Current Diagnostic Approaches to Chronic Diarrhea  
(part 1 of 2)  
Written by Marion D. Haber, DVM, DACVIM

Cardiologists: Taking care of the Plumbing  
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Why do Corneal Ulcers Worsen?  
Written by Clara O. Williams, DVM, MS, DACVO

Veterinary Herbal Therapy  
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DIARRHEA IS DESCRIBED as an increase in fecal mass, specifically volume, frequency and/or fluidity and it is an important clinical sign of intestinal disease. Diarrhea as a clinical sign can be found with both small and large intestinal disease. There are several differentiating factors (See Table 1). Often signs localizing to both the large and small intestine may be present in one clinical case. It is important to note however that small intestinal disease can be present without the actual presence of diarrhea.

CHARACTERIZING DIARRHEA
To help in further characterizing diarrhea it may be helpful to employ a fecal scoring system such as the one provided by Purina, Inc (See Fig. 1). A fecal scoring system not only helps with characterization at the time of diagnosis, but can also aid in judging response to treatment. It is also important to define duration of diarrhea. Diarrhea that has been occurring for less than 7-14 days is considered acute whereas diarrhea occurring greater than 21 days is considered chronic. Gathering this information along with an appropriate history and physical examination helps in forming a plan to establish an appropriate diagnosis.

DIAGNOSTIC APPROACHES TO CHRONIC DIARRHEA
Fecal examination is a key component to the diagnosis of diarrhea. The most common fecal testing is a fecal floatation to identify ova or cysts. Repeat testing of up to three separate fecal samples is important to diagnose intermittently shedding parasites. In cases of chronic diarrhea, prophylactic deworming should be considered even if fecal testing has been negative.

Direct fecal examination evaluates for excess fungal or bacterial elements (e.g. Clostridium spp) but results can be misleading and need to be interpreted with other patient information. Some patients will have higher than normal spores or bacteria and not have evidence of diarrhea. Special stains for fat, starch, or muscle fibers can be applied to fecal smears to identify features of malabsorption. A fecal wet mount can be used to evaluate for Campylobacter spp as well as trophozoites, such as seen with Giardia spp. Rectal scraping for cytology should be evaluated for evidence of inflammation as well as for evidence of fungal elements. Fecal culture should be pursued if inflammatory cells are noted on cytology or if significant hemorrhagic diarrhea and pyrexia are associated with diarrhea. Fecal culture, most commonly for Salmonella, Campylobacter jejuni, and Clostridium difficile, should be interpreted in light of other clinical signs. This diagnostic technique should not be used to aid in the diagnosis of small intestinal bacterial overgrowth. ELISA tests are commercially available for the detection of C. perfringens and C. difficile toxins, Giardia spp, feline panleukopenia virus, and Cryptosporidium spp. Testing for these infections should be performed if indicated in those cases where exposure to these organisms appears likely such as patients frequenting a boarding facility. PCR testing for Tritrichomonas spp in cats should be pursued in any cat with chronic large bowel diarrhea that is otherwise healthy. More information about this infection will be provided in the next newsletter.

The fecal alpha1-proteinase inhibitor test is used to help in the diagnosis of protein losing enteropathy. It can be used to mark protein loss and is viewed as a more sensitive marker than serum albumin. This diagnostic test requires three fresh fecal samples and it is important to note that gastrointestinal bleeding will cause this diagnostic test to be invalid.
Bloodwork

In cases of chronic unresponsive diarrhea where fecal testing is inconclusive, complete blood work including complete blood count, and chemistry profile including thyroid testing should be pursued to evaluate for other disease processes of the body. In cats evaluation for FeLV and FIV should be part of a complete evaluation. Radiographic imaging is important for identification of intestinal obstruction or displacement, masses, free gas, ileus, and serosal detail. Contrast imaging can also be helpful in the diagnosis of motility disorders, ulceration, and obstruction.

Ultrasound

Ultrasound is now more commonly used due to speed of evaluation and increased information obtained by this imaging modality. Ultrasound evaluation assesses intestinal wall thickness and layering as well as for presence of masses, effusion, and other organ changes. Please see Figure 2 for an example of intestinal wall thickening. It is important to note that a lack of intestinal wall change on ultrasound does not exclude the possibility of a patient having inflammatory bowel disease or lymphoma. Any data that is gathered has to be interpreted in light of the patients presenting clinical signs as well as other diagnostic testing.

Localization of Intestinal Disease

Evaluation of digestive function can be helpful in localization of intestinal disease. Trypsin-like Immunoreactivity (TLI) testing measures trypsinogen but also detects trypsin and some trypsin molecules bound to proteinase inhibitors. This test is used for evaluation of adequacy of pancreatic function and is used for diagnosis of exocrinepancreatic insufficiency (EPI). Pancreatic lipase immunoreactivity (PLI) is alternatively suited for diagnosis of pancreatitis. This immunoassay measures pancreatic lipase and is highly specific for pancreatic function. There is a larger residual amount of pancreatic lipase remaining in the vascular space compared to trypsinogen and therefore PLI testing is not used for the diagnosis of EPI. Intestinal function can in part be assessed using quantification of serum Cobalamin (Vitamin B12) and Folate. Vitamin B12 deficiency is a marker for distal small intestinal disease and is secondary either to the inability to absorb Vitamin B12 due to mucosal malabsorption or binding of Vitamin B12 by bacteria, such as may be seen with small intestinal bacterial overgrowth. Serum folate blood concentration evaluates for proximal small intestinal disease where deficiency is an indicator of malabsorption and excess is an indicator of bacterial overgrowth. Vitamin B12 deficiency usually worsens the signs of the GI disease that are already present. Rarely neurologic signs can be seen. Differentials for Vitamin B12 deficiency include severe, chronic small intestinal disease, pancreatic insufficiency, or hereditary causes. Breeds in which hereditary Vitamin B12 deficiency has been diagnosed include Giant Schnauzer, Beagle, Border Collie, Australian Shepherd and Chinese Shar Pei. Vitamin B12 deficiency has also been diagnosed in cats.
Current Diagnostic Approaches to Chronic Diarrhea

**Endoscopy and/or Surgery**

For definitive diagnosis of chronic diarrhea, biopsy may be necessary and it is important to decide between obtaining surgical or endoscopic biopsies. Endoscopy allows for gross examination including mucosal granularity and friability and levels of erythema, evaluation for erosions and ulcers, retained food as well as mass lesions. Please see Figure 3 for an example of increased granularity and friability in the duodenum in a case that was diagnosed with severe inflammatory bowel disease. Endoscopy allows for collection of multiple tissue samples although these samples do not penetrate all of the layers of the intestines. It can also aid with removal of foreign bodies and at times parasites may be visualized on examination. While there are many benefits to endoscopy, there are also limitations including the inability to obtain full thickness biopsies or reach the jejunum, and in smaller dogs and cats, the ileum. Ultrasound is very important in aiding to localize disease especially localizing what part of the intestine may be affected as well as what layers of the intestines. Surgical biopsies are usually recommended for cases where endoscopic biopsies will likely not provide an accurate diagnosis for the cause of the diarrhea. Additional benefits to surgical biopsies include evaluation of other organs and the potential for corrective surgery. Specific disadvantages to surgery include surgical risk, dehiscence, as well as the need for a delay before starting steroids to avoid a delay in healing. Once histopathology results are obtained via either surgical or endoscopic method, treatment is pursued. There are some rare cases where histopathology shows no abnormalities. In these cases differential diagnoses to be considered include small intestinal bacterial overgrowth, food sensitivity, toxin exposure, motility disorder, patchy mucosal disease or congenital disease.

Diagnosis of diarrhea can often be difficult, and due to client and patient considerations, a complete evaluation may not be possible. Trial with different treatments may be necessary. In the upcoming article (January 2011) there will be a full discussion on treatment options for chronic diarrhea, as well as a more detailed update on two causes of chronic diarrhea.

**REFERENCES AVAILABLE UPON REQUEST**
Cardiologists: Taking Care of the Plumbing

THE MAIN THING I LOVE ABOUT the specialty of cardiology is that so many different aspects are incorporated into our daily practice. We get to act as diagnosticians, imaging specialists, and even do some plumbing and electrical work! What I mean is that we get to address some of the diseases we treat directly through the use of catheter based interventional procedures. This has been a part of veterinary cardiology for many years but lately has blossomed with many advances which we will be making available here at Massachusetts Veterinary Referral Hospital.

Cardiology is a field that is predominated by diseases that are treated by medical means, i.e. congestive heart failure with furosemide and enalapril; however there are some diseases, such as bradyarrhythmias, pulmonic valve stenosis and patent ductus arteriosus, that can be treated using a more direct approach. I would like to share some advances in the interventional field related to the treatment of these diseases.

RE-WIRING THE HEART: PACEMAKER THERAPY
A pacemaker was first used to treat a bradyarrhythmia in a dog in 1968 and therapy has been steadily improving ever since. The first pacemaker was implanted in the abdomen and attached to the epicardium. Today, the vast majority of units are implanted subcutaneously and the lead is passed through the right jugular vein to contact the myocardium at the endocardial surface. The exception to this is in most feline patients. While ease of placement was a great advance some of the more recent changes have allowed a more natural function of the heart through the use of technology.

The simplest alteration in pacemaker use that has improved treatment has been the advent of rate responsive programming, which allows the pacemaker unit to increase the heart rate in response to movement. This allows an increase in cardiac output with exercise and further eliminates the likelihood of exercise induced syncope. While very beneficial, this is one of the more basic advances in therapy recently advocated in veterinary medicine.

An even more useful advance is the use of a sensing lead in the atrium to synchronize atrial and ventricular activity. Leads can be implanted in both the right atrium and right ventricle, or a single ventricular lead with a "floating" atrial sensing component can be used. The basic concept of these systems is to create an artificial atrioventricular node, with the pacemaker sensing atrial activity then depolarizing the ventricle after a set period of time.

These seemingly simple advances in pacemaker therapy have not only improved management, but have reduced complications. A rare but serious side effect of artificial pacing is pacemaker syndrome, which leads to systolic dysfunction and potentially heart failure. Simply varying the heart rate alone will reduce remodeling of the myocardium and prevent some incidence of pacemaker syndrome. More importantly, using therapy that allows the atrium to contribute to the ventricular preload with every beat helps to prevent complications and improves cardiac output. As we continue to improve our ability to utilize pacemakers we can expect an increased use in multiple chamber pacing and some centers are already utilizing implantable defibrillators in very specific cases.

Robert Schutrumpf, DVM, DACVIM(Cardiology)

Dr. Robert Schutrumpf practices at Massachusetts Veterinary Referral Hospital in Woburn, MA.
OPENING THE SLOW DRAIN- VALVULOPLASTY FOR PULMONIC STENOSIS

Pulmonic stenosis is a common congenital disease that most practitioners have dealt with, predominantly in the small canine patient. Balloon valvuloplasty has been used for many years to treat stenoses, with the most success in cases of primary valvular stenosis with no narrowing of the valve annulus or coronary artery anomalies. Over the years, valvuloplasty has progressed to replace surgery, in the form of patch grafting or valvulectomy, as the treatment of choice for this common congenital disease.

Recent advances in treatment of pulmonic stenosis have involved an evolution of the catheters used. The basic low pressure balloon catheter is usually adequate in valvular stenosis, however cases of annular stenosis often responded poorly with little to no decrease in the trans-valvular gradient. Recently, advances in the use of multiple balloon procedures, to increase the effective dilation radius, and in high pressure balloon catheters has improved outcome in these cases. Though still challenging cases, these new options give us more tools in treating the more complicated stenoses. Unfortunately, there is still not a safe and effective treatment for stenosis caused by aberrant coronary artery formation.

Other exciting advances in development are the use of stents in extreme cases of stenosis, and the branching out of balloon catheters into the treatment of other congenital disease. Though experience is limited, balloon catheters have been used to dilate membranes in diseases of atrial formation, such as cor triatriatum dexter. As experience increases in the veterinary community expect to see further advances in treatment of pulmonic stenosis and other less common congenital disease.

STOPPING THE LEAK- PATENT DUCTUS ARTERIOSUS OCCLUSION

Patent ductus arteriosus is the most common congenital abnormality seen in dogs and is infrequently seen in cats as well. In the past this disease was treated via thoracotomy and surgical ligation. In the past decade the use of thrombogenic coils arose as an alternative to surgery, but presented their own set of problems. Coil occlusion required pain-staking, often long procedures which might result in total occlusion or continued patency of the ductus and pulmonary embolization was common. In the past five years a very successful alternative has been developed.

The Amplatz canine ductal occluder™ was developed specifically for canine use and is modeled on a device commonly used in human medicine. The device itself is made of a mesh of a metal alloy known as nitenol (a combination of nickel and titanium) and functions as a plug placed in the pulmonic opening of the ductus. I have always compared it to putting the cork back in a champagne bottle. One flange is positioned in the pulmonary artery with a waist in the ductal orifice and a second flange within the ductus itself. A screw-on delivery cable allows deployment and retraction as needed to optimize placement.

This new, easy to use system has reduced the incidence of device embolization and reduced procedure time significantly. Studies and personal experience have yielded excellent results with complete closure occurring commonly. Though rare, embolization is possible and infection of the device still carries a guarded prognosis.

Unfortunately size is the major restriction for
treatment candidates with a general minimum of 3 kilograms being the current cut-off point. Despite these facts, patent ductus arteriosus occlusion is fast becoming the standard of care based upon a comparable surgical time with a reduction in morbidity and hospitalization time. In the future it may become more practical to use similar devices to treat other shunts such as atrial and ventricular septal defects, both of which are under investigation at this time.

SEE YOU IN THE FUTURE
Performing catheter based interventions requires proper equipment, proper training, and most importantly a fluoroscopy unit. We are excited that Massachusetts Veterinary Referral Hospital has acquired a fluoroscopy unit and can now offer these options for the treatment of cardiac disease. In the future our service will be growing and we will be expanding into other areas of interventional medicine. We look forward to providing the best possible care in all fields for your patients.

REFERENCES AVAILABLE UPON REQUEST

CARDIOLOGY SERVICES
We are pleased to announce that the cardiology department has expanded. For your clients’ convenience our doctors are available for consultations 6 days per week, including evening appointments 4 days per week.
The Cardiology Team Includes:
Dr. Laura Hatton, DVM (practice limited to Cardiology)
Dr. John MacGregor, DVM, DACVIM (Cardiology)
Dr. Trey Schutrumpf, DVM, DACVIM (Cardiology)

OPHTHALMOLOGY SERVICES
In January 2011 the ophthalmology department will be available 7 days per week for regularly scheduled appointments.
The Ophthalmology Team Includes:
Dr. Nancy Cottrill, DVM, MS, DACVO
Dr. Patrick M. Welch, DVM, MBA, DACVO
Dr. Clara Williams, DVM, MS, DACVO

Bios for all of our doctors are available on our website: www.IVGMassVet.com
WHERE IT ALL BEGINS:

“Hello Dr. Smith, this is Dr. Williams, from Mass Vet. I’m calling with an update on Fluffy, the 8 year old Shi Tzu you referred to us complaining of a deepening corneal ulcer.”

“Oh yes, hello Dr. Williams. Initially, it was a simple superficial corneal ulcer, I had been treating it with triple antibiotic three times per day. However, at the one week recheck this morning, the ulcer looked really deep that’s why I referred the owner to Mass Vet. .... I’m very confused, why did the corneal ulcer worsen despite topical treatments?

One of the most frequent referrals to the Ophthalmology department at Mass Vet are cases of complicated corneal ulcers. The conversation outlined above is actually a very frequent dialog we have with our referring veterinarians. Given this, I felt that maybe it was time we discussed one of your most frequently asked questions: "Why do corneal ulcers become deeper?"

PRIOR TO ANSWERING THE QUESTION...

We first have to understand the following:

1. How does the cornea manage to stay healthy (and not develop corneal ulcers)?
2. Why do corneal ulcers occur?

1. HOW DOES THE CORNEA STAY HEALTHY?

Let’s review the basic anatomy and physiology of the cornea:

- The cornea is an exquisite three layered tissue consisting of the endothelium, stroma and epithelium. Transparency is achieved thanks to a perfect arrangement of collagen fibers, a relative degree of dehydration and the absence of vascularization and fibrosis.

- The cornea depends on the tear film, the upper, lower and third eyelids for its protection.

- The corneal epithelium is physiologically abraded by normal blinking and desiccation.

The cornea remains healthy thanks to the balanced mechanisms of epithelial regeneration and surface protection.

2. WHY DO CORNEAL ULCERS OCCUR?

A corneal ulcer occurs when the corneal protection is inadequate, when there is excessive epithelial loss or when there is abnormal epithelial regeneration. Usually a corneal ulcer has multiple causes.

In fig. 1 you can see how trauma, the most mentioned culprit, is only one of the many exogenous causes of excessive epithelial loss. A truly traumatic corneal ulcer, can only be diagnosed after ruling out abnormalities of the epithelial regeneration and surface protection mechanisms.
Determining whether a corneal ulcer is complicated or uncomplicated is a function of its **healing time** and **size**.

If the corneal ulcer fails to heal after seven days (time) and if it has become wider and deeper (size), it is now a complicated corneal ulcer.

A simple (uncomplicated) corneal ulcer should heal (re-epithelialize) without involvement of the stroma within seven days. A topical antibiotic will ensure control of surface pathogens.

**FINALLY WE CAN ANSWER THE QUESTION:**
**WHAT ARE THE MECHANISMS THAT CAUSE CORNEAL ULCERS TO BECOME DEEPER?**

Ulcers deepen either because:

- We missed the initial cause of the ulcer, leaving it undiagnosed and untreated. This is true whether the cause had been a protection mechanism abnormality, or an endogenous or exogenous abrasion cause.
- Or simply because the ulcer had become infected and the corneal stroma is undergoing collagenolysis (melting).

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**Fig. 1:** Corneal protection, normal epithelial loss and regeneration depend upon the functions of multiple components.

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**Fig 2:** This is an example of an endogenous cause of excessive corneal abrasion. An ectopic cilium.

**Fig. 3:** A deep stromal ulcer that started as an uncomplicated, superficial ulcer. (Descemetocoeles).
Complicated corneal ulcers are:

- **Non-healing superficial corneal ulcers** (excessive healing time) that may require a grid keratotomy or even superficial keratectomy. (See fig. 4)

- **Deep or anterior stromal corneal ulcers** with or without inflammatory infiltration (abscessed ulcer), that require topical and systemic antibiotic treatment.

- **Melting corneal ulcers**, initially superficial, progressing to deep ulcers that can, without appropriate treatment, lead to corneal perforation.

- **Descemetoceles**, that usually require corneal surgery (placement of physical support, most often a conjunctival or corneoconjunctival graft with or without an exogenous collagen graft), (See fig. 5).

The repair of the corneal stromal ulcer requires a balanced synthesis, degradation and remodeling of the extracellular matrix (ECM). A melting ulcer occurs when there is excessive degradation of the stroma by proteinases (You may have heard about matrix metalloproteinases - MMPs).

The MMPs are produced by epithelial and inflammatory cells, fibroblasts and infectious agents. They literally `melt’ the corneal stroma if uncontrolled.

**Treatment of Complicated Ulcers**

Medical treatment of complicated corneal ulcers includes broad spectrum coverage with antibiotics. The frequency of the application depends upon the severity of the condition and the need to stop collagenolysis.

1. Topical quinolone antibiotics every four to six hours. In severe cases, this can be every one to two hours

2. Cefazolin 50 mg/ml (requires refrigeration) every 6 hours. In severe cases every two hours alternating with the topical quinolone.

3. Oral Clavamox or Doxycycline. The advantage of Doxycycline is its anticollagenolytic action.

- **Deep corneal ulcers do not occur all of a sudden.**
- **Identification of the ulcer’s cause will help in the proper management of the condition.**
- **Most ulcers are not caused by trauma.**
- **Non-healing corneal ulcers, descemetoceles and many infected, deep stromal corneal ulcers require referral to a specialist.**

**REFERENCES AVAILABLE UPON REQUEST**
TRADITIONAL CHINESE HERBAL MEDICINES are remedies that have been used for thousands of years, becoming very refined in the process. Acupuncture treatment is often combined with these herbal medicines. The advantages of Chinese herbal medicines include their low incidence of side effects. This stems from the fact that they are combinations of many ingredients.

These combinations, small amounts of various ingredients, are far less likely to cause problems. They also have been shown to create “synergy” with each other when combined, so they tend to create better results than if using each of the ingredients individually.

The herbs found in these traditional remedies vary widely. Most are plant-based, though rarely some are mineral or animal based. Diet and lifestyle changes are often recommended to minimize the need for acupuncture and herbal medicines.

Some herbal medicines are for short term use, others can be long term, depending on your pet’s condition. Often medicines are started slowly and increased or changed over time. It can sometimes take longer to see improvement than when using more conventional medications, especially with chronic conditions. It can also take time to determine the correct combination of herbs. However, the end result can certainly be worth it!

SOME CONDITIONS TREATED WITH HERBAL REMEDIES INCLUDE:

• Gastrointestinal Disorders (Vomiting, Diarrhea, Nausea, IBD)
• Cardiovascular and Respiratory Diseases
• Urinary diseases (Chronic Renal Failure, Glomerulonephritis, Recurrent Cystitis, Feline Lower Urinary Tract Disease, Urinary Incontinence)
• Behavioral disorders (Anxiety, Cognitive Dysfunction)

We recommend that a complete blood screen be performed prior to starting any medications. This is to ensure that there is a good understanding of what is going on internally. This also helps to track any changes once your pet has begun treatment with herbal medicines.

There has been much research into the pharmacologic properties of the many herbs used in traditional medicines. They have many antioxidant, antiinflammatory and antimicrobial uses individually and their combinations have shown great promise. More and more studies abound as to the pharmacology, clinical research and toxicology of active ingredients and combinations can be found in resources such as PubMed and Chen and Chen’s Chinese Herbal Formulas and Applications. There are now herbal companies that specialize in veterinary formulas that are both palatable and dosed specifically for dogs and cats. They also follow Good Manufacturing Practices and are manufactured in the United States.
IVG is dedicated to providing referring veterinarians and their clients with an unparalleled range of emergency and specialty services.

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References for all articles available upon request.