Disclaimer: Meeting Notes that may, or may not, have much to do with what is actually presented at the meeting!
OVERVIEW

Historically, Inflammatory Bowel Disease (IBD) has been considered the most common “cause” of chronic diarrhea and vomiting in dogs and cats. Unfortunately, by definition, idiopathic IBD isn’t a cause at all; it’s a convenient umbrella meant to cover all of those cases for which we don’t know or haven’t figured out what is causing the clinical signs, but we need a target to aim our treatment towards. The first principle of dealing with these clinical signs is to address the underlying disease process as specifically and effectively as possible. One small step towards that goal may be something as simple as changing our vocabulary. Recently (more so in Europe than the United States) the term “Chronic Enteropathy” has appeared in the literature as a term used to encompass those diseases of the gastrointestinal tract that result in chronic diarrhea, vomiting, and/or weight-loss. There are certainly still cases of idiopathic chronic enteropathy, and idiopathic IBD is an entry in the list of rule-outs for pets with a chronic enteropathy. But the term is a reminder that there are many other more specific causes of chronic GI signs to be considered (and potentially diagnosed!) as a guide to the aim of our treatment.

Jamie Lee Curtis tells us that probiotics will make us regular, so it must be true! Along with a shift in terminology from IBD to Chronic Enteropathy has come a subtle shift in research emphasis which hopefully will continue to help the veterinary profession direct treatment based on actual evidence; evidence-based medicine (EBM) for treating various chronic enteropathies. Unfortunately, if we limited ourselves to treatments for which there was solid supporting evidence we would all be out of a job rather quickly. However, although we are sworn to “do no harm”, it would also benefit our patients and our client’s bank accounts if we would develop treatment plans based on randomized-placebo-controlled-double-blinded studies, case controlled studies, expert opinion, or laboratory research…in that order!

BACKGROUND

Evidence-based medicine is just that, practicing medicine based on the evidence available to us. A more formal definition comes from the Sackett el al. text on Evidence-based medicine: “Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values.” In this scheme the available evidence is the limiting factor, and in veterinary medicine, that can be a significant limitation. That being said, with the obvious advances in electronic access we are orders of magnitude more able to pursue the evidence that is out there and incorporate it into our treatment protocols. Much of what we find is still expert opinion supported by anecdotal observation. In some cases we find that the research confirms what we have known and practiced all along, which is comforting. Sometimes we find a published failure-to-support what we know does actually work, and we have to choose between statistics and our own documented successes. Regardless, it is incumbent upon us to make the effort, and the following are examples of where that effort leads us in the treatment of GI disease in our veterinary patients.

- First Principles: Treating the Underlying Disease Requires a Diagnosis

Trichobezoars (Hair balls) are usually of minimal clinical consequence, although the cat often sounds like it is going through the throws of death to bring one up, and 2am seems to be the preferred time for expulsion. However, Barrs et al. (JFMS 1999) remind us that trichobezoars can cause partial or complete intestinal obstruction if the cat inappropriately tries to pass them out the wrong direction. At risk are long-haired cats (makes sense), both young and old, with a proclivity for ingesting non-digestible plant material. The cat may or may not have a concurrent disease process, and the abdominal mass identified on physical examination can be mistaken for a neoplastic process; representing a significantly different prognosis if misdiagnosed! Even if the cat is attempting to remove the hairball in the appropriate direction by vomiting, there are a number of reports of those attempts being unsuccessful (esophageal foreign body or stricture).
Surgery is the preferred method of removing an obstructing trichobezoar (as opposed to an endoscopic attempt) and clinicians should take that opportunity to obtain intestinal biopsies and histopathology. Even without an obstruction necessitating an abdominal explore, the persistent or frequent vomiting of hairballs should motivate the clinician to consider underlying gastrointestinal disease, such as an inflammatory condition leading to altered GI motility. As Dr. Keith Richter once said – “Hairballs are not due to deficiency of GI grease”.

- **First Principles:** Signalment, History, Physical Examination

Dr. Jody Gookin wrote the book (or I should say published the articles) that introduced feline practitioners to Tritrichomonas, a flagellated protozoan causing large bowel diarrhea (video available online at [www.jodygookin.com](http://www.jodygookin.com)). It is seen most frequently in cats < 2 years of age, often coming from shelters, catteries, or multi-cat households. Clinical signs include chronic waxing & waning malodorous large bowel diarrhea, or the kittens (and older cats) may be asymptomatic. The stool is semi-formed to liquid or cow patty, containing mucus and fresh blood, accompanied by flatulence. The kitten often strains to defecate (tenesmus) frequently enough to develop perianal inflammation, but is otherwise in good body condition with a normal appetite. The only dewormer demonstrating efficacy is Ronidazole (30 mg/kg PO q24hr 14d, potential neurotoxicity), although Dr. Gookin now reports strains that are resistant to this attempt!

- **First Principles:** Food First.

The terminology in veterinary medicine is evolving and it is now common place for clinicians to refer to “Food Responsive Diarrhea.” This term is able to encompass the classic food allergy and food intolerance while taking into account the observation that some cats will respond well to diets that are not actually designed to target a disease! A number of research efforts and publications over the last 10 years or so have highlighted the importance of early dietary intervention in cases of feline chronic diarrhea and vomiting. One of the most clinically significant findings of that research is that unlike a dermatologist, a gastroenterologist only needs about 2 weeks to determine if a diet trial has had an effect (8-12 for the dermatologist). So we can (and probably should) get the owner on board for attempting several food trials before we give up on seeing a beneficial effect, because it also appears that individual cats can respond to very specific diets; what diet works for one may not work for another, and visa-versa. The list of potentially beneficial diets is also expanding just about as fast as the pet food companies can produce them; hypoallergenic, hydrolyzed, no-grain, highly digestible, canned or dry, high protein-low carbohydrate, gluten free, lactose free, preservative free, etc. Dietary intervention can also include dietary supplementation, another list that is fast outpacing the research available to support its use – but including cobalamin, liquid “toppings” of vitamins and micronutrients, fiber, omega-3 fatty acids, antioxidants, prebiotics, probiotics, etc.

- **First Principles:** The most important diagnostic tool you have is you.

**CHRONIC ENTEROPATHIES - THE EVIDENCE**

*Food Responsive Diarrhea*

“Pharmaceutical agents are often given inappropriate precedence in the treatment of gastrointestinal tract diseases… manipulation of the diet provides clinicians with a powerful therapeutic strategy” (W. Grant Guilford, J Nutrition, 1994). The veterinary profession (with the persistent prodding of pet food companies) is expanding the clinical definition (a bit faster than our basic understanding) of the impact diet has on gastrointestinal disease. Even the language is evolving to acknowledge the fact that diet plays a role in GI health well beyond the simple classification of allergy or intolerance. Cataloging dietary components as a cause or contributor to GI disease has evolved from “It’s the beef” to looking at the potential role of grains, gluten, preservatives and preparation. Prescribing dietary intervention as a contributor to the cure for GI disease has evolved from single-source Lamb & Rice to diets incorporating most any creature on the planet, exotic vegetables, prebiotics, probiotics, a spectrum of digestibility, combinations of fibers and various volumes of fat, essential ingredients as well as essentially eliminated ingredients.

Dr. Guilford and many others have continued to contribute strong research evidence for the impact of diet as both the cause and potential cure for GI conditions. Several key take-home points from this effort are that 1) a significant percentage of cats and dogs with GI disease will respond favorably, if not completely, to dietary intervention; 2) a diet trial for a gastroenterologist lasts about 2-weeks, compared to the same effort for a dermatologist, which lasts 2-3 months;
3) although the standard dietary intervention remains the hypoallergenic/hydrolyzed diet, a much more diverse array of dietary options should be considered; 4) sometimes it is a matter of matching a specific diet with a particular patient, regardless of what research tells us about what should work.

**Cobalamin**

As we race to give the injection of our current “do no harm” poster child, vitamin B12, do not lose sight of the fact that cobalamin levels can be used as a diagnostic tool. Many cats with chronic gastrointestinal signs receive cobalamin supplementation regardless of their endogenous level, and so that level is often left unmeasured. But research suggests that the lowest cobalamin levels are frequently found in cats with GI lymphoma, and gastroenterologist are forever struggling with the important distinction between IBD and GI lymphoma. Of course it is not that easy – cats with IBD can have very low cobalamin levels, and cats with GI lymphoma can have normal cobalamin levels, but we start with a clinical diagnosis and test to support or refute that diagnosis. In that capacity, the initial cobalamin concentration could be an important clue.

It was the Ruaux et al. study of 2005 (JVIM) that alerted the profession to the importance and impact of cobalamin supplementation (250 micrograms SQ once weekly) in cats with GI disease and marked hypocobalaminemia (≤ 100 ng/L). Since that seminal study cobalamin levels are being measured in cats with a wide variety of non-GI diseases and hypocobalaminemia may be a significant contributor to a number of conditions. In 2007 Allenspach et al. (JVIM) identified hypocobalaminemia (≤ 200 ng/L) as a significant risk factor for a negative outcome for dogs with chronic enteropathies, highlighting the importance of this simple substance in the canine population as well.

**Probiotics**

Our knowledge of the GI microbiome is still incomplete. We know there are normal inhabitants, such as Firmicutes, Bacteroidetes, Fusobacteria, etc.; we know there are pathogens including various Clostridium, Campylobacter, Salmonella, and Escherichia spp; and we know that “dysbiosis” is a common finding in dogs with chronic diarrhea as a result of GI disease.

What we know about the use of probiotics in GI disease is even more incomplete. We know that to have any chance of being beneficial, the probiotic supplement must 1) contain a lot of organisms – current human trials are often using orders of magnitude higher doses than those found in veterinary studies; 2) those organisms must be alive; 3) probiotic effects are likely to be rapid onset with minimal staying power once discontinued; 4) probiotics are assumed to work by changing the make-up of the intestinal microbiota, but may in fact exert effects in other ways; 5) fortunately, like cobalamin, probiotics seem to belong on the same “do no harm” poster, with very few and very extra-ordinary exceptions.

**Antibiotic Responsive Diarrhea**

Private practitioners have used antibiotics to treat diarrhea for ages, to variable effect. Just as there is marked variability in the characteristics of the diarrhea seen from patient to patient, there are numerous differentials for the cause of diarrhea from patient to patient. So it is no wonder that a single class of treatment (antibiotics) would have variable results. The general benefit of antibiotics in cases of diarrhea are frequently attributed to rather mysterious non-antibiotic properties – the immunomodulatory effect of metronidazole, for example. Perhaps antibiotics are impacting the microbiota? Ironically, one of the most commonly reported side-effects of antibiotic administration in veterinary patients is GI upset, either vomiting or diarrhea! But there is no denying the anecdotal expertise that certain cases of diarrhea respond to antibiotics. Westermarck et al. (JVIM 2005) was one of the first to put academic effort into this anecdotal observation and determined that some dogs simply suffered from Tylosin-responsive chronic diarrhea. These were middle-aged large-breed dogs with chronic diarrhea. Place them on tylosin and their diarrhea resolves within day(s). Take them off tylosin and their diarrhea returns within a month. Prednisone does not cure it, probiotics do not cure it, but put ‘em back on tylosin and the diarrhea resolves. So our profession now has its very own example of the broader category of disease known as antibiotic-responsive diarrhea or ARD. Why does tylosin work? Who knows (not us). And before we reach for the prescription pad, be aware of the fact that the Westermarck group screened these dogs for parasites, exocrine pancreatic insufficiency, inflammatory bowel disease, small intestinal bacterial overgrowth, enteropathogenic bacteria (Salmonella spp., Campylobacter spp., Yersinia spp., or Lawsoni intracellularis), Clostridium perfringens enterotoxin and Clostridium difficile A toxin, prior to settling in on their diagnosis!
**Boxer Success Story**

Charting the history of the Boxer and this breed’s struggles with colonic disease serves as a source of pride for the veterinary profession. It was a predominantly unplanned but truly collaborative effort that took diarrhea in young Boxers from a death sentence to a simple fix. Today every veterinary clinician must have Boxer Colitis on their list of differentials for the appropriate presentation, and must have Baytril as a component of the therapy for this condition once the diagnosis is confirmed. As with most happy endings, the story is not really over, questions remain, and problems are possibly on the horizon. Fortunately our profession, led by researchers like Dr. Kenny Simpson at Cornell, is continuing to investigate this disease.

**SUMMARY**

- “Ready, Aim, Fire” is always the preferred sequence if you want to hit the target
- An accurate clinical diagnosis impacts the positive predictive value of your diagnostic tests
- Hold yourself responsible for remaining responsive to current and advancing research
- Allow your education, not your sales rep, to guide your use of dietary therapy
- Expand your definition of dietary intervention and thoughtfully consider alternatives
- Be a proud member of a profession where individuals make a difference in the quality of life of an entire breed

[Note: Important Acute conditions are not covered in this presentation or this table - for example, the importance of abdominal radiographs in acute vomiting; Parvo +/- Distemper titers in acute puppy diarrhea, PCV/TP in acute hemorrhagic K9 diarrhea, etc.]

<table>
<thead>
<tr>
<th>Canine</th>
<th>Feline</th>
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<tr>
<td><strong>Signalment, History, Physical Examination</strong></td>
<td><strong>An Effective Diagnostic Pathway is Dictated by a Sound Clinical Diagnosis</strong></td>
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<td><strong>The Use and Timing of Therapeutic Trials is Guided by the Severity of the Clinical Condition</strong></td>
<td>(dose recommendations can be highly variable; check current formulary prior to administration)</td>
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<td><strong>Canine</strong></td>
<td><strong>Feline</strong></td>
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<tr>
<td>Fecal centrifugation flotation and wet mount</td>
<td><em>Giardia/Cryptosporidium</em> IFA or <em>Giardia</em> ELISA</td>
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<td><strong>Rectal scraping (fungal colitis)</strong></td>
<td><em>Tritrichomonas foetus</em> PCR or InPouch culture</td>
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<td>[R]onidazole 30mg/kg q24hr 2 wks</td>
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<td><strong>Empirical Deworming, Broad-spectrum anthelmintic</strong> (Fenbendazole 50mg/kg/day for 5 days)</td>
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<td><strong>Food Responsive Diarrhea:</strong> Diet Trial 2-3 weeks per dietary intervention</td>
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<td>Hypoallergenic/hydrolyzed, Easily Digestible, Low Fat, Hi Fiber</td>
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<td><strong>Biochemical profile (fasted), CBC, Urinalysis</strong></td>
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<td>HypoT4 – Thyroid panel w/free T4</td>
<td>HyperT4 – total T4</td>
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<td>Addisons: Basal Cortisol, ACTH stim test</td>
<td>CKD – IRIS staging</td>
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<td>TX A&amp;M GI Panel (fasted and species specific): TLI, PLI, Folate, Cobalamin</td>
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<td><strong>Other Species-Specific Diagnostic Considerations:</strong> Examples</td>
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<td>Min Schnauzers – fasted [Triglyceride]</td>
<td>FeLV/FIV</td>
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<td>SCWT – Urine Protein:Creatinine Ratio</td>
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<td>Lundehunds, Basenjis – TX A&amp;M [fecal α-protease]</td>
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<td><strong>Antibiotic Responsive Diarrhea (ADR):</strong></td>
<td>Tylosin&lt;sup&gt;®&lt;/sup&gt; 10 mg/kg q24hr 6-12 wks</td>
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<td>Imaging: Abdominal radiography (+/- air or contrast), Ultrasound</td>
<td>Ultrasound-guided Fine Needle Aspirate: low morbidity, low yield</td>
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<td>Ultrasound Guidance: Infiltrative disease – Inflammatory vs. Neoplastic</td>
<td>Histopathology: Endoscopy (mucosal) vs. Surgical/Laparoscopy (full-thickness)</td>
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<tr>
<td>H&amp;E stain, Giemsa, Gram, acid-fast, GMS, PAS, Warthin-Starry stains</td>
<td>IHC, FISH, PCR, PARR</td>
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### Idiopathic Inflammatory Bowel Disease

**Dietary Intervention:****Hypoallergenic or Hydrolyzed**
- **Antibiotics:** Tylosin<sup>®</sup> 10 mg/kg q24hr
- Metronidazole<sup>*</sup> 10 mg/kg q12hr
- Prednisolone 1-2mg/kg BID, taper per clinical signs & side-effects
- Budesonide 1 mg (cats, toy breeds) – 3 mg (mid-lg breed) total dose q24hr, then taper
- Cyclosporine 5 mg/kg PO q24hr
- Frozen, w/food if GI upset on empty stomach
- Azathioprine 2 mg/kg PO q24hr then taper
- Chlorambucil 2mg total/cat q4d
- If cat < 2kg, 2mg total/cat q1wk
- Azathioprine not recommended in cats

**Lymphangiectasia** (rotties, yorkies, maltese, shar-pei, GShep)
- Low-fat diet (alt Hydrolyzed for easily digestible)
- Prednisolone 1-2mg/kg BID, then taper (Rutin 50 mg/kg PO TID)
- Cobalamin, parenteral fat-soluble vitamins, low-dose aspirin

### GI Lymphoma

**Consult with Oncology**
- Chlorambucil 15 mg/m<sup>2</sup> PO q24hr for 4 days q3wks
- Prednisolone 3 mg/kg PO q24hr, then taper

**Additional Therapies to Consider as Warranted**
- E-tube placement, Probiotics, canned Pumpkin, metanucil, *Helicobacter* Rx
- Mirtazapine 0.6 – 1.0 mg/kg BID
- Mirtazapine 15mg tab, ¼ tab q24hr (1/8th in CKD)
- Cerenia 1.0 mg/kg/day IV, SQ; 2.0 mg/kg/day PO (reduce dose 50% with liver failure);
  may be given for > 5 consecutive days
  may be given to young animals
- Cerenia 1.0 mg/kg/day IV, SQ; 2.0 mg/kg/day PO (reduce dose 50% with liver failure)

*Tylenol®Soluble = 100gms per bottle; 1 tsp (5ml) = 2.5-2.7gms; 1/8<sup>th</sup> tsp = 325mg; bitter, rec’d capsules
*1mg of metronidazole base = 1.6mg of metronidazole benzoate
SCWT = soft-coated Wheaton terrier; IHC = immunohistochemistry; FISH = fluorescence in situ hybridization; PCR = polymerase chain reaction; PARR = PCR for antigen receptor gene rearrangement
INTRODUCTION

Feline Panleukopenia

Feline “Panleuk” is a viral infection seen most often in non-vaccinated kittens, caused by feline parvovirus that results in an acute presentation of predominantly gastrointestinal signs: vomiting, diarrhea, anorexia, dehydration and lethargy. This condition is often terminal. Like Parvo in puppies, the virus attacks the rapidly dividing cells of the GI mucosa, destroying the normal architecture and function of the villi and crypts. The CNS and retina can be affected, and the disease derives its name from the panleukopenia seen on CBC.

The virus is very stable in the environment and extremely contagious, although the disease is extremely unlikely in well-vaccinated kittens. Hence the classic “at-risk” population is young kittens (< 6 months of age) in a shelter environment, often with an unknown or inadequate vaccination history.

The panleuk posture is one of severe dehydration, weakness and lethargy, with the head flat on the floor or hanging into a water bowl, similar to the hypokalemic cat. Abdominal palpation may elicit discomfort and reveal intestines that are too firm or too soft, but either way, just not right. As with many acute and severely ill cats, body temperature is more likely to drop than register as a febrile as the condition progresses. If the kitten was infected very early on the presentation may include cerebellar signs such as hypermetria and a wide-based stance. A fundic exam should be performed to look for retinal dysplasia. The viral destruction of leukocytes makes these kittens susceptible to secondary infection and some number of them are likely to present with concurrent respiratory signs – the triad of a distemper dog: GI, respiratory, and CNS.

Severe panleukopenia is present on the CBC of these kittens and the biochemical profile may reflect the patient’s dehydration and GI signs. The fecal CPV antigen immunoassay, a canine parvovirus assay, detects the feline panleukopenia virus in feces. Paired serum samples would demonstrate a rising antibody titer over a 2-3 week period. Viral isolation and electron microscopy are used less frequently.

Treatment is largely supportive:

- Hydration – often severely dehydrated
- Electrolytes – abnormal secondary to diarrhea and vomiting
- Nutrition – patients are often anorectic, consider nasogastric tube for support
- Transfusion – sometimes used for oncotic support
- Secondary bacterial infections – broad spectrum antibiotic

The persistence of the virus in the environment is problematic and requires significant attention to all areas of potential shedding, using a 1:32 dilution of household bleach. The KEY to control is vaccination of all cats (those that survive the infection appear to be protected for life). There are a variety of products available, and the last “kitten” vaccine should be administered at 16-20 weeks of age (see AAFP Guidelines and Disease Information Fact Sheet (Dr. Margie Scherk), www.catvets.com).

FeLV

Feline leukemia virus (FeLV) is a retrovirus that infects the intestinal crypt epithelial cells, although most famous its effect on cells of the bone marrow and immune system. Cats appear particularly susceptible if they spend time outdoors or are from a multi-cat household. Grooming, biting, and sharing life (or more
Specifically, saliva) with other cats increases the likelihood of transmission. FeLV is a differential for persistent diarrhea in a young cat, particularly if accompanied by concurrent infections. Lymphoma is also common in young FeLV-positive cats.

The CBC often reflects the hemolymphatic aspects of infection, resulting in anemia, abnormal lymphocyte counts, neutropenia, and thrombocytopenia. Biochemical changes are non-specific. The IFA assay will identify an FeLV antigen, although may not detect the virus for up to 12 weeks post-infection. The ELISA assay may detect the same viral antigen earlier in the disease progression.

Treatment is again largely supportive (as above) although these patients are more likely to require blood transfusions for their anemia. More specific drugs to consider for the treatment of these cats include:

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<tr>
<th>Drug</th>
<th>Dosage/Details</th>
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<tr>
<td>Zidovudine</td>
<td>5-15 mg/kg PO BID</td>
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<td>alpha-interferon</td>
<td>30 U/day PO for 7 days every other week</td>
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<tr>
<td>Propionibacterium acnes</td>
<td>0.5 mL/cat IV once or twice weekly</td>
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<td>acemannan</td>
<td>100mg/cat/day</td>
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<tr>
<td>Oxytetracycline (Mycoplasma haemofelis)</td>
<td>15 mg/kg PO TID</td>
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<tr>
<td>Doxycycline (Mycoplasma haemofelis)</td>
<td>5 mg/kg PO BID</td>
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<tr>
<td>Erythropoietin</td>
<td>35-100 IU/kg SC q48 hours</td>
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<tr>
<td>rhG-CSF</td>
<td>5 ug/kg SQ q24 hours</td>
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For FeLV vaccination at CSU we use the canarypox-FeLV recombinant vaccine, always testing the cat for FeLV status prior to vaccination. Decreasing exposure to other cats is another strategy. (see AAFP feline retrovirus management guidelines).

**FIP**

Another viral disease of high mortality in cats, FIP, a mutated coronavirus, does most of its damage through an immune-mediated process where one of the body’s defenses, macrophages, actually help spread and perpetuate the disease, which is classically pyogranulomatous in nature. Anorexia, weight-loss, and diarrhea are clinical signs associated with GI involvement, but usually the other effected tissues result in the clinical signs that are most suggestive of the diagnosis. Panleukopenia is actually another differential to consider in these cats as they may have neurological and ocular signs, but FIP cats also often have swollen bellies full of fluid and granulomatous masses, and are frequently icteric. Elevated globulins and a viscous, straw-colored abdominal fluid are highly suggestive of the disease, although histopathology (intestines, liver, kidney) is the gold standard.

Treatment is supportive, but FIP is almost invariably a terminal disease. Vaccination is not generally recommended by the American Association of Feline Practitioners, and prevention is best done through the reduction of possible exposure.

FIV is another retrovirus that can cause significant GI signs, usually transmitted between cats through bite wounds, but the prevalence of this virus actually increases with age so we do not include in our discussion of kitten diarrhea.

**Tritrichomonas**

“Good news Mrs. Smith, your kitten’s diarrhea is likely to resolve all on its own in just 6 months to 2 years!”

_Tritrichomonas foetus_ is a motile flagellated protozoal cause of diarrhea, found predominantly in young cats. One of its best friends appears to be _Giardia_, as they are commonly found hanging out together. Both are
most often transmitted by the fecal-oral route. The clinical presentation is usually one of persistent or recurrent large bowel diarrhea with few other problems besides a very sore bum, maybe even rectal prolapse. Although rare, some kittens can present in much worse shape, with anorexia, weight-loss, fever, fecal incontinence and abdominal pain. Another common aspect of the presentation is that a battery of dewormers has failed to have the desired effect. The classic history includes an environment of exposure; shelters, cat shows, breeders, or catteries.

Diagnosis starts with an index of suspicion based on the clinical presentation. A wet mount of fresh feces (the fresher the better, no refrigeration, use 40x magnification) may reveal the organism – the classic distinction between *Tritrich* and *Giardia* is based on motion: *Tritrichomonas* appears to have a jerky movement and spindle-shaped undulating membranes, *Giardia* with a spiral motion and a concave ventral disc. Direct examination is, however, low yield. Fecal culture for protozoal organisms is available (InPouch TF), one advantage being that Giardia organisms do not grow in the pouches (incubated at 37°C for 48 hours or room temperature for 12 days, examine daily) while at CSU we frequently use PCR to identify the presence of the organism (the Colorado Diagnostic Laboratory offers a duel PCR assay for both Tritrich and Giardia, again emphasizing that the 2 are often found in the same cat). Again, we start with a clinical diagnosis, since we have found adult cats PCR positive for *Tritrichomonas* where the organism is less likely to be causing the cat’s diarrhea. Testing all cats in a household does help to identify carriers.

There are a lot of drugs that won’t treat *Tritrichomonas*; the one that seems to have the most success is Ronidazole (30 mg/kg/day for 14 days), although recent work by Dr. Jody Gookin (who first identified this organism as a cause of diarrhea in kittens) suggests that some degree of resistance to Ronidazole is emerging in this population of bugs, much as there is an increase in resistance of *Giardia* to metronidazole. Like metronidazole, adverse side-effects of ronidazole include neurotoxicity (ataxia and seizures). *T. foetus* is easily killed in the environment with most disinfectants, so regular cleaning of “infected” households is important – asymptomatic carriers are common. This is one reason for therapeutic failure, in addition to inappropriate dosing of ronidazole or emerging resistance of the organism to this treatment. Some practitioners will use a high fiber diet in these patients because of the large bowel aspect of the disease. Probiotics are frequently recommended, and a recent prospective, double-blinded, placebo-controlled study found that adding probiotics (*Enterococcus faecium*) to Ronidazole for the treatment of *Tritrichomonas* significantly reduced the likelihood of relapse following treatment, compared to treatment with Ronidazole alone (Lalor & Gunn-Moore, International Society of Feline Medicine abstract, 2012). There is some question regarding the safety of Ronidazole in kittens and it is generally not recommended for use in kittens less than 12 weeks of age, but in this abstract the range of the treated patients started at 2 months of age and no adverse side-effects were reported. Capsules are stored in the freezer and owners should use precautions when handling the drug (use gloves, do not open or crush capsules) as it is considered a carcinogen.

**Giardia**

*Giardia* is a flagellate protozoan parasite that most often causes acute, small bowel diarrhea, but should also be a differential for acute or chronic large, small, or mixed bowel diarrhea – in other words, diarrhea (oh, and occasionally pets will vomit). Young cats are more likely to be clinically effected than older cats, and the condition may be severe in kittens.

As with *Tritrichomonas*, kittens from population-dense environments (kennels, catteries, and cat shows) are at increased risk, a number of dewormers appear ineffective against *Giardia*, and resistance to metronidazole also appears to be an emerging problem.

Trophozoites can be found in fresh feces where the “falling leaf” motility and concave surface distinguishes them from the “herky-jerky” movement of *Tritrichomonas*. Cysts are shed intermittently but can be revealed through zinc sulfate and centrifugal flotation of fresh feces (3 samples, 2 grams of feces mixed with 15 ml of a 33% zinc sulfate solution, strained, filled with additional zinc sulfate, and centrifuged for 3-5 minutes at 1500 rpm with the tube covered with a coverslip; Lugol’s iodine may be added to the centrifuge tube to make identification easier). Various fecal ELISA assays are available, and at CSU we often employ PCR.
Therapy can be attempted with:

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<tr>
<th>Therapy</th>
<th>Dosage and Duration</th>
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<tr>
<td>Fenbendazole</td>
<td>50 mg/kg PO q24 hours for 5 days</td>
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<td>Pyrantel, praziquantel, febantel</td>
<td>56 mg/kg (febantel) q24 for 5 days</td>
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<tr>
<td>Furazolidone suspension</td>
<td>4 mg/kg BID for 7-10 days</td>
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<td>Metronidazole benzoate</td>
<td>10-25 mg/kg PO BID for 5-7 days</td>
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<tr>
<td>Tinidazole</td>
<td>30 mg/kg PO q24 hours for 3 days</td>
</tr>
<tr>
<td>Quinacrine</td>
<td>11 mg/kg PO, q 24 hours, 12 days</td>
</tr>
</tbody>
</table>

Therapeutic failure and relapse is common, suggesting misdiagnosis, inappropriate dosing, lack of client compliance, reinfection, or concurrent disease.

**Cryptosporidium parvum**

*Cryptosporidium* is a coccidian parasite that can cause anything from nothing to transient to life-threatening disease. Diagnosis is made with a fecal ELISA or IFA, although be aware that like Giardia, Cryptosporidium is shed intermittently. There are very few treatment options available in cats; azithromycin (5-10 mg/kg PO q 24 hours for 14 days) has been successful in anecdotal reports.

**Summary**

- A number of viral causes of kitten diarrhea have not been covered (calicivirus, rotavirus, astrovirus, enteric coronavirus; definitive diagnosis is difficult and treatment is largely supportive care
- A number of bacterial causes of kitten diarrhea have not been covered (salmonella, campylobacter, clostridium, colibacillosis; definitive diagnosis is difficult and treatment is largely supportive care
- Kittens are particularly susceptible to the effects of dehydration, lack of nutrition, and thermoregulation; once again highlighting the importance of all aspects of supportive in these small patients.

**References**


*Tritrichomonas* information found at [http://www.cvm.ncsu.edu/docs/personnel/gookin_jody.html](http://www.cvm.ncsu.edu/docs/personnel/gookin_jody.html)
INTRODUCTION

The vast majority of cases of Inflammatory Bowel Disease in humans are either Ulcerative Colitis or Crohn’s Disease, two reasonably well defined conditions. In contrast, as already mentioned, the term Inflammatory Bowel Disease in veterinary medicine refers to an Idiopathic condition that often serves as an umbrella term for a variety of clinical conditions – all of those for which we haven’t found a cause. At the recent 2011 ACVIM meeting in Denver CO, Dr. Al Jergens defined feline IBD as having the following features: 1) the presence of persistent (> 3 weeks) gastrointestinal signs which are characterized by cyclic periods of active and inactive disease; 2) inadequate response to dietary trials and symptomatic therapies alone; 3) failure to document other causes for gastrointestinal inflammation; and 4) histopathologic evidence of mucosal inflammation.

The veterinary profession is undergoing a subtle but important shift in terminology. Whereas previously a diagnosis of “Inflammatory Bowel Disease” or IBD was often given to any cat with diarrhea when time, patience, or finances precluded an actual diagnosis, we now tend to start with the term “Chronic Enteropathy”. From there we move forward diagnostically and therapeutically in an organized manner that allows us to add important qualifiers, such as Chronic Enteropathy – Food Responsive Diarrhea. Only when we have exhausted the differential list and procured histopathology do we settle for a diagnosis of IBD (NOTE: the real name is idiopathic inflammatory bowel disease and it is a histopathologic diagnosis). One consequence of this shift in vocabulary is a shift in our choice of trial therapies, moving away from early intervention with glucocorticoids (IBD) to a renewed appreciation for the power and importance of dietary therapy.

1) Identify the patient as having a Chronic (you pick, 3 weeks, 2 months?) Enteropathy (diarrhea, vomiting, weight-loss, change in appetite, etc.); signs attributable to a dysfunction of the enteric system because non-enteric causes have been ruled-out (Diagnostic Step One, often referred to as the Minimum Data Base, with a number of tests thrown in for good measure; PLI, TLI, cobalamin, abdominal ultrasound, etc.). With a stable patient:

2) Fecal examination and prophylactic deworming (Step Two).

3) Diet trial (Step Three – ruling out an Adverse Reaction to Food)

4) Antibiotic trial (Step Four – ruling out an Antibiotic Responsive Condition)

5) The Chronic Enteropathy persists – Tissue Diagnosis (Step Five) to rule out Neoplasia.

Histopathology is/was/maybe considered the “gold standard” for diagnosis of Inflammatory Bowel Disease, although ironically, many studies show very little correlation between histopathologic severity and clinical reality, so what’s the point? (Encourage your pathologist to look into the recent guidelines produced by the WSAVA, www.wsava.org). Perhaps the single most critical function of our pathologist is to distinguish
between IBD and Neoplasia for us, our patient, and their owners. But even that distinction has clearly been shown to be a difficult one for the naked eye looking through a microscope – and it can be very difficult to get two eyeballs to agree (especially if they belong to two different pathologists). To make matters worse, the two may not be as separate and distinct as we would like. An overlap between IBD and alimentary lymphoma in cats has been suggested with some cases of IBD suspected of progressing to alimentary lymphoma (as has been demonstrated in humans). Fortunately, the information that can be derived from a piece of tissue is rapidly extending beyond a classical histopathologic description. Particularly relevant technological advances include immunohistochemistry and flow cytometry, both designed to more give much more detailed and sophisticated names to the cells that are present in the tissue specimen. Although currently of little practical importance, we are also able to identify differences at the biochemical level between cytokines and Toll-like receptors that likely have clinical implications. One of the more effective treatments for Crohn’s disease is an antibody directed at TNF-alpha (tumor necrosis factor), a long way away from the non-specific biochemical atom bomb known as prednisone.

The major players in the etiopathogenesis of inflammatory bowel disease have seemingly been identified: Antigenic Stimulation, the Microbiota, the Enteric Architecture and Protective Functions, and the Immune System. New players are joining the ranks as research continues – particular enteropathic bacterial species, specific toll-like receptors, an array of cytokines and chemical messengers, breed-specific genetic mutations, etc. It makes for a fascinating quagmire of literature that renders us “idiopathic”.

6) **Diagnosis** = Inflammatory Bowel Disease (or a histopathologic surprise from a pathologist with a sense of humor that sends you reeling back towards square one).

IBD treatment – now that you’ve got it diagnosed, sort of, how to treat?

**Diet** (there it is again and a crucial component of IBD therapy): novel protein, hydrolyzed, highly digestible diet, with dietary fiber, polyunsaturated fatty acids (n-3 FA), and prebiotic/probiotic supplements. There, did I leave anybody out? At various ends of the spectrum, an inappropriate immune response to dietary antigens may constitute an Adverse Reaction to Food, a Food Allergy, or simply an antigenic component of IBD. The only real way to tell is to rechallenge the cured cat with the previously offending diet and see if the diarrhea returns to the new carpet…sure.

**Rx**: corticosteroids (prednisolone 2 mg/kg/day, taper over 6-12 weeks; budesonide 1-3 mg/day) and metronidazole (15 mg/kg BID) are the most frequently prescribed drugs for IBD. As an additional immune-modulator in cases that persist in the face of glucocorticoids, chlorambucil (2 mg every 4 days in cats > 2 kg) is gaining in popularity, and appears particularly important if the IBD is actually low-grade lymphoma – the two look disturbingly similar.

**Vomiting**: Vomiting may be the only sign or a concurrent condition in cats with IBD. α2 adrenergic antagonists (chlorpromazine 0.2-0.4 mg/kg subQ or IM TID) and 5-HT3 antagonists (ondansetron 0.1-1.0 mg/kg or dolasetron 0.5-1.0 mg/kg, orally or IV q12-24 h) act as effective anti-emetics in cats, while metoclopramide (dopaminergic antagonist, 1-2 mg/kg CRI) is less effective as an anti-emetic (although still a prokinetic, in theory at least). At CSU we frequently reach for the NK-1 receptor antagonist, maropitant 0.5 – 1.0 mg/kg q24 h intravenously, subcutaneously, or orally).

**History Lesson**

“Pharmaceutical agents are often given inappropriate precedence in the treatment of gastrointestinal tract diseases. Nutrients have marked influences on the gastrointestinal tract and manipulation of the diet provides clinicians with a powerful therapeutic strategy to be used alone or concurrently with drug therapy”
As early as 1994 Dr. Guilford recognized that different diseases of the GI tract were likely to respond to different dietary manipulations. Simply characterizing the clinical condition was an important first step towards deciding on the best fit amongst diet choices. For example, for chronic small bowel diarrhea Dr. Guilford recommended a “highly digestible, gluten-free, hypoallergenic, isosmolar, low in fat and low in lactose” diet. That should just about cover it!

We have long recognized the cat as an obligate carnivore but we continue to debate just exactly what impact that status should have on what we actually feed this species. Bear in mind that if left to their own devices, and assuming they more closely resembled a contestant on Hunger Games as opposed to the Couch Potato so many of us are accustomed to dealing with, cats would consume a diet high in protein, with low to moderate amounts of fat and minimal carbohydrate. A cat’s obligate daily protein requirement (30% DMB) is over twice that of a dog (12%) and cats have specific requirements for particular proteins (ex. taurine) as well as a number of vitamins, arachidonic acid, carnitine, and vitamin D.

**Acute Gastroenteritis**

Historically the first principle in the nutritional management of acute gastroenteritis has been no nutrition at all – “rest” the GI tract with a 24-48 hour fast. In addition to diarrhea, nausea and inappetence, the patient was often vomiting upon presentation, adding to the argument against putting anything (ie. food) down the pet’s throat. The potential contribution of acute pancreatic inflammation and the concern over stimulating the pancreas with food also fuels the fasting paradigm. Following the period of fasting, small quantities of a “bland” diet are gradually introduced as we hold our breath hoping the offending etiology has passed. A somewhat more scientific justification for a period of fasting would be the concern over antigen exposure in the gut during a period of inflammation, potentially creating a “food allergy” where previously there had been none. With cats this approach can be problematic. For one thing, a high protein/low carbohydrate diet does not fit the usual definition of a “bland” diet. The canine bland diet contains a small amount of highly digestible protein, a low fat content, and moderate to large amounts of highly digestible carbohydrate (ie. white rice). In addition, cats frequently can be anorectic for several days before their owner’s realize what’s (not) happening and present them to the veterinarian, and anorexia in a cat can have much more severe consequences than anorexia in a Labrador retriever. Not feeding a cat for 24 hours is still considered a viable way to “rest” the GI tract in cases of acute gastroenteritis, but the clinician must be aware of the likelihood that the clock on that 24-hour window may well have already run out by the time the patient is in your office.

Several recent pharmaceutical advances are of tremendous benefit to the cat with acute gastroenteritis, and the clinician attempting to care for that patient. Metoclopramide still may have a place as a pro-motility agent in the cat, but it has largely been replaced by cisapride (5mg per cat, two to three times daily) for that function. The pharmacology of the cat’s emetic center is simply not amenable to metoclopramide as an effective feline anti-emetic. Fortunately, ondansetron (0.5 mg/kg IV or PO once daily) and maropitant (1mg/kg daily, subcutaneously or orally – 1/4th of a 16mg tablet) appear to be very effective anti-emetics in the cat. So if needed, we can stop the cat with acute gastritis from vomiting. What about getting them to eat? Cyproheptadine (2-4mg per cat, once or twice daily) has long been used as an appetite stimulant in cats, with variable success. More recently, mirtazapine (1/4th of a 16mg tablet once daily, reduce the dose in cats with chronic kidney disease) has been shown to be an effective appetite stimulant in many cats, and may have some anti-emetic properties as well. Contrary to the original dosing information (every 3 days), research by Dr. Quimby at Colorado State University has shown that the pharmacokinetics of mirtazapine in cats would require daily administration of the drug for full effect. It appears safe to mix and match the various anti-emetics and appetite stimulants, and the most effective combination will likely differ for different patients.
Finally, if a feline patient at CSU is approaching 48 hours without having been convinced to take on nutrition voluntarily (or with the help of pharmaceutical intervention), we will move relatively quickly towards “assisted feeding” through either a nasoesophageal feeding tube (liquid diet such as CliniCare at 1 kcal/ml, or the human product Ensure, also 1 kcal/ml), or quite frequently, an esophageal feeding tube (E-tube) with a blenderized diet, particularly if we are trying to get the cat out of the hospital.

Dietary intervention for acute gastritis in cats:

- High quality protein
- Highly digestible diet (>90%), single ingredients, no additives or flavorings
- Moderate energy density, small amounts of highly digestible carbohydrate
- High moisture content
- Fat for palatability
- 3-4 meals/day

The quality of the protein source in the diet is perhaps the single key ingredient for the successful passage and placation of an inflamed feline GI tract. Any poor-quality, undigested protein enters the colon as food for the bacterial microbiota that reside there. This may result in a change in the quantity and quality of the colonic bacterial population (“there goes the neighborhood”), stimulates the secretion of water into the GI lumen, and increases the amount of ammonia produced and thereby further damages an already diseased GI mucosa. In short, exacerbates both the feel (softer) and smell (bad) of the problem (diarrhea).

Food Responsive Diarrhea, a Chronic Enteropathy of Cats

The veterinary profession (with the persistent prodding of pet food companies) is expanding the clinical definition (a bit faster than our basic understanding) of the impact diet has on gastrointestinal disease. Even the language is evolving to acknowledge the fact that diet plays a role in GI health well beyond the simple classification of allergy or intolerance. Cataloging dietary components as a cause or contributor to GI disease has evolved from “It’s the beef” to looking at the potential role of grains, gluten, preservatives and preparation. Prescribing dietary intervention as a contributor to the cure for GI disease has evolved from single-source Lamb & Rice to diets incorporating most any creature on the planet, exotic vegetables, prebiotics, probiotics, a spectrum of digestibility, combinations of fibers and various volumes of fat, essential ingredients as well as essentially eliminated ingredients.

Dr. Guilford and many others have continued to contribute strong research evidence for the impact of diet as both the cause and potential cure for GI conditions. Several key take-home points from this effort are:

- A significant percentage of cats with GI disease will respond favorably, if not completely, to dietary intervention
- A diet trial for a gastroenterologist lasts about 2-weeks, compared to the 8-12 week effort for a dermatologist
- The standard dietary intervention remains the hypoallergenic/hydrolyzed diet
- A much more diverse array of dietary options should be considered
- Sometimes it is a matter of matching a specific diet with a particular patient, especially with cats

Fiber

- Non-digestible plant carbohydrate

Soluble, fermentable fiber (ex. beet pulp) is easily broken down by GI bacteria into short-chain fatty acids (SCFA), an essential nutrient for repairing and maintaining a healthy GI mucosa. Soluble fiber will also
slow down digestion, delay gastric emptying, inhibit absorption of nutrients and cholesterol, slow GI transit time, increase fecal water content, and shift the microbial balance towards “healthy” bacterial species (*Lactobacilli* and *Bifidobacter*) from unhealthy species (*Clostridium* and *E colii*).

- Oatmeal, oat cereal, lentils, apples, oranges, pears, oat bran, strawberries, nuts, flaxseeds, beans, psyllium, carrots
- Metamucil: psyllium, 1/8th – 1/4th teaspoon twice a day

Insoluble, poorly fermentable fiber (ex. cellulose) adds bulk to the stool, and may help normalize motility and act as a laxative. Colitis is the GI condition that appears to be most responsive to this action, hence the proliferation of “fiber-responsive” diets. Fiber-responsive diets high in insoluble fiber should be avoided in cats prone to constipation (chronic kidney disease) or obstipation (megacolon).

- Whole wheat, whole grains, wheat bran, seeds, nuts, barley, brown rice, zucchini, broccoli, carrots, green beans, root vegetable skins
- Canned pumpkin: 90% water, 3% fiber, 1-2 teaspoons per meal

For those constipated cats approaching megacolon, fiber-enriched diets are particularly important as dietary fiber may increase fecal consistency, bind potential colonic irritants, improve abnormal colonic motility, and produce beneficial short-chain fatty acids which nurture large bowel structure and function. Fermentable fibers (beet pulp, psyllium, soy fiber, or oat bran) is recommended for maintenance of colonic health.

**Probiotics**

Our knowledge of the GI microbiome is still incomplete. We know there are normal inhabitants, such as Firmicutes, Bacteroidetes, Fusobacteria, etc.; we know there are pathogens including various *Clostridium*, *Campylobacter*, *Salmonella*, and *Escherichia* spp; and we know that “dysbiosis” is a common finding in dogs with chronic diarrhea as a result of GI disease.

What we know about the use of probiotics in GI disease is even more incomplete. We know that to have any chance of being beneficial, the probiotic supplement must 1) contain a lot of organisms – current human trials are often using orders of magnitude higher doses than those found in veterinary studies; 2) those organisms must be alive; 3) probiotic effects are likely to be rapid onset with minimal staying power once discontinued; 4) probiotics are assumed to work by changing the make-up of the intestinal microbiota, but may in fact exert effects in other ways; 5) fortunately, like cobalamin, probiotics seem to belong on the same “do no harm” poster, with very few and very extra-ordinary exceptions.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Population (n)</th>
<th>Key</th>
<th>Reported Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marshall et al AJVR 2006</td>
<td>Healthy adult cats (12)</td>
<td>2</td>
<td>↑ Lactobacillus, ↓ Clostridium &amp; Enterococcus</td>
</tr>
<tr>
<td>Veir et al Vet Ther 2007</td>
<td>Kittens (9)</td>
<td>1</td>
<td>↑ CD4+ cells</td>
</tr>
<tr>
<td>Lappin et al JFMS 2009</td>
<td>Chronic FHV-1 cats (12)</td>
<td>1</td>
<td>lessened morbidity</td>
</tr>
<tr>
<td>Rishniw et al JFMS 2011</td>
<td>CKD cats (10)</td>
<td>3</td>
<td>Failed to ↓ azotemia sprinkled on food</td>
</tr>
<tr>
<td>Garcia et al FEMS 2011</td>
<td>Healthy cats &amp; dogs (12/12)</td>
<td>4</td>
<td>↑ abundance of probiotic bacteria in feces</td>
</tr>
<tr>
<td>Bybee et al JVIM 2011</td>
<td>Shelter dogs &amp; cats (&gt;100)</td>
<td>1</td>
<td>Cats sig fewer episodes ≥ 2 days</td>
</tr>
<tr>
<td>Hart et al JFMS 2012</td>
<td>Feline chronic diarrhea (53)</td>
<td>4</td>
<td>70% perceived improvement in diarrhea</td>
</tr>
</tbody>
</table>

1 Enterococcus faecium SF68 (FortiFlora); 2 Lactobacillus acidophilus; 3 Azodyl; 4 Proviable-DC (Nutramax)
Consider possible application of Probiotics to:
- acute onset idiopathic diarrhea
- diarrhea associated with over-crowding, shelter environment, young animals
- chronic diarrhea whose response to therapy is less than satisfactory
- in anticipation of stressors, diet change, travel?
- antibiotic-associated diarrhea (concurrent use?)
- antibiotic-responsive diarrhea (useful adjunct?)
- diarrhea secondary to GI parasites? (adjunct?)

consumerlabs.com - a source for unbiased information on probiotics and other nutraceuticals (small fee).

**Cobalamin**

As we race to give the injection of our current “do no harm” poster child, vitamin B12, do not lose sight of the fact that cobalamin levels can be used as a diagnostic tool. Many cats with chronic gastrointestinal signs receive cobalamin supplementation regardless of their endogenous level, and so that level is often left unmeasured. But research suggests that the lowest cobalamin levels are frequently found in cats with GI lymphoma, and gastroenterologist are forever struggling with the important distinction between IBD and GI lymphoma. Of course it is not that easy – cats with IBD can have very low cobalamin levels, and cats with GI lymphoma can have normal cobalamin levels, but we start with a clinical diagnosis and test to support or refute that diagnosis. In that capacity, the initial cobalamin concentration could be an important clue.

It was the Ruaxx et al. study of 2005 (JVIM) that alerted the profession to the importance and impact of cobalamin supplementation (250 micrograms SQ once weekly) in cats with GI disease and marked hypocobalaminemia (≤ 100 ng/L). Since that seminal study cobalamin levels are being measured in cats with a wide variety of non-GI diseases and hypocobalaminemia may be a significant contributor to a number of conditions. In 2007 Allenspach et al. (JVIM) identified hypocobalaminemia (≤ 200 ng/L) as a significant risk factor for a negative outcome for dogs with chronic enteropathies, and a cobalamin less than 150 ng/L is suggestive of GI lymphoma in cats.

**Summary**

- Dietary intervention may not be the only therapy, but it must be a part of an effective plan
- It takes 3 strikes before a cat is out; even a different version of a diet-type may hit the mark
- 2 weeks, not 12, or “Thank Heaven I’m not a Dermatologist!”, for a GI diet-trial
- Expand the definition of Dietary Intervention beyond Diets

**References**


I. Definitions

Occam’s Razor (from Wikipedia): Occam's razor (or Ockham's razor), often expressed in Latin as the lex parsimoniae, translating to law of parsimony, law of economy or law of succinctness, is a principle that generally recommends selecting the competing hypothesis that makes the fewest new assumptions, when the hypotheses are equal in other respects. When discussing Occam's razor in contemporary medicine, physicians speak of diagnostic parsimony.

Diagnostic parsimony advocates that when diagnosing a given injury, ailment, illness, or disease a doctor should strive to look for the fewest possible causes that will account for all the symptoms. “When you are in Texas and you hear hoofbeats, think horses, not zebras.”

Hickam’s Dictum: Hickam’s dictum states that “patients can have as many diseases as they damn well please.” It is often statistically more likely that a patient has several common diseases, rather than having a single rarer disease which explains their myriad symptoms. Also, independently of statistical likelihood, some patients do in fact turn out to have multiple diseases, which by common sense nullifies the approach of insisting to explain any given collection of symptoms with one disease.

II. Occum’s Razor

Feline Chronic Kidney Disease – One Cause of a Myriad of Symptoms

Anemia: normochromic/normocytic, non-regenerative, erythropoietin deficiency, chronic GI loss  
   r/o chronic disease, Renal disease, gastric ulceration, BM, neoplasia, etc.
Anorexia: anorectic factor, leptin  
   r/o Primary (CNS), secondary, Renal disease, liver disease, GI disease, pancreatitis, etc.
Hypertension: impaired autoregulation, RAAS activation  
   r/o Primary, secondary to Renal disease

Hyperparathyroidism: phosphorus retention, low calcitriol  
   r/o Primary hypoparathyroidism, secondary to Renal Disease, hyperphosphatemia
Hyperphosphatemia: decreased GFR  
   r/o: Renal disease, postrenal, hemolysis, hyperthyroidism, intoxicatino, dietary, iatrogenic, osteolysis,  
   hypoparathyroidism
Proteinuria: tubulointerstitial injury, upregulated inflammatory products  
   r/o GN, amyloidosis, Renal Disease, inflammation, infection, neoplasia, immune-mediated

PU/PD: loss of concentrating ability, increased solute load, ADH-insensitivity  
   r/o: Primary, Renal disease, hyperthyroidism, pyelonephritis, leptospirosis, hypoadrenocorticism, pyometra,  
   hepatic failure, hypercalcemia, hypokalemia, drugs, diabetes insipidus, diabetes mellitus, psychogenic, behavioral,  
   CNS
Hypokalemia: decreased intake, increased loss  
   r/o: Renal disease, alkalosis, dietary, drugs, GI, hyperadrenocorticism, hyperaldosterone, insulin, periodic,  
   renal tubular acidosis
Uremia/Metabolic acidosis: impaired excretion (H+) and/or catabolism, increased secretion
r/o Renal disease
Vomiting: uremic toxins, CRTZ, uremic gastroenteritis, ischemia, biliary reflux
r/o: Primary or secondary GI, FB/obstruction, dietary, inflammation, infection, neoplasia, motility disorder, pancreatitis, Renal disease, liver disease, cardiac, CNS

III. Hickam’s Dictum

Uncontrolled Feline Diabetes Mellitus – Diabetic Ketoacidosis – DM + Concurrent Disease(s)


23% Hyperadrenocorticism  13% Acute pancreatitis
21% Urinary tract infection  5% Neoplasia
16% Dermatitis  4% Hypothyroidism


84% Bacterial pyoderma  42% Malassezia
58% Otitis externa  29% Hyperadrenocorticism
49% Allergic dermatitis  22% No concurrent endocrinopathy/allergy


69% One or more concurrent disorder  20% Urinary tract infection
41% Acute pancreatitis  15% Hyperadrenocorticism


93% Concurrent disorders; hepatic lipidosis, cholangiohepatitis, pancreatitis, chronic renal failure, urinary tract infection, neoplasia


37% present in Diabetic Ketoacidosis

22% have a concurrent disorder; hyperthyroidism, IBD, eosinophilic granuloma complex

IV. The Conundrum Case

Sig: 7 yo FS DSH

CC: Febrile & Elevated ALT

Diagnosis: Cholangiohepatitis

CC: Diarrhea

Diagnosis: Inflammatory Bowel Disease

CC: Anorexia & Lethargy

Diagnosis: Pancreatitis
Hickam’s “Triaditis” Dictum or The Ultimate Occam’s Razor?

Weiss DJ et al. Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cats. JAVMA 1996

“The prevalence of IBD (83%) and pancreatitis (50%) was greater for cats with cholangiohepatitis, compared with cats without inflammatory hepatic disease. Thirty-nine percent of cats with cholangiohepatitis had IBD and pancreatitis. Evidence of IBD in association with cholangiohepatitis was characterized by infiltration of lymphocytes and plasma cells into the lamina propria; however, neutrophilic infiltrates also were found in 40% of cats with cholangiohepatitis. CLINICAL IMPLICATIONS: Cats with a diagnosis of cholangiohepatitis should be evaluated for IBD and pancreatitis.”
Inflammatory Bowel Disease (IBD): Inflammation of the small or large intestine for which no underlying etiology can be identified. Histiocytic, granulomatous, and chronic fibrosing enteritis are similar conditions that are rare in cats but that mimic lymphoplasmacytic IBD. Conditions with a clinical presentation similar to IBD include hyperthyroidism, alimentary lymphoma, parasites (giardia, cryptosporidium, clostridium), food allergy or intolerance, renal failure, FeLV/FIV associated disease, concurrent hepatic and pancreatic disease (“triaditis”), systemic mastocytosis.

Lymphoplasmacytic enteritis is the most common form of IBD in the cat. It affects middle-aged to older cats most frequently (no breed or sex predilection), but can be seen in cats less than 1 year of age.

Eosinophilic enteritis appears clinically the same as lymphoplasmacytic IBD, although GI bleeding is more common in this condition. The patient may have a peripheral eosinophilia. Differentials that mimic eosinophilic IBD include mast cell tumor, hypoadrenocorticism (rare in cats), and endoparasites. Eosinophils may infiltrate other organs (spleen, liver, lymph nodes, and bone marrow). This condition (feline hypereosinophilic syndrome) carries a poor prognosis.

Lymphosarcoma is the most common intestinal tumor in cats. Adenocarcinoma and mast cell tumors are other frequently seen GI neoplasms. All have a clinical presentation (vomiting and weight loss) that is similar to IBD.

Clinical signs:
- Vomiting (often intermittent)
- Weight loss
- Decreased appetite/anorexia
- Lethargy
- Diarrhea (not as common as in the canine)
- Hematochezia (large intestinal disease)

Physical Examination:
- Normal
- Loss of muscle mass
- Thickened intestinal loops
- Mesenteric lymphadenopathy

Clinical Pathology:
- Hemoconcentration, anemia
- Lymphopenia, leukocytosis or leukopenia
- Increased ALT, hypocholesterolemia
- Hypoalbuminemia (rare in cats), hyperglobulinemia

Diagnosis:
- CBC, Biochemical profile, Urinalysis, TT4, FeLV/FIV, fecal float (Giardia ELISA), fecal smear, fecal fat (Sudan stain)

- Plain films WNL
- Contrast radiographs (Low yield for the time, effort, and expense)

- Ultrasound – poor intestinal wall layer definition, mesenteric lymphadenopathy, localized or focal intestinal thickening – operator dependent!
Endoscopy – definitive diagnosis??
- Gross observation: gastric ulceration, cobblestone mucosa, loss of texture, exudates, friable, spontaneous bleeding
- Biopsy: multiple biopsies at same site ("PacMan")
- Rule of 8; magic number (?) from any one area for reliable pathological assessment
- Avoid crushing or shoveling (how?!), processing artifacts
- Collect from different areas (stomach, duodenum, jejunum; colon)

Interpretation – normal vs. abnormal numbers of inflammatory cells
- Architectural disruption and mucosal epithelial changes;
- Lymphocytic and plasmacytic infiltrates,
- Crypt distortion, villous blunting, atrophy and fusion,
- Lamina propria fibrosis, epithelial cell or glandular necrosis

How Specific?? (i.e. IBD vs. food allergy/intolerance vs. lymphosarcoma)

The GI Laboratory
College of Veterinary Medicine and Biomedical Sciences
4474 TAMU
Texas A&M University
College Station, TX  77843-4474

Telephone: (979) 862-2861
FAX: (979) 862-2864
e-mail: gilab@cvm.tamu.edu
www.cvm.tamu.edu/gilab

Ship samples using UPS or FedEx, not US Mail or DHL, TLI and PLI assays are species-specific, you MUST indicate species, Separate serum from clot before shipping samples, Both hemolysis and lipemia may interfere with test performance

Cobalamin Dose
Recommended dosages of cobalamin for dogs and cats

<table>
<thead>
<tr>
<th>Animal BW Range</th>
<th>Dose/injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cats, dogs up to 5kg</td>
<td>250 µg</td>
</tr>
<tr>
<td>Dogs, 5-15kg</td>
<td>500 µg</td>
</tr>
<tr>
<td>Dogs &gt; 15kg</td>
<td>1000 µg</td>
</tr>
</tbody>
</table>

1x/wk for 6 wks; 1x/2 wks for 6 wks; then monthly

Most generic cobalamin preparations are 1mg/ml, i.e. 1000µg/ml. Multi-vitamin and B-complex injectable formulations contain much lower concentrations of cobalamin, and often cause pain at the injection site. Their use is not recommended.

Cobalamin is non-irritating and may be given subcutaneously or intramuscularly; most clinicians deliver it subcutaneously.
Top Figure: Input to the Emetic Center, showing different classes of neurotransmitter receptors. D dopaminergic, α adrenergic, 5HT serotonergic, M cholinergic, H histaminergic, ENK enkephalinergic, ω opioid, MOT motilin. Bottom Figure: Those emetic and pro-kinetic receptors not thought to play an important role in the feline are circled or lined-out.

Consequences (examples):

- Apomorphine (D2-dopamine receptor agonist) = good in dogs, poor emetic in cats
- CRTZ D2-dopamine receptors probably not important for emesis in cats
- Metoclopramide (D2-dopamine receptor antagonist) not a good feline antiemetic
- Compared to xylazine (α2-adrenergic agonist); side-effect in cats = emesis
Histaminergic receptors found in CRTZ of dogs, but not cats. Antagonists such as diphenhydramine are ineffective antiemetics for motion sickness in cats, so consider α2-adrenergic antagonists (i.e. chlorpromazine) for motion sickness in cats.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>FELINE DOSE</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucralfate</td>
<td>250mg BID</td>
<td>For gastric ulceration (avoid Pepto-Bismol)</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>2.5 mg/kg IV BID</td>
<td>H2-blocker, decrease acid secretion</td>
</tr>
<tr>
<td></td>
<td>3.5 mg/kg PO BID</td>
<td>For ulcers</td>
</tr>
<tr>
<td></td>
<td>1-2 mg/kg PO TID</td>
<td>Prokinetic</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>5-10 mg/kg PO TID</td>
<td>H2-blocker, inhibits P450 liver enzymes</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>0.7 mg/kg PO q24hrs</td>
<td>Proton-pump inhibitor, safe but avoid chronic use</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>0.5 mg/kg TID SQ</td>
<td>Hypotension; avoid in dehydrated animal</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>0.5 mg/kg TID IV, SQ</td>
<td>May cause extrapyramidal symptoms</td>
</tr>
<tr>
<td>Yohimbine</td>
<td>0.25-0.5 mg/kg BID</td>
<td>Xylazine reversal agent</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>1-2 mg/kg/24hr CRI</td>
<td>Questionable efficacy in the cat</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>0.1 mg/kg BID</td>
<td>Slow IV push. Some rec’d against using in cats</td>
</tr>
<tr>
<td>Cisapride</td>
<td>2.5-5.0 mg/cat TID</td>
<td>Safe in cats (diarrhea and abdominal pain possible)</td>
</tr>
<tr>
<td>Prednisone/Prednisolone</td>
<td>1-2mg/kg/day</td>
<td>Taper (↓ %25 q2-4wks until EOD therapy)</td>
</tr>
<tr>
<td>Budesonide</td>
<td>1.0 mg/cat q24hrs</td>
<td>Locally active GI steroid (high first pass metabolism)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.22 mg/kg/day</td>
<td>Cats tolerate higher doses with fewer side effects</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>20mg/cat</td>
<td>Adverse effects with long-term use still possible</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>0.3 mg/kg q48hrs</td>
<td>Use With Caution: Bone Marrow Toxicity</td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>1 - 4 mg/kg/day divided</td>
<td>Neoral (trough levels of 500 ng/ml)</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>1-2 mg/cat; 2-3x/wk</td>
<td>Recheck WBC counts</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>10-20 mg/kg q24hrs</td>
<td>Use with caution, cats sensitive to salicylates</td>
</tr>
<tr>
<td>Fenbendazole</td>
<td>50 mg/kg PO q24hrs</td>
<td>Rx for 3 days: Broad spectrum anthelmintic</td>
</tr>
</tbody>
</table>

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**Cisapride**

Phone: (719) 481-2209  
Toll-Free: (800) 595-7565  
Fax: (719) 481-4971

**Headquarters:**  
115 C 2ND Street  
P.O. Box 467  
Monument, CO 80132

**Email:**  
Customer Service: custserv@monumentpharmacy.com  
Sales: sales@monumentpharmacy.com  
General Information: info@monumentpharmacy.com
I. Diagnostic Testing

Sensitivity – the proportion of true positives that are correctly identified by the test
Specificity – the proportion of true negatives that are correctly identified by the test

- True positive: Sick pets correctly diagnosed as sick
- False positive: Healthy pets wrongly identified as sick
- True negative: Healthy pets correctly identified as healthy
- False negative: Sick pets wrongly identified as healthy

Positive Predictive Value (PPV) - The ratio of true positives to combined true & false positives; the proportion of pets with positive test results who are correctly diagnosed. It is the most important measure of a diagnostic method as it reflects the probability that a positive test reflects the underlying condition being tested for. Its value depends on the prevalence of the disease.

II. Protein-losing Enteropathies

Hypoalbuminemia

- Elevated Globulins
  - Protein-losing nephropathy
  - Liver Failure
  - Malabsorption
  - Maldigestion
  - Starvation

- Decreased Globulins
  - Protein-losing enteropathy (PLE)
  - Blood loss
  - Proteinaceous exudate

Protein-losing Enteropathy Differentials

- Severe inflammatory bowel disease
- Granulomatous disease
- Alimentary tract lymphoma
- Lymphangiectasia
- Chronic intussusception
- Parvovirus
- Salmonellosis
- Histoplasmosis
- Pythiosis
- Purulent enteropathy
- 2° mucosal edema
- Severe parasitism
  - Hooks, whipworms
  - Mucosal crypt ectasia

Hypoalbuminemia

Although the combination of hypoalbuminemia and hypoglobulinemia is “textbook” for a protein-losing enteropathy (PLE) – assuming the dog is not bleeding out in front of you or has presented with 3° degree burns over most of its body – it should be noted that a normal, or even elevated globulin level should never be the only reason to take PLE off a list of differentials that was generated by a History and Physical Examination. It should also be noted that PLE is not really a diagnosis at all, but simply a description of the consequences of the severity or chronicity of the actual underlying problem. The diagnostic work-up can begin by adjusting the above list of PLE differentials based on the breed and age of the dog, with IBD being more common in older animals, lymphosarcoma being less particular, and lymphangiectasia preferring certain breeds. Parvovirus and intussusception often occur together in young dogs, as does heavy GI parasitism, while histoplasmosis has a geographical distribution.
Once hypoalbuminemia is noted on the biochemical profile and globulins are assessed the clinician needs to confirm that there is no significant loss of protein in the urine (urine protein:creatinine ratio) and the liver is capable of producing adequate protein (other biochemical indicators of liver function followed by a bile acids test if necessary). Other common laboratory abnormalities consistent with PLE include lymphopenia, hypocholesterolemia, hypomagnesemia, and hypocalcemia. It would be unusual for an animal with a PLE not to present with diarrhea, and a thorough fecal examination is an essential part of that diagnostic work-up. In addition, feces can be submitted (Texas A&M GI Laboratory) for measurement of fecal α1-protease inhibitor enzyme quantification, a molecule that is of similar size to albumen but is not degraded in it’s journey through the GI tract, and hence, and indirect marker of albumen loss and a relatively sensitive (more sensitive than serum albumen?) marker of protein-loss through the GI tract. Be aware of possible significant and clinically relevant electrolyte abnormalities in Ca++ and/or Mg++, as well as either Secondary Hyper- or Hypoparathyroidism.

The most direct route to a diagnosis in cases of PLE is histopathology. The advantages and pitfalls of the various techniques available (endoscopy, laparoscopy, and exploratory surgery) is beyond the scope of these notes. It is common for lesions suggestive of lymphangiectasia AND inflammatory bowel disease to be present within the same biopsy sample – the bursting of lacteals and release of their contents is likely to set up an inflammatory response, and the crowding of the interstitial space with cells of the immune system is likely to impede normal lymphatic flow. This makes the site (ileum versus ileum), depth (mucosal versus full-thickness), and quality of the biopsy of significant importance in final interpretation. The potential diagnostic yield provided by abdominal ultrasound prior to any of the above-listed techniques is also beyond the scope of this discussion, as the literature continues to debate the significance and sensitivity of certain ultrasonographic abnormalities, such as a loss of normal intestinal wall architecture, intra-mural “speckles”, or enlarged mesenteric lymph nodes.

--------------

Sig: 1.5 yo FS Yorkshire Terrier
CC: “Big belly”
Ascites, peripheral limb edema, and dyspnea secondary to pleural effusion suggest an albumen concentration < 1.5 g/dL.

III. Lymphangiectasia  Breed predisposition: Yorkshire and Soft-Coated Wheaten terriers

NOTE: If endoscopy is planned and lymphangiectasia is a primary differential, administration of corn oil one hour prior to the biopsy procedure may increase the likelihood of documenting dilated lacteals (Drs. Willard and Zoran, Texas A&M).

<table>
<thead>
<tr>
<th>Treatment Options for Lymphangiectasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPN or PPN</td>
</tr>
<tr>
<td>Low-fat Diet</td>
</tr>
<tr>
<td>Medium chain triglyceride oil (MCT)</td>
</tr>
<tr>
<td>Corticosteroids</td>
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<tr>
<td>Oncotic Pressure</td>
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<tr>
<td>Rutin</td>
</tr>
</tbody>
</table>
IV. Inflammatory Bowel Disease, Alimentary Lymphosarcoma

<table>
<thead>
<tr>
<th>Treatment Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
</tr>
<tr>
<td>Hypoallergenic</td>
</tr>
<tr>
<td>Hydrolyzed</td>
</tr>
<tr>
<td>Ultra Low-fat</td>
</tr>
<tr>
<td>Elemental</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Plasma – colloid, coag factors</td>
</tr>
<tr>
<td>Immunomodulatory</td>
</tr>
<tr>
<td>Prednisone/Prednisolone</td>
</tr>
<tr>
<td>Chlorambucil</td>
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<tr>
<td>Azathioprine</td>
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<tr>
<td>Cyclosporin</td>
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<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Antibiotic</td>
</tr>
<tr>
<td>Metronidazole</td>
</tr>
<tr>
<td>Tylosin</td>
</tr>
<tr>
<td>Cobalamin</td>
</tr>
</tbody>
</table>

*Zoran, Texas A&M

V. Exception to “The Rule”

Sig: 3.0 yo MC Basenjis
CC: V/D, weight-loss

Immunoproliferative Enteropathy of Basenjis

- < 3 years of age
- Chronic intermittent diarrhea
- Severe progressive weight loss
- Diarrhea, occasional vomiting
- Hypoproteinemia
  - Severe hypoalbuminemia
  - Hyperglobulinemia
- Mature neutrophilia, non-regen anemia
- Moderately increased hepatic enzymes

VI. Mirtazapine (Remeron®)

Appetite stimulant, anti-anxiety, anti-emetic (5-HT3 antagonist)
Remeron SolTab (generic) 15mg tablets

Cat dose 1/8th tablet q24hr (EOD if CKD)
Dog dose 15-30mg/dog PO q24hr
VII. Hypereosinophilic Syndrome

Eosinophilic infiltrates in intestinal tract and parenchymal organs (ie., spleen)
Cats > 7 yo, diarrhea (bloody) & weight-loss, thickened small intestines
Eosinophilia (2,000 - 60,000 cells/μl)
Poor prognosis; Prednisolone (6-8 mg/kg/day) + adjuct immunosuppressives

VIII. Feline Promotility

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>0.2-0.2 mg/kg TID-QID</td>
<td>Efficacy in Question</td>
</tr>
<tr>
<td>Cisapride</td>
<td>1.25 – 5.0 mg/cat TID</td>
<td>Compounding Pharmacy</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>1-2 mg/kg PO BID-TID</td>
<td>Stim feline colonic activity</td>
</tr>
<tr>
<td>Lactulose</td>
<td>2-3 ml PO TID</td>
<td></td>
</tr>
<tr>
<td>Psyllium</td>
<td>1-4 tsp q12-24hr</td>
<td></td>
</tr>
<tr>
<td>Canned Pumpkin</td>
<td>1 tbsp BID</td>
<td>Not Pumpkin Pie filling</td>
</tr>
<tr>
<td>Kristalose</td>
<td>¼ to 1 tsp BID</td>
<td>Powdered lactulose</td>
</tr>
<tr>
<td>Miralax granules</td>
<td>¼ tsp BID</td>
<td>GoLytely minus electrolytes</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>25-50 μg/day</td>
<td>PGE1 stim intestinal motility</td>
</tr>
</tbody>
</table>

IX. Negative Abdominal Explore

Esophageal Foreign Bodies

Greenies – Leib & Sartor JAVMA 2008; small dogs 84%, distal esophagus 74%, overall mortality 26%, esophageal stricture formation 24%
Potential complications – Burgos-Rodrigues et al. JAVMA 2003; perforation, pneumomediastinum, pneumothorax, pleuritis, mediastinitis, pneumonia, esphagobronchial fistulas;use nonionized iodinated contrast agent
Indications for surgical retrieval – Sale et al. JAAHA 2006; (bones, chew toys, fish hooks, carrots) immovable foreign body, high risk of causing/worsening perforation

Sliding Intussusception

Dysautonomia

Dysautonomia is a neuropathy of unknown etiology that affects all aspects of the autonomic nervous system. It was originally described as a disease of cats in the United Kingdom, but has subsequently been reported in dogs in the United States, with Kansas appearing to be an “epi-center” but numerous cases diagnosed in Colorado. Traditionally it appears to be a “seasonal” disease affecting mostly young dogs from rural settings. Although this would appear to narrow the search towards particular causes (environmental exposure, toxin ingestion, etc.), as of yet no culprit has been identified. To complicate matters, at CSU we are seeing the disease in dogs somewhat outside the norm; older animals and some breeds hardly known for their rugged rural lifestyle.

Clinical signs consistent with a diagnosis of dysautonomia include poor body condition, lethargy, constipation and/or diarrhea (rarely to the point of fecal incontinence), regurgitation and/or vomiting, and anorexia. Signs of urinary dysfunction (i.e. incontinence) can also occur. In addition to overall poor body condition (although at CSU we’ve also seen dogs that look quite healthy on the outside) physical examination often reveals dry mucus membranes, dilated pupils and raised 3rd eyelids, slow or absent papillary light reflexes, an inappropriately low heart rate, and poor anal tone.

The initial diagnostic pathway often hinges on whether vomiting or regurgitation is determined to be the presenting or most prominent problem. Baseline blood work shows non-specific changes consistent with vomiting, malnutrition, or muscle wasting. Plain thoracic films will often reveal megaesophagus, or fluoroscopy/barium contrast shows esophageal hypomotility. Abdominal films can be particularly striking. The bladder is often large (and flaccid) and the stomach
maybe chalked full of food hours after the last meal. The appearance of the intestinal track is frequently interpreted as consistent with a GI obstruction, or in their most extreme state, a mesenteric torsion. This explains why one of the more frequent “diagnostic tests” in cases of dysautonomia is a negative abdominal exploratory surgery. Often the degree and extent of intestinal distention is actually an important clue – if there is an obstruction, where would it be to cause this pattern?!

It requires a high index of suspicion and an attentive history and physical examination to support a clinical diagnosis of dysautonomia. But once dysautonomia makes it on to the list of differentials there are a number of ancillary diagnostics to perform while resisting the urge to open the animal’s abdomen. A Shirmer tear test may reveal “dry eyes”, the dog’s bradycardia is minimally responsive to atropine, intra-dermal histamine (compared to saline control) fails to elicit a wheal or flare, and dilute pilocarpine (compared to the non-dysautonomic dog in the next cage) leads to an extremely mitotic pupil (denervation hypersensitivity). The simplistic nature of this battery of tests makes us uncomfortable, but if we’re lucky, the combination of bizarre results makes us confident in our diagnosis, there just aren’t many other conditions that fit. The problem arises if we fail to consider dysautonomia in the first place, or the diagnostics come back inconclusive.

Supportive care (e.g., artificial tears, elevated feedings, expressing the urinary bladder, antibiotics, etc.) is the basis of therapy, as well as parasympathomimetic drugs such as bethanechol and metoclopramide. A low-profile gastrostomy feeding tube can be placed to help the owner provide adequate nutritional support if the patient’s megaesophagus precludes effective oral intake. The prognosis for dysautonomic pets is grave and the owner must be committed to providing extensive nursing and supportive care. Even with partial recovery of some faculties, complete recovery is highly unlikely.
I. Feline Physiology

A. Cats are Carnivores
   1. Protein metabolism
      a. enzymes
      b. energy
   2. Protein requirement
   3. Adaptive insulin resistance

B. Cats Fed Carbohydrates
   1. Glucose Toxicity
      a. potentially reversible
   2. Amyloid deposition
      a. irreversible
      b. β cell dysfunction
      c. impaired insulin release
      d. peripheral insulin resistance
   3. Obesity
      a. reversible
      b. peripheral insulin resistance

C. Transient Diabetes
   1. Clinical demonstration of Pathophysiology
      a. Prediabetic → NIDDM ↔ IDDM → Absolutely require insulin

D. Dietary Intervention
   1. Mickey Mouse
      a. Childhood Hero or High Protein, Low Carbohydrate Meal
   2. Dry versus Canned
      a. CHO sticks like glue
   3. Fun with Fiber
      a. w/d
   4. The Variety
      a. m/d
      b. DM
      c. Wellness
II. Feline Frustration

A. PU/PD, Polyphagia, Weight-loss

B. Fat Boy to Frail Flower

C. Diabetic Ketoacidosis (DKA)
   1. “You are never alone.”
      a. concurrent disorders

D. Initial Treatment
   1. Reverse the Reversible
      a. Dearth
      b. Diet
      c. Insulin
   2. Insulin Options
      a. PZI
      b. Glargine

E. The Maze of Monitoring
   1. The Delightful Dog
   2. Glucose Curves
   3. Fructosamine
   4. In-hospital or At-home
   5. How much is too much?
      a. Reasons and Rationale
      b. Goals of Therapy
      c. Hypoglycemic happenings
With the advent of the internet there are a tremendous number of sources for information on pet food content. There is also the potential for a tremendous amount of misinformation. Entire lectures are now devoted to reading pet food labels, and attempting to pry user-friendly information out of the manufacturer can be frustrating at best. This is in no way meant to be an endorsement of any particular site, and I make no claim whatsoever as to the accuracy of this particular site, but one site I’ve found that seems to pretty extensive is

```
Algorithm: Monitoring with fructosamine
Measure BG and Fructosamine (FR)

FR < 400
BG < 180

FR > 400
BG < 60
Somogyi
Excellent control

FR < 400
BG < 60
Over regulation

FR < 400
BG > 180
Stress induced hyperglycemia

FR > 400
BG > 180
Poor control
```

---
Protocol for Glargine use in Cats

Adapted from Dr. Jacquie Rand, Center for Companion Animal Health
University of Queensland, Australia  www.uq.edu.au/vetschool/centrecah

**Initial Dose**

If fasting BG > 360 mg/dl → 0.5 U/kg ideal body weight BID
If fasting BG < 360 mg/dl → 0.25 U/kg ideal body weight BID

Do not increase dose for 1st week;
Decrease dose if BG curve or clinical signs suggest hypoglycemia.

[Dr. Rand recommends keeping the cat in hospital for 3 days to check the patient’s initial response to insulin, or alternatively, obtain at-home BG curves for the first 3 days]

Recheck at 1, 2, 3, and 4 weeks – “as required” after that.
Expect little change in the first 3 days, good glycemic control by day 10.

**Subsequent Dose Adjustments**

If pre-insulin BG > 216 mg/dl → increase by 0.25-1 U/injection
If nadir BG > 180 mg/dl → increase dose by 0.5-1 U/injection

[Ideal nadir in well controlled cat 72-145 mg/dl]

If pre-insulin BG 90-160 mg/dl and/or if nadir 90-160 → no change in dose

If pre-insulin BG < 180 mg/dl → 0.5-1 U/injection
If nadir BG < 54 mg/dl → 1 U/injection

Dr. Rand recommends using clinical signs, water intake, and urine glucose to make additional adjustments in insulin dose if pre-insulin BG =198-252 mg/dl or if nadir = 54-72 mg/dl.

**Remission**

If nadir = 72-126 mg/dl or pre-insulin BG < 180 mg/dl = gradually reduce Glargine by 0.25-1 U/injection until total dose is 0.5-1 U/injection once daily

If cat is stable with pre-insulin BG < 180 mg/dl at insulin dose of 0.5-1 U per day, withhold insulin and perform 12-hour BG curve.  If subsequent pre-insulin BG > 200 mg/dl continue at 1 U/injection BID; if pre-insulin BG < 200 mg/dl continue with no insulin and recheck in 1 week.  Monitor water intake and urine BG.

NOTE: These recommendations are based on a relatively small number of cases.
MITOTANE: alias O,P’-DDD, alias Lysodren® (Bristol-Myers Oncology)

“Adrenal cytotoxic agent used for medical treatment of pituitary-dependent hyperadrenocorticism.” (Plumb)

Mechanism of action: Severe, progressive necrosis of the zona fasciculata and zona reticularis (within days of starting therapy). [Zona glomerulosa may be affected (aldosterone) – not clinically significant]

TRILOSTANE: alias Vetoryl®, alias Desopan® or Modrenal® (Dechra)

“May be useful in dogs for treatment of pituitary dependent hyperadrenocorticism, adrenal dependent hyperadrenocorticism…” (Plumb)

Mechanism of action: Competitive inhibitor of 3-beta hydroxysteroid dehydrogenase…reducing synthesis of cortisol, aldosterone, and adrenal androgens…rare case report of hypoadrenocorticism and death

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MITOTANE: (O,P’-DDD) Lysodren® (Bristol-Myers Oncology)</td>
</tr>
<tr>
<td>• “Adrenal cytotoxic agent used for medical treatment of PDH.” (Plumb)</td>
</tr>
<tr>
<td>• Severe, progressive necrosis of the zona fasciculate and zona reticularis</td>
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</tbody>
</table>
Administer with Prednisone???

• 0.2 mg/kg/day during initial treatment
• Mask clinical markers of Rx “endpoint”
• Withdraw 2-3 days prior to ACTH stim
• Required ~ 5% of patients
• Not warranted

Side-Effects

• Lethargy
• Ataxia
• Weakness
• Anorexia
• Vomiting
• Diarrhea
• ~ 23%
• “usually mild”

• Stop Mitotane
• Start Prednisone

Schedule

• 25 mg/kg PO BID w/food
• Until
  – < 60 ml/kg/day of water
  – > 10 – 30 minutes longer to finish meal
  – Vomiting, lethargy, diarrhea
Monitoring Therapy

- Phone calls
- 8-9 days
  - Hx, PE
  - ACTH stim test, BUN, Na/K, glucose, liver enzymes, CBC
- Stop, Continue, Maintenance?
- 7 – 10 days (max. usually 16 days)

Maintenance Therapy

- If < 10 days
  - 25 mg/kg every 7 days (divided doses)
  - Recheck ACTH stim every 1-3 months
- If > 10 days
  - 50 mg/kg every 7 days (divided doses)
  - Recurrent signs or post-ACTH cortisol > 5 μg/dl – repeat induction

Trilostane

- Competitive inhibitor of 3-β hydroxysteroid dehydrogenase
- Decreased synthesis of cortisol, aldosterone and adrenal androgens
- PDH and Adrenal tumor (AT)
- Must be imported
“Relatively well tolerated in dogs”

- Lethargy
- Inappetence
- Vomiting
- Electrolye abnormalities
- diarrhea

- Rare case reports of hypoadrenocorticism and death

Schedule

- Same for PDH or AT
  - < 5 kg = 30 mg q 24 hrs
  - 5-20 kg = 60 mg q 24 hrs
  - > 20 kg = 120 mg q 24 hrs
- May require BID dosing
  - 3 mg/kg BID
- Adjust dose

Monitor

- Clinical effects
- Adverse effects
- Electrolytes
- ACTH stim test (4 – 6 hrs post-dose)
  - At 10-14 days, 30 days, 90 days
  - Every 3 - 6 months when stable
Dose Adjustments

• < 0.72 μg/dl = d/c drug
  – Restart in 24-48 hrs at lower dose
• > 7.2 μg/dl = increase dose
• Inbetween
  – Clinical control = no change
  – Not clinically controlled = BID