems | **Dietary** problems |
| **Parasites** | **Parasites** less common but always possible |
| - nematodes | - nematodes |
| - protozoa (*Giardia*, *Trichomonads*) | - protozoa (*Giardia*, *Trichomonads*) |
| - coccidia (including *Cryptosporidium*) | - coccidia (including *Cryptosporidium*) |
| **Viral and bacterial** | Viral causes uncommon in older animals |
| **Clostridium perfringens enterotoxicosis** | **CPE** (common in older animals) |
| **(CPE)** | **Acute colitis** (fairly common cause of diarrhea in older animals) |

*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, a*ccurate* 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* enterotoxicosis 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)**

**Acute Diarrhea – DOGS (initial screening)**

- ☐ Direct smear in house (fresh sample (perform by <1hr)
- ☐ $ZnSO_4$ w/centrifugation
- ☐ Giardia antigen test
- ☐ Parvo test if indicated

**Later if Persistent:**

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

**Acute Diarrhea – CATS (initial screening)**

- ☐ Direct smear in house (fresh sample (perform by <1hr)
- ☐ $ZnSO_4$ w/centrifugation
- ☐ Giardia antigen test

**Later if Persistent:**

- ☐ Repeat all of the above
- ☐ Cryptosporidium IFA
- ☐ Clostridium perf enterotoxin assay
- ☐ Large bowel signs??
  > R/O Tritrichomonas foetus (special tests)

****Negative results do not rule-out any parasite. Be persistent, as retesting can be very important.**

## Diagnostic Approach to Acute Nonspecific Diarrhea

1. **Differentials:** First consider dietary problems, GI parasites, bacterial/viral infections, acute colitis. Test for parvovirus if clinical presentation warrants.
   ***Make sure the client checks the home environment carefully to ensure there has not been ingestion of any toxins or other foreign material that could cause diarrhea, including plants and shrubs.
2. To rule-out parasites, test as indicated above in the box. If fecal tests are positive for parasites, treat accordingly.
3. If dietary sensitivity or indiscretion is considered a possibility, feed a controlled diet for GI problems, for 1-3 weeks.
4. Options on other therapies that can be tried include: metronidazole (bacterial diarrhea), probiotics (to help normalize the GI flora and competitively exclude pathogens), and motility modifier drugs (as long as there is not an infectious cause). If these therapies do not resolve the problem fairly quickly, other diagnostic testing should be undertaken.

# 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.
**KEY POINT:** 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. This is not a sensitive test, but it is quick and inexpensive and if trophozoites are seen, a diagnosis can be made quickly.

### 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. While zinc sulfate with centrifugation can be done in the hospital lab, our preference for many years has been to send fecal samples to a commercial lab for analysis. This is 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. For this reason many practices in the United States 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 subsequently begin to shrink and will be more difficult to recognize. **Since animals shed *Giardia* on an intermittent basis it is recommended that a series of 3 zinc sulfate concentration tests be run over a 3 to 5 day period, IF the *Giardia* antigen test is not run concurrently, in order to maximize chances of accurately diagnosing or ruling out *Giardia* in animals with chronic diarrhea. If there are 3 negative tests within 5 days, it is not likely the patient has *Giardia.*** Diagnostic efficiency increases to 90-95 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*.

**Alternatively, however, an antigen test can be run at the same time as the centrifugation test to help increase diagnostic efficiency and accuracy. This is what I recommend now as a standard practice, as the diagnostic sensitivity is higher (greater than 95%) and definitive results are obtained earlier. This is also more convenient (testing is done on one fecal sample on one day) and economical that doing 3 centrifugation assays over a 5 day period.**

**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)
- The best overall test to perform on a single fecal sample is a combination of zinc sulfate centrifugal flotation and a *Giardia* antigen test.

**Giardia Antigen Testing**

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 centrifugal flotation. 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, and these tests are often performed at a commercial laborary rather than in the hospital setting (WHY? Significantly better quality control and more economical).** 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 involved metronidazole. For dogs in which metronidazole proved ineffective, other drugs such as fenbendazole or albendazole (Valbazen) were used. More recently it was shown that albendazole 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, bone marrow suppression, 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, is very effective against *Giardia* and is currently our primary therapy in most cases. 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 good 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 mg/kg orally every 12 hours for 5 to 7 days). *The total dose of metronidazole should never 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 benefical 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: <u>Will Probiotics Help</u>?**

- ❑ *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 exists 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 most 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 e 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:**

Gookin JL: Tritrichomonas. In Bonagura JB and Twedt DC, eds: Current veterinary therapy XIV, St. Louis, 2009, Elsevier, p. 509-511.

Gookin JL, Foster DM, Poore MF, et al: Use of a commercially available culture system for diagnosis of *Tritrichomonas foetus* infection in cats. J AM Vet Med Assoc, 222 (10), 2003.

****Website for periodic updates and video clips of motile trophozoites: www.JodyGookin.com. There is an excellent reference section titled AN OWNERS GUIDE TO DIAGNOSIS AND TREATMENT OF CATS INFECTED WITH *TRITRICHOMONAS FOETUS.***

## *Clostridium Perfringens* Enterotoxicosis

Over the last 20 years *Clostridium perfringens* enterotoxicosis (CPE) has been 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.

*C. 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. 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.* DNA testing is now also available from several commercial laboratories as part of a fecal panel.

**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 ¼ 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 to12 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 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 (if 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 *Cryptosporidia* 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** | **Feline** |
|---|---|
| **Azithromycin** 5-10 mg/kg, BID orally, for 14-28 days | **Azithromycin** 7-15 mg/kg, BID, orally, for 14-28 days |
| **Paromomycin** 150 mg/kg, SID orally, for 5 days | **Paromomycin** 150 mg/kg, SID orally, for 5 days |
| **Tylosin** 15 mg/kg, BID orally, for 21-28 days | **Tylosin** 15 mg/kg, BID orally, for 21-28 days |

## Diagnostic Approach for Cats with Chronic Diarrhea

***PRE-BIOPSY work-up***

**CBC, biochemical profile, UA, FeLV/FIV**

**T4 (investigate for hyperthyroidism)**

- **Fecal analysis**
  - **Direct smear for Giardia trophozoites and trichomonads**
  - ***Giardia* (ZnSO4 w/centrifug. *and* Ag test)**
  - ***Clostridium perfringens* enterotoxin assay**
  - ***Cryptosporidium* IFA**
  - **Rectal or fecal cytology (examine for inflammatory cells)**

**Cobalamin assay (vitamin $B_{12}$**

**fTLI (blood test for exocrine pancreatic insufficiency)**

**Biopsies of the intestines** are done to evaluate for inflammatory bowel disease and intestinal lymphoma. Biopsies can be obtained via either endoscopy or exploratory laparotomy

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# INFLAMMATORY BOWEL DISEASE (IBD) IN DOGS – DIAGNOSIS AND THERAPY

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA Antech

## 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 presumptive diagnosis of IBD is made on the basis of history, physical exam and elimination of other disorders by laboratory tests and other studies such as radiography and ultrasonography. 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.

Although inflammatory bowel disease is not breed specific, the Sharpei breed requires special consideration because they can develop a severe type of IBD. Most Sharpei dogs with IBD will present with a ravenous appetite, chronic diarrhea and weight loss. They often have intestinal dysbiosis (bacterial overgrowth) and other intestinal problems as well. Sharpeis with diarrhea, even for short durations of 3 to 4 weeks, due to IBD seem to be at increased risk of developing hypoproteinemia.

Early clinical investigation in these patients should always include a complete blood count and complete biochemical profile.

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 radiographic 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. In fact, *Giardia* antigen testing is very sensitive and can identify infections that may be missed on one or two zinc sulfate centrifugation tests with centrifugation or where there is incorrect interpretation of the identity of cyst structures (a common error in clinical practice). 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. Endoscopic and surgical biopsies are discussed in a subsequent section.

**Diagnostic Imaging of the Intestinal Tract**
**(Diagnostic Imaging section contributed by Dr. David S. Biller, DACVR, Kansas State University)**

**Normal Radiographic Anatomy of the Small Intestine**
The small intestine should be evaluated for margination (serosal surface definition). The margin should be smooth. It will normally be visible due to fat in the serosa except when the animal is young (< 6 months) or emaciated or if abdominal fluid or cellular infiltrates are present. The normal diameter of the small intestine in dogs is < 2–3 rib widths, or less than the dorsoventral dimension of the second lumbar vertebral body.

The small bowel should be evenly distributed throughout the abdomen, occupying space not taken up by other organs. As organomegaly occurs, whether normal (distended stomach or urinary bladder) or abnormal (e.g., mesenteric lymphadenopathy, pancreatic enlargement, splenic mass), the intestine will be displaced. The direction helps to determine the differentials for the mass causing the displacement. In obese cats, it is common for the intestines to be localized in the ventral abdomen to the right of midline. The small bowel should have a smooth, continuous, curved appearance.

It is often necessary to have contrast studies (upper GI series) to identify normal or abnormal shape or diameter of small bowel. The radiopacity of the bowel loop is dependent on whether it is fluid-filled, gas-filled, or filled with a combination of fluid and gas. Fluid-filled loops of bowel appear as white rope-like structures. Gas-filled loops appear as black, thin-walled tubes. A small amount of gas above fluid appears as a narrow, radiolucent band with an apparent thickening of the bowel wall. A larger volume of gas reflects wall thickness more accurately and therefore bowel wall thickness should never be evaluated on survey films but only with use of contrast (whether negative or positive).

In dogs, barium should enter the duodenum in 13–20 minutes, the jejunum in 30 minutes, the jejunum and ileum in 60 minutes, and the ileocolic junction in 90–120 minutes. Barium should clear the upper GI tract and enter the ileum and colon in 3–5

hours.

The appearance of the mucosa or wall of the small bowel is best evaluated using positive contrast material. The mucosa should appear as a smooth, even surface or as a finely fimbriated edge. This fimbriation is due to barium dissecting between groups of aggregated villi. In normal young dogs, the mesenteric border of the duodenum has numerous or single, usually square or conical depressions, in the bowel overlying lymphoid follicles. These are pseudoulcers and considered normal. They are not seen in cats.

**Abnormal Anatomy of the Small Intestine on Survey Radiographs**
Ileus is an obstructive condition of the intestine and is either mechanical or functional. Mechanical ileus is also referred to as “dynamic” (or obstructive) ileus. It is usually simple and nonstrangulating. The radiographic signs may be influenced by the degree, location, and duration of obstruction. Dilatation of small intestine secondary to mechanical obstruction results from swallowed air and saliva and accumulation of mucosal secretions in the digestive tract.

Functional ileus, also referred to as paralytic or adynamic ileus, can be localized or generalized and may be a sequelae to mechanical ileus. The stages of development of functional ileus include muscle fatigue allowing stretching of the intestine, muscle ischemia secondary to stretching, and muscle necrosis. Functional ileus has numerous causes, such as extrinsic (which tend to be more generalized) that include spinal cord injury, reflex to pain, peritoneal trauma or irritation, or vascular compromise, and intrinsic (which is most often regional). Intrinsic causes include edema, amyloidosis, and acute inflammation or enteritis.

Survey radiographs of inflammatory bowel disease are usually normal or luminal fluid maybe increased.

**Abnormal Anatomy of the Intestinal Tract on Contrast Radiographs**
Intraluminal disorders usually appear as radiolucent areas surrounded by positive contrast medium. They often delay intestinal transit time and cause ileus proximal to their location. Intramural disorders should be evaluated with an upper GI series (positive contrast/barium).

The following questions should be answered while evaluating the upper GI series:

1. whether the lesion projects into the lumen, causes a narrowing or constriction;
2. whether the lesion projects away from the lumen, causing an enlargement of the diameter of the lumen as a result of a defect in the bowel wall;
3. whether thickening and rigidity of the bowel wall, irregularity at the serosal or mucosal surfaces, or a combination of these changes has occurred.

Radiographically, intramural disorders of the bowel may appear pedunculated, broad-based, smooth or irregular, and may expand the width of the bowel. Benign tumors tend to be smooth; malignant tumors tend to be irregular. The causes of

intramural lesions include neoplasia, granuloma, abscess, scar, and hematoma. Inflammatory diseases of the small intestine (enteritis) tend to increase the rate of intestinal motility (i.e., reduced transit time). Chronicity and severe enteritis may cause irregularity of the mucosal surface; chronic enteritis may also decrease the width of the bowel lumen. Chronic and very severe enteritis can cause alterations or erosion of the mucosa.

Barium studies of patients with severe/chronic inflammatory bowel disease may be characterized by the appearance of thumbprinting. Thumbprinting is described as irregularly arranged mural based indentations into the contrast column.

**Ultrasonography of the Normal Gastrointestinal Tract**

Until recently, ultrasonography was considered to be a poor choice for evaluation of the GI tract because of the ultrasonographic barrier caused by luminal gas. Over the past 5 years, however, it has been applied successfully in diagnosis of a number of GI disorders, including gastric and intestinal foreign bodies, intussusception, uremic gastropathy, chronic pyloric hypertrophic gastropathy, enteric duplication, and GI neoplasia. It has proven useful not only in the diagnosis of morphologic GI disease but also in the evaluation of GI function. Maximizing resolution by using a high-frequency transducer is critical in the examination of the GI tract. Fasting the animal before ultrasonography also improves the results of the examination.

**Normal Wall Thickness in Dogs**

| | |
|---|---|
| **Stomach** | **3-6 mm** |
| **Duodenum** | **3-5 mm** |
| **Jejunum** | **2-4 mm** |
| **Ileum** | **2-4 mm** |
| **Colon** | **2-3 mm** |

**Larger dogs have thicker walls.*

Ultrasonography enables differentiation of the layers of the stomach, which alternate in echogenicity. Under optimal conditions, five separate layers can be identified. They are the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic). The submucosa and subserosa–serosa are hyperechoic because of the presence of relatively more fibrous connective tissue. The mean number of peristaltic contractions in the stomach is 4–5 per minute.

The ultrasonographic appearance of the GI lumen depends on its contents. In a collapsed, state the bowel lumen appears as a hyperechoic core (“mucosal stripe”) surrounded by a hypoechoic halo of bowel wall. This core represents mucus and small air bubbles trapped at the mucosal–luminal interface. When fluid is present in the bowel lumen, an anechoic area is present between the walls of the bowel that appears tubular in long-axis views and circular in short-axis views. Gas in the GI lumen causes a highly echogenic interface with reverberation artifact. The presence of fluid in the bowel lumen improves the sonographer’s ability to evaluate the

mucosal and submucosal layers of the GI tract, whereas the presence of luminal gas hinders it.

As with the stomach, the layers of the intestine alternate in echogenicity. Under optimal conditions, five separate layers can be identified: the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic).

Real-time ultrasonography should be included in the examination of enteric motility. The mean number of peristaltic contractions in the intestine is 4–5 per minute. Contractions are not seen in the colon.

**Ultrasonography of the Abnormal Gastrointestinal Tract**
**Ileus**
Both mechanical and paralytic ileus have been described as ultrasonographic findings. Mechanical ileus occurs proximal to an area of obstruction; paralytic ileus can be generalized (e.g., viral enteritis, hypokalemia) or focal (e.g., duodenitis secondary to pancreatitis). When ileus is present, the bowel appears dilated and fluid-filled and GI motility is decreased or absent.

**Inflammatory Disease**
With inflammatory bowel disease, the intestine may be normal on ultrasound examination. The measurement of the intestinal wall thickness by ultrasound is neither specific or sensitive for diagnosing IBD. Changes, especially those of severe or chronic disease, have been reported as focal to diffuse thickening, altered echogenicity, poor intestinal wall layer definition, and mild enlargement of adjacent lymph nodes. Mucosal echogenicity may remain hypoechoic, appear hyperechoic with striations or hyperechoic with speckles and be associated with but nonspecific for IBD. Jejunal lymph node thickness of > 6 mm maybe consistent with IBD but nonspecific for the type of disease. Round, enlarged, hypoechoic LNs maybe more consistent with neoplasia, while inflammatory lymph nodes may be enlarged but tend to maintain their normal shape.
The most common finding with inflammation is extensive and symmetric wall thickening with the layering retained. In comparison, neoplasia is usually localized with greater wall thickness and loss of normal layering. These categories can overlap, and therefore cytology or histopathology is required for definitive diagnosis. Acute enteritis or inflammatory bowel disease may demonstrate corrugation of the intestine on ultrasound examination.

**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. Even expert endoscopists report that in some cases one-fourth to one-third of the biopsies they take from a patient will have some degree of damage to the tissue that may preclude the samples from being useful or representative. Therefore, 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. When a pediatric diameter endoscope is used this is possible in most dogs over 4 to 5 kg. If the ileum can not 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.

**Organ Biopsy Via Laparoscopy or Laparotomy**

Organ biopsy is required to confirm canine IBD, and full-thickness samples procure tissue samples that will help the pathologist make the most accurate diagnosis. Full thickness intestinal biopsies can be accomplished by laparoscopic techniques or open abdominal surgery. Laparoscopic techniques have been well described for visceral organ biopsy. They are minimally invasive and well-suited for tissue procurement; however, laparoscopy is not yet readily available as a tool in most small animal general practice hospitals. Surgery on the other hand is an excellent way to obtain liver, pancreatic, and full thickness intestinal biopsies. In addition to biopsy, liver, pancreas and bile aspirates can be obtained for culture and cytology.

## 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. It 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. Others include fluticasone propionate, tixocortol pivalate, and beclomethasone dipropionate.

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).

Use of other drugs may be indicated in some dogs with IBD. If large intestinal inflammation is present either metronidazole or 5-amino salicylic acid derivatives (sulfasalazine, osalazine, mesalazine) or both in combination will usually control large bowel diarrhea due to colitis. Corticosteroids are usually ineffective for controlling signs of large intestinal inflammation in dogs (although steroids are very effective for this purpose in cats). Other alternative therapies may include cyclophosphamide, chlorambucil, and cyclosporin. Omega 3 fatty acids (antiinflammatory effects) or vitamin E (antioxidant) may also be beneficial in some chronic cases.

**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. Previous therapy had included immunosuppressive doses of steroids in all dogs (starting dose of prednisolone was 2.2 mg/kg/day, administered for a range of 6 to 14 weeks before the dose was decreased). Other drugs tried in most of the dogs included metronidazole (range of 2 to 38 weeks).

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.

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# INTENSIVE CARE MANAGEMENT FOR DOGS WITH SEVERE VIRAL ENTERITIS

Todd R. Tams, DVM, Diplomate ACVIM
Chief Medical Officer
VCA

Puppies and Young Dogs - Parvovirus Enteritis

Disease caused by parvovirus in dogs (destruction of intestinal crypt epithelium, lymphocyte depletion, neutropenia) is generally more severe than that caused by coronavirus (destruction of intestinal villi). Coronavirus enteritis is often characterized by mild and self-limiting clinical signs. Intestinal mucosal injury due to parvovirus is more extensive, involving both crypt and villous epithelium. A combination of secretory and malabsorptive diarrhea results. Sepsis occurs commonly in dogs with parvovirus due to absorption of preformed bacterial toxins and intact bacteria across the damaged intestinal epithelium. Bacteremia is more likely to occur in severely leukopenic animals. Sepsis occurs infrequently in dogs with coronavirus enteritis.

## Treatment of Acute Infectious Diarrhea in Dogs (e.g., Parvovirus Enteritis)

### Fluid Therapy

Fluid replacement is one of the most important treatments for patients suffering from vomiting and diarrhea. Rate and route varies with each patient, but patients with hemorrhagic gastroenteropathy are often dehydrated at presentation and strong consideration must be given to intravenous fluid therapy. Restoration of an effective circulating blood volume is of primary importance in the management of hypovolemic and septic shock. Subcutaneous fluid administration provides slow, unreliable volume replacement, may induce hypothermia, and occasionally results in the formation of subcutaneous abscesses.

Initially, a buffered crystalloid solution such as lactated Ringer's or Normosol-R should be given, followed by fluids with glucose added (lactated Ringer's or Normosol-R with 5% dextrose) when dehydration becomes less severe (5-6%). Both lactated Ringer's and Normosol-R are mildly alkalinizing and may be beneficial in patients with metabolic acidosis, especially in animals with severe diarrhea. The buffer sources in Normosol-R are acetate and gluconate. An advantage of acetate and gluconate is that they do not require hepatic metabolism and they do not contribute to lactate levels.

The calculation of fluid requirements should be the sum total of: 1) daily maintenance requirements, 2) deficits due to dehydration, and 3) continued (contemporary) losses (vomiting and diarrhea). Generally, the average adult dog requires a maintenance volume of approximately 60 ml/kg body weight per day. Estimation of dehydration is at best crude, but is derived from an accurate history, physical examination, and laboratory data. Once calculated only 75-80% of this volume is replaced the first twenty-four hours with the remainder given the second day. Below is an example of typical fluid calculations.

Case Example:
A 20 kg dog with vomiting and diarrhea is estimated to be 10% dehydrated. The calculated 24 hour fluid requirement would be 2,850 ml

1. Maintenance: 60 ml/kg x 20 kg = 1,200 ml
2. Dehydration: 10% x 20 kg = 2.0 kg
   2.0 kg x 1,100 mg/kg (clinical approximation) = 2,200 ml
   2,200 ml x 75% replacement the first 24 hours = 1,665 ml
   1,200 ml maintenance + 1,650 ml dehydration = 2,850 ml
3. Ongoing losses: if vomiting or diarrhea continues during fluid therapy the volume lost is estimated and added to the original 2,850 ml calculated requirements. Too often dogs with severe viral enteritis are not adequately hydrated in clinical practice. One of the major reasons for this is that the importance of determining and replacing ongoing losses is not recognized. Inadequate volume replacement is one of the causes of a poor response to therapy.

If the animal is in critical condition, a "shock dose" of fluids is often given the first hour and is roughly up to 90 ml/kg (in the first one to two hours).

**Antibiotic Therapy**
Most cases of simple vomiting and diarrhea do not warrant any antibiotic therapy. However, patients with hemorrhagic gastroenteropathies should be given antibiotics because the severe intestinal mucosal inflammatory changes which occur allow the normal intestinal microflora to invade the intestinal mucosa and lead to septicemia. Antibiotics are specifically given to eliminate microflora invading the mucosa, to eliminate microflora causing septicemia, and to eliminate pathogens that have invaded.

Bacteria invading the mucosa to produce bacteremia are members of the normal intestinal microflora. Antibiotic treatment is directed against both groups of bacteria, the aerobes (especially *Escherichia coli*) and anaerobes (especially *Bacteroides* and *Clostridium* of bowel origin). The important source of the bacteremia is the anaerobes (outnumber the aerobes in the colon by 1,000 to 1). Penicillin is the most effective antibiotic against anaerobes invading from the colon.

If patients with hemorrhagic gastroenteropathy are only mildly ill, and have an adequate number of white blood cells, penicillins are a good initial choice. Amoxicillin (22 mg/kg IM or SC every 12 hours) or ampicillin provide adequate coverage. Antibiotics should not be administered subcutaneously in dehydrated animals because the rate of absorption will be delayed. Cephalosporins also provide good coverage for both aerobic and anaerobic bacteria. Cefoxitin (Mefoxin) is an excellent choice for more moderately affected animals (30 mg/kg IV or IM every 6 - 8 hours). Cefoxitin is sometimes administered in conjunction with a fluorquinolone (enrofloxacin 5 mg/kg every 24 hours IV). Cartilage abnormalities have been associated with enrofloxacin in young, large breed dogs. Clients should be warned about this possibility, but this is a rare occurrence.

Cefoxitin is usually classified as a 2nd generation agent. Unlike the first generation agents (e.g., cefazolin), it has good activity against many strains of *E. coli, Klebsiella, Campylobacter,* and *Proteus* that may be resistant to the first generation agents. In human medicine, cefoxitin's activity against many strains of *Bacteroides fragilis* has placed it in a significant therapeutic role. While *Bacteroides fragilis* has been isolated from anaerobic infections in veterinary patients, it may not be as significant a pathogen in veterinary patients as in humans.

Other combinations that can be used in moderately to severely affected animals are a penicillin or cephalosporin given in conjunction with an aminoglycoside (gentamicin 6 mg/kg every 24 hours IV or amikacin). Amikacin's spectrum of activity includes coverage against many aerobic gram negative and and some aerobic gram-positive bacteria, including most species of *E. coli, Klebsiella* spp., *Salmonella* spp., *Enterobacter* spp., *Serratia* spp., *Shigella* spp., *Mycoplasma* spp., and *Staphylococcus* spp. Several strains of *Pseudomonas auruginosa, Proteus,* and Serratia that are resistant to gentamicin will still be killed by amikacin. The aminoglycoside antibiotics are inactive against fungi, viruses, and most anaerobic bacteria. The recommended dose of amikacin in dogs for susceptible infections and empirical therapy is 15-30 mg/kg IV, IM, or SC once daily (Plumb's 2015). Septic patients may be started at 20-30 mg/kg once daily. Note: Dosage should be adjusted based on kidney function and serum levels when possible. Patients with parvoviral enteritis are generally younger dogs with normal renal function and are receiving aggressive fluid therapy as part of their therapeutic regimen. In very ill parvo patients aminoglycosides are generally administered for a period of 5-8 days, occasionally a little longer.

Aminoglycosides can cause acute renal tubular necrosis. Maintenance of normal blood volume is essential when using aminoglycoside antibiotics and patients should be evaluated for presence of renal disease prior to administration of an aminoglycoside.

Cefovecin (Convenia) is an extended spectrum semisynthetic cephalosporin with an extended duration of action. Due to the distinctive pharmacologic profile of cefovicin (Convenia), a single injection (8 mg/kg SC) provides a complete 14 day course of therapy. Convenia can be used in parvovirus cases where home care is required due to limited client finances, with the convenience of a single injection of antibiotic and no need to administer oral or injectable antibiotics at home (see detailed discussion on home care at the end of this document). Studies are continuing to evaluate this treatment more critically.

**Glucose**

It is not uncommon for hemorrhagic gastroenteropathy patients to be hypoglycemic at or shortly after the time of presentation. Glucose is required in adequate levels for normal white blood cell migration and phagocytosis and for treatment and prevention of hypoglycemia occurring with septic or endotoxic shock. A bolus of glucose (1 to 2 gms/5 kg, or approximately 1 ml 50% dextrose per 2 kg), is given slowly IV at the start of therapy and then added to the fluids as a 5% solution as dehydration nears resolution. A bolus of 25% dextrose is preferred over a 50% concentration because the latter is quite hypertonic and may induce vomiting.

**Antiemetics**
Antiemtetic therapy is important in vital enteritis patients. Many of these animals are vomiting frequently during the early stages of the disease and they are prone to fluid and electrolyte loss, discomfort associated with nausea (can be profound), aspiration pneumonia,and esophagitis. Maropitant (Cerenia) is the most effective antiemetic drug for parvoviral enteritis patients. It is described in detail elsewhere in these same proceedings notes (see Pharmacologic Control of Vomiting). Ondansetron and dolasetron are also good choices. Use of anticholinergic drugs must be avoided.

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 relatively new 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 experience has 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, 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 home care after the acute phase of the disease is under control. Maropitant has been approved for use in puppies as young as 8 weeks of age (initially the approval was for 16 weeks of age or older).

**Potassium**
Hypokalemia is a frequent occurrence in patients with anorexia, vomiting and diarrhea. Significant potassium losses also occur through the kidneys. As a result, potassium supplementation is a very important part of therapy for animals with hemorrhagic gastroenteropathies.

Early potassium supplementation is extremely important for successful management of dogs with severe parvovirus enteritis. Supplementation should be instituted before hypokalemia is detected because serum potassium concentration represents only a small fraction of total body potassium stores. Most patients receive 20 to 30 mEq per liter of fluids administered. Some dogs require supplementation at 40 mEq per liter. Potassium can be included in fluids administered subcutaneously (add 20 to a maximum of 35 mEq/L for SC administration).

**Corticosteroids**
Pharmacologic doses of glucocorticoids have been shown to have antishock effects in all forms of shock, especially septic. There is still no definitive evidence, however, to show

that these agents improve overall survival. Beneficial effects include improved tissue perfusion, decreased leukocyte margination and perivascular leukocyte degeneration, and reduced absorption of endotoxins. It seems advisable at this time that corticosteroids should be administered as early as possible in a septic shock state. Many parvo patients do not need this type of therapy, especially if adequate volume replacement therapy is instituted relatively early in the course of the disease and effective antimicrobial agents are administered. If a patient is considered to be in serious to critical condition, dexamethasone sodium phosphate can be administered at 2 to 4 mg/kg IV *after* an initial bolus of IV fluids is delivered. It may be necessary to repeat the dose at 8 to 12 hour intervals for 2 to 3 total treatments (decision based on patient response).

**Treatment Of Pronounced Hypoproteinemia**

Hypoproteinemia often develops rapidly in animals with severe diarrhea and small intestinal injury. Replacement of lost proteins by administration of fresh-frozen plasma may prove beneficial, especially when the total protein level drops below 3.5 g/dl. A plasma transfusion serves to both help in restoration of plasma oncotic pressure and to provide a source of immunoglobulins. Administration of fresh-frozen plasma from regularly immunized donor animals is a means of providing antibodies against circulating parvovirus. This is an effective means of neutralizing the virus in clinical patients. Use of fresh-frozen plasma may help reduce mortality in severely ill parvovirus enteritis patients.

A dose of 6 to 10 ml/kg of plasma is usually administered. This volume can be administered up to 2 times per 24 hours. An in-line filter is used to remove particulate material during plasma infusion. Plasma should be administered slowly for the first 10 to 30 minutes to monitor for signs of adverse reaction.

**Intestinal Parasite Control**

In addition to providing primary care for the sequelae of viral enteritis, it is important that any concurrent intestinal parasite problems be controlled as well. Intestinal parasitism, especially in puppies, can add significantly to the debilitation that viral or bacterial enteritis can cause. Fecal samples should be evaluated as early as possible for evidence of parasites. This should include using a Giardia antigen test to help improve diagnostic sensitivity for Giardia.

**Anthelmintic drugs** most commonly used include pyrantel pamoate (roundworms, hookworms) or fenbendazole (roundworms, hookworms, whipworms, and *Giardia*) at 50 mg/kg once daily for 3 consecutive days. For animals that are vomiting I prefer to use fenbendazole since it requires only one dose per day and has such a broad spectrum of activity (including *Giardia*).

**Reflux Esophagitis**

Significant reflux esophagitis probably occurs in animals with persistent vomiting much more commonly than we recognize. Dogs with parvovirus enteritis that are debilitated and recumbent are especially at risk. Vomited fluid that is retained in the esophagus is not cleared adequately in weak and recumbent animals. As a result, the esophageal mucosa is bathed with gastric acid and activated enzymes that will cause mucosal injury. Because

significant discomfort can result from esophagitis it is important that it be recognized and treated in a timely manner.

Treatment of esophagitis in animals with persistent vomiting includes use of an injectable histamine H2-receptor antagonist (e.g., famotidine), and a cytoprotective drug in suspension form (sucralfate). H2-receptor antagonists are used to decrease gastric acid production, thereby decreasing acid volume available for reflux. H2-blockers also reduce the volume of gastric juice that is produced. I most often use famotidine at a dose of 0.5 mg/kg IV every 12 hours, if I am concerned about esophagitis being present.

**Pain Management for patients with Parvovirus Enteritis**

Dogs with parvovirus enteritis, or any other cause of severe viral enteritis, can experience significant abdominal pain. Causes of pain include diffuse intestinal injury, cramping, and reflux esophagitis (described above).

Butorphanol will help provide relief in patients with mild pain and it also has some level of antiemetic activity. It can be used in conjunction with chlorpromazine or metoclopramide. Transdermal Fentanyl (Fentanyl patch) or injectable morphine (0.2-1.0 mg/kg every 6 hours SC or IM) or hydromorphone (0.1-0.4 mg/kg every 6 hours SC or IM) can be used in parvovirus enteritis patients that are experiencing moderate to severe abdominal pain. Notable changes in patient behavior that can be indicative of good pain relief often include more frequent assumption of a position of relief or comfort (less curling up, more laying out in a more extended or “sprawling” form), more effective antiemetic drug effects, and an earlier return of appetite. Butorphanol should not be given in conjunction with other opioids, including fentanyl, morphine, or hydromorphone, since it is a partial antagonist. It must be noted that both human and animal patients that receive the benefit of effective analgesia often have lower morbidity and mortality.

When a fentanyl patch is placed on a patient that is already in significant pain, morphine or hydromorphone are administered every 6 hours for 24-36 hours, so that the patient receives adequate analgesia while awaiting achievement of effective blood levels of fentanyl from the patch.

**Nutritional Support**

Early nutritional support is now recognized to be a very important part of therapy for parvoviral enteritis patients. Feeding will help improve GI mucosal integrity and prevent mucosal atrophy and bacterial translocation. In one study it was shown that early enteral feeding via nasoesophageal feeding tube using Clinicare liquid diet resulted in improved weight gain, fewer clinical signs, and a shorter hospitalization period. Ideally feeding should begin as soon as vomiting is significantly reduced. Use of effective antiemetic drugs as described earlier will help facilitate an earlier feeding schedule. Ideally, feeding is begun within 12-36 hours of hospitalization. One of the nutritional recovery formulas is fed every 6 hours, as tolerated by the patient, at around 1ml/kg per feeding (e.g., Hill’s a/d or Royal Canin Recovery RS).

**Outpatient Treatment of Patients with Parvoviral Enteritis**

In some cases clients are unable to financially support the costs for inpatient care of viral enteritis patients. Experience has shown that a significant number of patients can still be helped through outpatient care, with treatments administered by the client in the home environment.

The following guidelines are followed:

1. **Lab tests:** Try to perform at least a baseline PCV, total solids, glucose strip, and a blood smear for WBC estimation if a full CBC can't be run. A fecal exam for parasites should also be done, if at all possible, since many parvo patients also concurrently have GI parasites.
2. **Treatment is as follows:**
    a. **Initial fluid dose:** Administer one-quarter shock dose of crystalloid fluids for IV fluid resuscitation, over the first 2-3 hours. The patient isn't staying as an inpatient except for these first several hours when IV rather than SC fluids can be expected to make a significant difference in initial resuscitation. One-quarter shock does is 20 ml/kg.
    b. **SC fluid administration at home:** Add 20-30 mEq KCl/liter of fluids for SC administration. Do not exceed 35 mEq per liter.
    Fluid goal per 24 hours: Aim for 30 ml/kg/dose with 4 doses spread out evenly over each 24 hour period.
    c. **Antiemetics:** Administer Cerenia 1 mg/kg first dose at the hospital. Send home several loaded syringes for home administration. The client is instructed to keep the syringes refrigerated and to administer one dose each 24 hours. Once vomiting come more under control oral Cerenia is administered for an additional several days.
    **d. Antibiotics:** Administer cefovicin (Convenia) 8 mg/kg SC at the hospital. No other antibiotics are administered. Convenia is a third generation cephalosporin with bactericidal effect. The single injection at the hospital is more cost effective than sending home multiple loaded syringes of other antibiotics and also minimizes the number of injections that the client will need to give at home.
    **e. Feeding:** Begin early syringe feeding when it can be tolerated – as early as possible. Start with Hill's a/d or Royal Canin Recovery RS at 1 ml/kg every 6 hours. Gradually increase the volume over ensuing days.
    **f. Pain management:** Some visceral analgesia will be provided via the Cerenia treatments. Additional analgesia can be provided through administration of buprenorphine or placement of a fentanyl patch. If pain is detected on initial exam, an injection of morphine or hydromorphone can be given SC or IM at the hospital, and then a fentanyl patch is applied for ongoing analgesia. Use best judgment for each individual patient.
    **g. Anthelmintics:** Treat for any parasites identified on a fecal exam. If no fecal exam could be performed (cost containment), administer fenbendazole (Panacur) 50 mg/kg once daily for 5 days, starting when vomiting is subsiding.

h. **Communication:** Keep in close contact with the client to gauge progress and answer questions along the way.

**Summary**

Successful management of dogs with severe parvovirus enteritis requires a multifaceted treatment approach, a hospital staff that is dedicated to high detail patient care, and a committed pet owner. The success rate is very high when all of these factors are present.

# CHRONIC LARGE INTESTINAL DISEASE IN DOGS AND CATS

Todd R. Tams, DVM, DACVIM
Chief Medical Officer
VCA

## 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 maldigestion, 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 (cecocolic 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 antiinflammatory 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* enterotoxicosis, 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 that 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.

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## 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 obstipation. 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 cisparide (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 ion 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 liquify 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 awhile 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 managing cats with chronic constipation and megacolon. The diet was available earlier in Europe and reports were presented at ECVIM 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.

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