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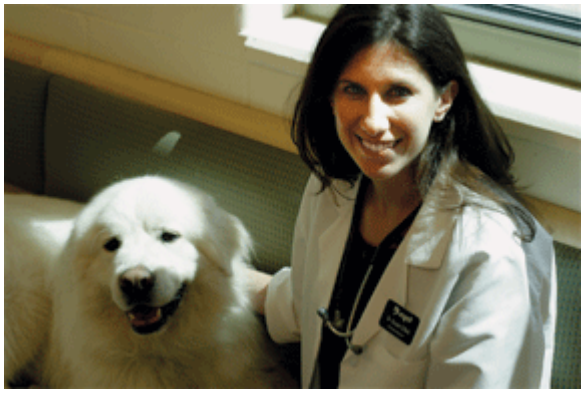
Management Options for Chronic Gastrointestinal Conditions in Geriatric Cats and Dogs



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Getting Started

Chronic gastrointestinal conditions can be frustrating for clients and clinicians alike, and so adding the element of advanced patient age into the mix can bring about some unique challenges.

One trap to avoid however is making assumptions or taking short-cuts based on patient age. That being said, you might consider an "accelerated" work-up or therapeutic trials in the interest of time. We assess patient weights at every single visit regardless of the reason for a visit. If you use an electronic record keeping system in particular, this can allow for easy observation of any significant trends in weight loss or weight gain. Train your assistants in thorough history taking and/or consider "flipping" your visit style and take your own histories while your assistants scribe for you. Have clients get in the habit of snapping photos of labels of food they are feeding at home and/or the containers they are using to measure out quantities of food. Sometimes they have deliberately (or unknowingly!) changed flavors resulting in significant changes in calories offered.

If you are like me, you breathe a huge sigh of relief once you see stable body weight in your patient at an office visit. Start here, weight loss (or weight gain) will trigger muscle memory patterns as you begin to complete your physical exam. Are my patients' senses intact? How significant is periodontal disease? Nasal congestion? Neck pain? Overt abdominal abnormalities? Muscle condition? Arthritis symptoms? Weight loss in itself is a very significant clinical sign regardless of whether or not

accompanied by other more classic GI signs such as vomiting, diarrhea, or decreased/absent appetite. Unless there is an obvious cause revealed during history-taking, try to obtain a minimum database at this visit: CBC, Chemistry profile, UA, fecal float, T4 (feline). For geriatric cats in particular, B12/Folate is part of my minimum database. Otherwise schedule a weight check for 2-4 weeks and plan on performing labwork at that visit. Encourage cat owners to purchase a baby scale for use at home.

Many of us are trained to keep routines intact for older patients, in particular our older cats. However, we might need to encourage clients to rethink the set up at home as cats age. Older cats may have difficulty getting to food without discomfort; this is often due to arthritis, but loss of muscle mass and function can be a contributing factor. Weight loss can occur due to reduced access to food or reduced intake due to a decline in the ability to taste, smell or see food. Do they need to jump on a counter or travel a set of stairs to get to their food, water, or litter boxes?

Most of what we discuss here applies to stable patients at home. If needed, supportive feeding should be considered when a patient has been hyporexic or anorexic for more than 3–5 days or is expected to have low voluntary intake for more than 3-5 days, and/or if severe underlying disease is discovered in the work-up process.

How to Approach Diarrhea

If diarrhea is the only symptom, right away try determine large bowel vs. small bowel diarrhea. Take a thorough diet and medication/supplement history. This is where you can save yourself time by taking your own history (rather than an assistant). If there is no significant weight loss, consider a diet trial of a high fiber diet such as Hill's w/d or Purina OM for cases of large bowel diarrhea. In the case of small bowel diarrhea, an easily digestible, lower fat diet such as Royal Canin GI LF or Hill's i/d could do the trick. If diarrhea is newly present in an older cat, although I might send home a new diet, I would get labwork pending and even schedule an abdominal ultrasound. Dogs seem like they could have more variables contributing (indiscretion, treats), so I might give diet and medication a try regardless of age before I assume anything more ominous is going to be diagnosed. This is what I call their "first strike." If they are not quickly improving with diets/meds, I recommend diagnostics to be sure there is not a primary issue (hepatic, pancreatic, renal, metabolic, endocrine disease). At some point in the treatment of chronic diarrhea, regardless of a negative fecal float, a course of dewormer (typically 5 days of fenbendazole) should be prescribed. With experience I have become a much bigger advocate of diet change alone. Clinical impression (and some studies) suggest up to 50% of dogs and cats with "nonspecific GI disease" will respond to dietary therapy alone. This is worth it to me, and many clients, and because responses can be seen within one to two weeks, we aren't losing precious time. Have an open conversation with clients. If you prescribe more than one therapy you will face the challenge of knowing which one worked! Food responsive diarrhea will tend to be present in younger patients, with more large bowel diarrhea, and without significant labwork changes (absence of hypoproteinemia). But again, given the frequency of "sensitive stomach" revealed in history taking, it's likely worth a try.

"Food Responsive" Gastrointestinal Disease

If labwork results from your visit are normal, and depending on clinical signs, consider a two week dietary trial. It would be unusual for dietary allergy or intolerance to first present itself in geriatric patients, but many patients have a history of chronic intermittent signs. These are the "sensitive stomach" cases or chronic intermittently vomiting cats or dogs. Furthermore, some cases of inflammatory bowel disease can improve from a novel protein or hydrolyzed diet trial. If you think your patient will eat it, I would jump right to a prescription hydrolyzed diet to avoid the possibility of prior antigen exposure. Despite this statement, we frequently offer Royal Canin limited ingredient diets in the Internal Medicine department because both canned and dry options are available and because we suspect they are quite palatable. Studies have shown that sometimes a quarter to a half of cats with chronic GI issues will respond to diet alone, sometimes with signs resolving within 2-3 days, perfect for a geriatric work-up. Other studies have shown two weeks is necessary, but certainly not 6-8 weeks. Royal Canin hypoallergenic formulas, Purina HA and Hill's formulas such as z/d and limited ingredient diets are also stocked at Angell. Two

weeks is often sufficient to look for improvement in signs. For dogs, this might be an instance where you consider having clients home cook a diet for a two week trial.

Medications for Diarrhea

1. Metronidazole

Metronidazole is frequently used in GI cases but more and more, it has been suggested that long-term administration and potential side effects make it less desirable than other options. Further, metronidazole has been shown to cause DNA damage to feline lymphocytes *in vitro*. There is also evidence in laboratory animals that it has carcinogenic potential. Do we still prescribe it? Yes! A suggested GI dosage for metronidazole in cats and dogs is 7.5 to 10 mg/kg given orally BID.

At Angell, fenbendazole (panacur) at 50 mg/kg SID with food for 5 consecutive days is the treatment of choice for giardiasis or other suspected cases of parasitism (as opposed to higher doses of metronidazole).You might save metronidazole for particularly challenging cases.

2. Tylosin

Tylosin is an oldie but goodie, and definitely in favor right now amongst veterinary internists. Tylosin is a macrolide, bacteriostatic antibiotic with activity against most gram-positive and gram-negative cocci, gram-positive rods, and *Mycoplasma*. Tylosin works by transiently changing the GI enteric bacterial population, probably by promoting the growth of beneficial commensal bacteria while suppressing "bad" bacteria. Like many wonder antibiotics, there is also a suggestion that tylosin may exhibit anti-inflammatory properties. Also of great use, tylosin appears to have almost no systemic or toxic side effects. It is even approved for use in poultry (i.e., safe for human consumption). The initial dose recommendation for tylosin in both dogs and cats is 15 mg/kg orally, BID, mixed with the food (has a bitter taste) or given via gelatin capsule. (A helpful note from Dr. Twedt: it comes as a powder and a #3 gelatin capsule holds 130 mg, a #1 capsule holds 240 mg, a #0 capsule holds 345 mg, and a #00 capsule holds 430 mg). For cases that respond, the long-term dose can be reduced to as low as 5 mg/kg/day. Tylosin is effective for most *Clostridium perfringens* and is considered by many to be the treatment of choice for suspected clostridial diarrhea. The biggest drawback is getting it into patients who aren't eating well, are sensitive to its presence in their food, and basically cats!

What Tests to Run?

Regarding weight loss in cats, you can get yourself down a bit of a rabbit hole. I would be sure to keep communication open with clients. Some clients may have noticed no symptoms at home and suddenly find themselves facing an exhaustive and expensive work up for weight loss. We sometimes ponder how a minimum database in cats should be redefined as CBC/Chemistry panel/T4/UA/SDMA/B12/Folate, abdominal ultrasound, echo and thoracic radiographs. You will eventually find something "wrong" and will need to use clinical experience and tracking to try to ascertain how significantly your finding is contributing to weight loss, changes in appetite, or other signs. For example, mild chronic kidney disease, a soft heart murmur, a mild elevation in a T4 might not be the primary issues but revealed along the way.

As mentioned before, if large bowel diarrhea is the only issue, I would trial diet and/or medications first before spending extensive resources on testing (other than fecal testing). For dogs and cats with chronic diarrhea I would not skip evaluation for parasitic infestation. Go ahead and deworm with a broad-spectrum dewormer (5 day course of fenbendazole). If diarrhea does not improve/resolve with diet/medication, and/or if vomiting is present, perform a CBC, serum chemistry profile, urinalysis, (and total T4 in cats). The reason is to try to rule out other primary disease processes. If signs persist without identifying another primary disease process, it is reasonable to submit TLI/B12/Folate. Pancreatitis in dogs often is accompanied by anorexia, vomiting, and abdominal pain, so these signs may help you decide whether or not to run a cPLI. As cats can so often have non-specific signs, you would be justified to submit serum fTLI, fPLI, cobalamin, and folate concentrations with any suspicion of chronic GI signs.

You might find conflicting evidence about hypocobalaminemia in hyperthyroid cats. As I often screen older cats with weight loss for B12 deficiency I would use your judgment in terms of submitting this test as part of your work-up.

Notes on TLI/PLI (adapted from Texas A&M GI Lab)

TLI: In dogs, values below 2.5 µg/L are diagnostic for EPI. Values between 3.5 and 5.7 µg/L are rarely if ever associated with signs of EPI but may reflect subclinical disease or part of the disease continuum. Consider repeating a TLI in one month if signs persist. Also be sure your patient is fasted 12-15 hours before a blood sample collected.

In cats, values equal to or below 8.0 µg/L are diagnostic for EPI.

Serum TLI values above 50.0 µg/L (dogs) and 100.0 µg/L (cats) may be associated with either acute or chronic pancreatitis or decreased renal excretion due to severe renal insufficiency. Elevated serum TLI concentrations are also seen in some malnourished patients (dogs usually) without evidence of pancreatitis, and in some cats with patchy pancreatic hypertrophy/atrophy (generally considered to be a benign age-related change). **Perform a PLI test before concluding a patient has pancreatitis.**

In cats increased serum TLI is often also observed with small intestinal disease. In these cases serum concentrations of **cobalamin and folate** should be determined for evaluation of the small intestine. I don't always submit a "TLI/B12/Folate" panel as part of my initial work-up in cats. My patients have not always been fasted for 12-15 hours at time of initial presentation. Furthermore, pricing is the same whether we run a TLI alone, or a "TLI/B12/Folate," so we could submit a TLI at a future appointment when the patient is fasted if we are suspicious of EPI.

Antech Canine CE-IBD Assay

This test uses ELISA technology and requires a small blood sample. The IBD Assay delivers one of two results – "consistent with IBD" or "not consistent with IBD." It also includes three biomarkers to substantiate and pinpoint diagnosis and monitoring:

Gliadin sensitivity (similar to gluten sensitivity)

Bacterial proliferation

Intestinal inflammation

In a study published in *JVIM*, March 2020, Estruch et al tried to identify serologic markers to differentiate dogs with chronic enteropathies, essentially an IBD blood test. Although there may be a place for this test in a diagnostic work-up, we have not adopted its use at Angell as of September 2020.

GI Neoplasia in Cats

Unfortunately, neoplasia is more commonly diagnosed in older patients than younger ones. Lymphoma, adenocarcinoma, and mast cell tumors (MCT) are the most common intestinal neoplasms in cats. The most common tumors in dogs are lymphoma, adenocarcinoma, gastrointestinal stromal tumor (GIST), and leiomyoma or leiomyosarcoma. Sometimes adenomas or adenomatous polyps are diagnosed in the colorectal area.

GI signs are common when neoplasia is present and include vomiting, weight loss, anorexia, and diarrhea. Studies have shown approximately 50% of dogs with lymphoma are anemic at the time of diagnosis. Additionally many dogs have significantly higher numbers of RBC anomalies compared to dogs with IBD instead. An even higher number of cats with GI lymphoma, may be anemic when GI lymphoma is present.

Lymphoma is the most common GI neoplasm in cats, and GI lymphoma is the most common form of lymphoma in cats.

Another common finding on labwork is hypocobalaminemia, present in 40-71% of dogs with small-cell intestinal lymphoma, and 78% of cats with low-grade lymphoma.

Cats with low-grade or small-cell lymphoma tend to have more chronic and less severe clinical signs compared to cats with large-cell or high-grade lymphoma. It can be helpful to obtain a specific diagnosis mostly because cats with low-grade lymphoma can have a much better prognosis. Some studies show complete response rates to treatment in half to most cats treated, with a median survival time close to two years or longer. The prognosis for large-cell/high grade GI lymphoma is poorer, with a median survival time reported in the literature of 7 weeks to 209 days.

Small cell Lymphoma sample treatment plan:

Prednisolone treatment: Starting dose is 1-2 mg/kg PO q 24 hrs, then gradually reduced to 0.5-1 mg/kg q 24 hrs.

Chlorambucil dosage options:

Continuous dose is 20 mg/m2 PO q 2 wks.

Intermittent dosage is 15 mg/m2 PO q 24 hrs for 4 days q 3 wks.

Another option is 2 mg PO q 48-72 hrs.

I have to remind myself not all cats gets lymphoma, but if initial labwork reveals low albumin and low B12 levels I become very suspicious. I would not skip an abdominal ultrasound prior to obtaining biopsies, but keep lines of communication open with clients. If clients are limited in finances and/or in how aggressive they want to be with diagnostics, there is a chance you may find something you can aspirate at the time of an ultrasound. Normal test results can be frustrating and feel “wasteful” to clients if they are left without a diagnosis. Unless imaging strongly points you to surgery, most of our internists recommend endoscopy before surgical biopsies. Dr. Lisa Gorman’s 2018 article discusses the differences between endoscopic and surgical biopsies in detail.

“Steroid-Responsive” Gastrointestinal Disease

Corticosteroids are well accepted as highly effective drugs for treatment of inflammatory bowel disease (IBD). Recall that some cats have better clinical responses to use of the metabolically active drug prednisolone compared to the pro-drug prednisone. For this reason we prescribe prednisolone for all cats just in case they fall into this category. Studies also suggest that prednisolone dosing should be based on lean or ideal body weight if cats or dogs are over-conditioned.

It is estimated that about 30% of the dogs that fail diet and antibiotics will respond to corticosteroids. Generally, oral prednisolone 1–2 mg/kg q 24h PO is given that is then tapered over an 8-week period. However, the side effects of glucocorticoids can be marked and I try to never exceed a total of 40 mg per day in large-breed dogs.

Budesonide is a novel glucocorticoid that is reported to have a high first-pass hepatic metabolism and exerts a "local effect" on the intestine with minimal systemic effects. An enteric-coated formulation is used for humans with IBD, but a non-enteric coated formulation made by a compounding pharmacy should be used so that the drug targets the small intestines. There is plenty of apparent anecdotal efficacy using budesonide in dogs and cats. Some systemic steroid effects are possible, but it might be a safer choice in patients in which you are hesitant to try steroids (patients with cardiac disease or diabetes mellitus, for example). Recommended dose is 1 mg every 24 hours in cats and toy breeds, and up to 3 mg every 12 hours for large-breed dogs.

Additional GI Medications

When trying to manage chronic GI conditions, you could certainly consider medication trials, but there are pros/cons in doing this depending on what medications you trial. For example, I rarely prescribe an appetite stimulant in cats without also treating presumed nausea. Although there is some evidence mirtazapine can have mild anti-nausea effects in people, I reserve it primarily for its appetite stimulant benefits. So, if I am going to prescribe it for such, I also try to add Cerenia (maropitant) at least to start. Another pitfall of course is that if you send home multiple medications and recommend a diet change, you may be hard pressed to know which one is actually helping.

Fortiflora I happily send home to almost any cat or dog. Many of our clinicians swear by Fortiflora as an appetite stimulant in some cats. Fortiflora SA just came out and we are trying it amongst ourselves first before switching over. We also stock Visbiome, which appears to be one of the pre/probiotics of choice of many internists. It is a little bit more expensive and needs to be refrigerated but is an excellent choice.

Cobalamin Therapy

Cats and dogs with gastrointestinal disease can have tissue-level cobalamin deficiencies. Furthermore, a study published in the Journal of Feline Medicine and Surgery pointed out that geriatric cats in particular, independent of diet are at an increased risk of cobalamin deficiency. Studies have demonstrated overall weight gain, as well as resolution, or at least improvement in clinical signs such as vomiting or diarrhea, with the introduction of cobalamin supplementation alone. Certainly if exocrine pancreatic insufficiency is diagnosed, cobalamin levels should be checked, or empiric supplementation started. Cobalamin may also have a pharmacologic effect as an appetite stimulant. Anorectic feline patients with cobalamin deficiency often start to eat again once they are being supplemented. I will often give a first dose SC at the time of the appointment.

Cobalamin should be supplemented whenever serum cobalamin concentration is in the low normal range (i.e., less than approximately 400 ng/L) in both dogs and cats. Per the Texas A & M website: For either oral or parenteral supplementation, serum cobalamin concentration should be supranormal at the time of reevaluation. However, if serum cobalamin concentration is within the normal range, treatment should be continued at least monthly (for parenteral supplementation) and the owner should be forewarned that clinical signs may recur sometime in the future.

For parenteral cobalamin supplementation

Protocol: weekly injections for 6 weeks, then one dose a month later, and retesting one month after the last dose.

Dose: SC injection of 250 µg per injection in cats and, 250-1500 µg per injection in dogs, depending on the size of the patient:

Dogs weight	Below 10 lbs	10 lbs-20 lbs	20 lbs-40 lbs	40 lbs-60 lbs	60 lbs-80 lbs	80 lbs-100 lbs	Above 100 lbs
Dose of Cobalamin	250 µg	400 µg	600 µg	800 µg	1000 µg	1200 µg	1500 µg

For oral cobalamin supplementation:

Protocol: daily administration for a total of 12 weeks and re-check serum cobalamin concentration one week after finishing supplementation. Dose: 250 µg in cats and 250 – 1000 µg in dogs, depending on the size of the patient (follow package insert for Cobalequin).

Fortunately since cobalamin is a water-soluble vitamin, excess cobalamin is excreted through the kidneys. Complications due to "over-supplementation" should not occur and has not been reported.

Folate

Deficiency: In theory, folate deficiency can have clinical consequences, so if it is diagnosed on B12/Folate result, you should consider supplementation. How severe a deficiency is present and the reality of supplementing your patient will impact your decision to recommend it though. Over the counter folic acid supplements would be used. A recommended dose of 200 mcg for cats and smaller dogs (<20 kg BW) and 400 mcg for larger dogs (20 kg BW) orally once daily for 4 weeks would be a good starting point. The primary significance of severely low folate however would be undiagnosed proximal small intestinal disease.

Excess: Small intestinal bacterial dysbiosis (from EPI or other chronic enteropathies) may result in increased serum folate concentrations. However, this does not appear to predict whether patients will respond favorably to antimicrobials alone. I would still proceed with a diet trial and potentially antimicrobials, probiotics, and/or prebiotics (fermentable fibers) if the clinical picture justifies it.

Mirtazapine

Mirtazapine is a 5-HT3 receptor antagonist with appetite-stimulant properties. Recent pharmacodynamic studies have shown it is safe and can be an excellent appetite stimulant. Higher doses, however, are commonly associated with side effects, such as vocalization, hyperexcitability, and tremors. Thus, the recommendation is use of smaller, more frequent doses. Dosing cats has become much easier with the FDA approval of a transdermal ear gel for cats (Mirataz). The dose ends up being around 2 mg per cat when a 1.5 inch strip is applied to alternating inner ear flaps (dosing ruler is included with the packaging). Dog dosing ranges from 3.75 mg to 30 mg once daily depending on the size of the dog, not to exceed 30 mg per dose (~1.1-1.3 mg/kg every 24 hours).

Maropitant

Cerenia (Maropitant by Zoetis) is a neurokinin-1 (NK-1) receptor antagonist that acts in the central nervous system by inhibiting substance P, the key neurotransmitter involved in vomiting. Maropitant suppresses both peripheral and centrally mediated emesis. The injection is approved for the prevention and treatment of acute vomiting in dogs and for treatment of vomiting in cats. The oral tablets are indicated for the prevention of acute vomiting and vomiting due to motion sickness in dogs.

Maropitant has been effective for controlling vomiting secondary to a variety of stimuli, including reducing chemotherapy-induced nausea. It has also received fame as a “wonder cure” for all sorts of ailments and may ameliorate visceral pain. It should be used before anesthesia/sedation and can be used in conjunction with chemotherapy.

Capromorelin

Capromorelin (ENTYCE - Aratana Therapeutics) mimics the action of the hunger hormone ghrelin which causes growth hormone secretion and appetite stimulation, resulting in an increase in lean body mass. Capromorelin is an orally active small molecule that has more sustained effects than its naturally found counterpart and has been shown to increase food intake and weight gain. Although studies suggest this drug is safe to use in both cats and dogs we reserve its use for dogs only at Angell. Capromorelin oral solution is dosed at 3 mg/kg orally up to every 24 hours (dog dose). It can cause salivation and be a little challenging to administer in dogs. We avoid its use in cats due to anecdotal reports of hypotension and bradycardia (plus ptyalism can be dramatic).

In Conclusion

With both geriatric dogs and cats, take into consideration which medications and supplements they are already taking. How easy will it be to medicate them? Does your hospital offer compounded medications and/or easy to administer formulations?

GI work-ups can be frustrating in even our youngest patients. Keep communication open with your clients and recognize the unique needs posed by advanced age. Consider when you might have the luxury of trialing different diets or medications, and what will be reasonable to employ in a patient more likely to have comorbidities or other challenges such as finicky appetite, arthritis-related discomfort, or failing senses.