The GI Lab at Texas A&M | VETERINARY MEDICINE & BIOMEDICAL SCIENCES TEXAS A&M UNIVERSITY

Promoting Gastrointestinal Health in Companion Animals

Newsletter - Spring 2015

Editors: JM Steiner & JS Suchodolski

What's inside:

The Gastrointestinal Laboratory at Texas A&M University

News from the GI Lab

As we have done for the last few years, we start every new year with a newsletter and it has been my privilege to summarize the new developments at the GI Lab for you. As you are all acutely aware, our profession is a people profession and it is ultimately the people of any veterinary practice or lab that make the difference. As such, we are very fortunate to have a fabulous team of laboratory managers and supervisors, technicians, researchers, administrative staff, graduate students, and student workers. While our team is already a great team we have been very fortunate to have several new additions. Dr. Jonathan Lidbury, originally from England, joined the GI Lab 7 years ago, after completing two clinical internships (one in England and one with Steve Ettinger in Los Angeles) to pursue a combined residency/PhD program. Jonathan completed his residency 3 years ago, is board certified by both the American and European Colleges of Veterinary Internal Medicine, and he is in the process of putting the finishing touches on his PhD. I am pleased to announce that starting in January of 2015 Jonathan will start as a tenure-track assistant professor in small animal internal medicine. As such, he will become an integral part of the leadership team of the GI Lab. Jonathan will be on the clinic floor at the Small Animal Clinic at Texas A&M University, but he will also continue to pursue his interest in gastroenterology and his special interest in hepatic diseases in dogs and cats. As you are probably aware, the number of small animal hepatologists is unfortunately small and thus Jonathan will fill a very important role. Jonathan will also continue to participate in our free consultation service. We are very much looking forward to adding another faculty member to our staff! Also, recently, two new PhD students have joined our lab, Sina Marsilio and Yuri Lawrence; both are board-certified with the American College of Veterinary Internal Medicine and both will do some clinic duty while pursuing their PhD program within the GI Lab. Yuri and Sina will also start to partake in our consultation services, so there is a chance you will be talking to one of them in the future.

As far as our laboratory services, we have successfully developed several new assays to assess small animal patients with chronic enteropathies. We now have two markers for neutrophilic infiltration of the GI mucosa, one marker for eosinophilic infiltration, and one marker for mast cell degranulation. While all of these assays have shown initial promise, their exact use in clinical practice will need to be further evaluated before we offer them to you for routine use. We also now have an assay for the measurement of serum motilin concentrations in dogs, but again the clinical utility of measuring motilin in dogs with GI disease needs to be further evaluated. Over the last few years we have been measuring methylmalonic acid concentrations in dogs and cats with hypocobalaminemia. Interestingly, we were able to show that a significant number of dogs and cats with serum cobalamin concentrations in the low normal range have an increased serum MMA concentration, an indicator of cobalamin deficiency on the cellular level. While this assay is time-consuming and expensive we have decided to offer this test to you going forward. While we do not anticipate that you would use this assay in all patients with chronic enteropathy, we believe there could be value in certain situations, such as a patient not responding to cobalamin supplementation or patients enrolled in clinical trials, among others. Please let us know if you have any questions concerning this new assay. As you can see, things are moving forward at the GI Lab – though let there be no mistake, many questions regarding small animal gastrointestinal disease remain. However, we have learned a lot over the recent years and we learn a little more every day – this is why small animal gastroenterology is such an exciting field to work in! Thank you for your continued patronage as without your submissions to our lab, none of the research we do would be possible. Thank you!

(Jörg M. Steiner)

Jonathan Lidbury, BVMS, MRCVS, DACVIM, DECVIM-CA
Assistant Professor in Small Animal Medicine

Feline Exocrine Pancreatic Insufficiency (EPI)

We would briefly like to draw your attention to what we believe to be an underdiagnosed condition in cats – exocrine pancreatic insufficiency (EPI). Only 20 years ago feline EPI was considered to be an extremely rare disease. However, over recent years the GI Lab at Texas A&M has diagnosed well over 1,000 cats with this condition *per annum*. While this incidence is much lower than the incidence of EPI in dogs, a considerable number of cats are diagnosed with this condition. Despite this, many veterinarians still consider feline EPI to be extremely rare and do not routinely test for it, which would suggest that the actual incidence is even higher.

EPI in cats is usually caused by chronic pancreatitis, though other causes, such as acinar pancreatic atrophy, pancreatic duct obstruction, or pancreatic hypoplasia have all been suspected in isolated cases. The age of onset of clinical signs varies widely and cats of virtually any age can be affected. Clinical signs of EPI in cats are similar to those in dogs, however, the clinical presentation can vary widely with clinical signs such as diarrhea or loose stools (Figure 1), weight loss and/or sarcopenia (Figure 2), ravenous appetite, and greasy soiling of the haircoat. However, some cats may show anorexia, vomiting, or even polyuria/polydipsia. Some of these cats may have concurrent diabetes mellitus, which further complicates the condition.

The measurement of feline trypsin-like immunoreactivity concentration in serum is considered the diagnostic test of choice for feline EPI. The reference interval of this assay is 12-82 µg/L and values of less or equal 8 µg/L are considered diagnostic of EPI.

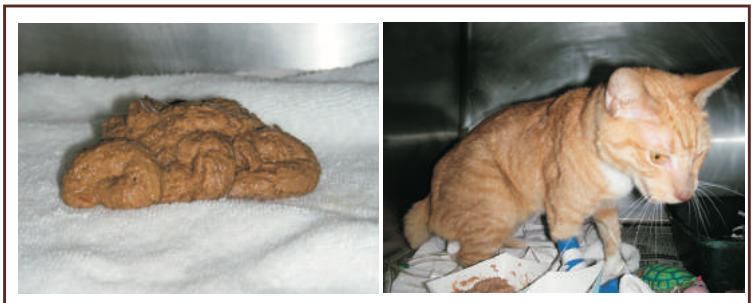

Figure 1 and 2. Loose stools and weight loss/sarcopenia in a cat with clinical signs of EPI. (Pictures courtesy Dr. Kenneth Jones, Jones Animal Hospital, Santa Monica, CA

Figures 3 and 4. Normalization of stools and body condition after successful treatment for EPI (Pictures courtesy Dr. Kenneth Jones, Jones Animal Hospital, Santa Monica, CA

Treatment of feline EPI is with enzyme supplementation (1 teaspoon per meal of an enzyme supplement containing approximately 70,000 lipase units per teaspoon of enzyme powder). In contrast to dogs, some cats will refuse to consume cat food sprinkled with pancreatic enzyme powder. In these cats it may help to first mix the powder with a small amount of a highly palatable food or even fish oil. Another alternative is the use of freshly frozen pancreas from cows, pigs, or even game. Almost all cats with EPI are cobalamin deficient and serum cobalamin concentration should routinely be measured in cats with EPI. Cobalamin supplementation should be instituted in all cats with cobalamin deficiency (see our website for a dosing schedule). Some cats with EPI have secondary small intestinal dysbiosis and may benefit from a 6-week course of tylosin (at 25 mg/kg q 12 hrs compounded into capsules). If the cat does not respond to therapy, the patient should be evaluated for concurrent conditions such as inflammatory bowel disease and if none can be identified trial therapy with omeprazole (at 0.7 to 1.0 mg/kg q 12 hrs orally) is recommended.

Most cats require lifelong therapy, but the majority of them can be successfully managed and will have normal stools (Figure 3) and a normal body condition (Figure 4). (Jörg M. Steiner)

Just Another Cat with Vomiting and Diarrhea? A Quick Case Report

Tigger, a 5-year old male-neutered Maine Coon cat presented to Texas A&M University for evaluation of vomiting and diarrhea of 1 month's duration. The diarrhea was characterized as being small intestinal in nature and had progressively become worse since it was first noticed. The frequency of the vomiting had also increased and prior to presentation Tigger was vomiting about four times a day. His owners were unable to assess whether his appetite had changed as they own several cats. There had been no response to empirical treatment with metronidazole and famotidine.

On physical examination Tigger was bright, alert, and responsive and his vital signs were within normal limits. Although his body condition score was judged to be 6/9 on palpation he was assessed to be moderately sarcopenic. No important abnormalities were found upon thoracic auscultation, abdominal palpation, or the rest of his physical examination.

No clinically important abnormalities were found on a plasma biochemistry profile, urinalysis, or complete blood count. Mildly enlarged jejunal and paracolic lymph nodes were found during abdominal ultrasound examination. No ova or parasites were found upon fecal floatation. Tigger's serum cobalamin concentration was markedly decreased (<150 ng/L; reference interval: 290-1,499), suggesting distal small intestinal disease or exocrine pancreatic insufficiency and his serum folate concentration was increased (33.7 µg/L; reference interval: 9.7-21.6) suggesting small intestinal dysbiosis or consumption of a diet high in folate. Measurement of his serum trypsin-like immunoreactivity concentration was diagnostic for exocrine pancreatic insufficiency (2.9 µg/L; reference interval 12-82).

Treatment with pancreatic enzyme powder (Viokase-V), at a dose of 1 teaspoon mixed with canned food twice daily and cyanocobalamin at 250 µg given by subcutaneous injection once weekly were started. Additionally, his diet was changed to a highly digestible canned diet.

(continued on next page)

A Quick Case Report - continued

Two months after diagnosis, Tigger's owners reported that the diarrhea and vomiting had resolved. His body condition was unchanged. However, his muscle mass was judged to be slightly lower than optimal on physical examination. His serum cobalamin concentration was >1,000 ng/mL and his serum folate concentration was 21.0 µg/L. The pancreatic enzyme powder was continued as was the highly digestible diet. The frequency of the cobalamin injections was decreased to once a month. Tigger continues to do well 18 months after diagnosis.

Tigger represents a cat with EPI that does not have all of the typical clinical signs described in the literature (see above). Instead, Tigger showed chronic vomiting in addition to diarrhea and sarcopenia. While in some of these cats the vomiting maybe due to concurrent inflammatory bowel disease, this is not diagnosed in all the cats who show this clinical sign. In other cats the vomiting maybe due to residual chronic pancreatitis.

Regardless, Tigger is a great example why EPI should be considered as a potential differential diagnosis in all cats with chronic signs of gastrointestinal disease. (Jonathan Lidbury)

Consultant Corner

Does renal disease affect the results of serum TLI concentration?

Serum TLI is a highly sensitive and specific for the diagnosis of EPI in both dogs and cats. However, trypsinogen and trypsin are small molecules that are both excreted by the kidneys. Therefore, TLI might be falsely normal or in rare instances increased in patients with EPI and concurrent advanced renal failure.

Do you recommend evaluating cats for EPI?

Once considered a rare disease in cats, feline EPI is now recognized more frequently. Since the introduction of an assay for the measurement of serum feline trypsin-like immunoreactivity concentration (fTLI) in cats in 1995, the frequency of a diagnosis of feline EPI has been steadily increasing. While in 2002 there were 23 cats diagnosed with EPI through measurement of serum fTLI concentration at the Gastrointestinal Laboratory at Texas A&M University, in 2004 there were 225 cats, in 2008 there were 476 cats, and in 2013 there were 942 cats (unpublished data, 2014). These data clearly show that EPI occurs with considerable frequency in cats and also point to the fact that the recognition of EPI is still increasing. EPI can affect cats of any age, gender, and breed. Common clinical signs include weight loss (91%), loose stools (62%) to diarrhea (28%), poor hair coat (50%), anorexia (45%), polyphagia (42%), depression (40%), and vomiting (19%). Feces may appear yellow- to clay-colored, semi-formed, voluminous, and malodorous but are not typically watery or greasy. In summary, these data suggest that in cats with unexplained weight loss or chronic diarrhea, their serum fTLI concentration should be measured to diagnose or rule out EPI.

How should I interpret increased PLI in a clinically normal dog?

An increased serum PLI concentration in a clinically normal dog or cat suggests subclinical pancreatic acinar cell damage. In some instances acinar cell damage may be an incidental finding and in most of these patients serum PLI concentration should be re-evaluated 2-3 weeks later. If the increase in PLI concentration persists, further work-up for pancreatitis, including abdominal ultrasound examination and evaluation of the patient for risk factors for pancreatitis is indicated.

Does PLI correlate with disease severity and can it be used for monitoring purposes?

Because of its sensitivity for pancreatic inflammation, PLI concentrations can also be used for follow-up. Serum PLI concentrations should be repeated at different intervals, depending on the severity of the disease process. With acute severe pancreatitis, it may be useful to evaluate the patient every several days, while re-evaluation every few weeks is sufficient for dogs and cats with mild disease. Care should be taken not to over interpret small changes in serum PLI concentration that occur over time. For, example in a dog whose serum cPLI increases from 500 to 560 µg/L this is not a clinically important increase, whereas if it decreased to 190 µg/L, this would be an important change.

What is the recommended protocol for folate supplementation if a result is abnormally low?

Folic acid is a water-soluble vitamin that is required for many metabolic processes and a patient with a subnormal serum folate concentration may benefit from oral supplementation with folate. However, the effects of not supplementing such a patient with folic acid are not as clear as they are for cobalamin. Also, the exact amount required for supplementation is not clear. We currently, suggest supplementing small and medium-sized dogs and cats with 200 µg orally once a day and larger dogs with 400 µg once a day for one month. Folate or folic acid for oral supplementation is available from many health food stores or the vitamin section of any grocery or department store. Over-supplementation is not a concern as excess folate is excreted in the urine.

How long does a patient have to be off of antacids before the concentration of serum gastrin can be measured?

Hypergastrinemia does occur after the administration of proton pump inhibitors such as omeprazole or pantoprazole and to a lesser extend following administration of histamine-2 receptor antagonists such as famotidine. However, a recent study in dogs showed serum gastrin concentrations returning to baseline levels 7 days after cessation of treatment with omeprazole or famotidine. Therefore, discontinuation of any antacid therapy for at least 7 to 14 days prior to the measurement of gastrin is considered sufficient in order to get reliable results.

How long do patients need to be held off food before measurement of serum TLI concentration?

Serum TLI may be slightly increased after feeding in healthy dogs and cats, and therefore both cats and dogs should be held off food for 12 hours before collection of a blood sample.

What are the age restrictions for measurement of fecal alpha1-proteinase inhibitor (alpha1-PI) concentration?

The fecal alpha1-PI concentrations in dogs <1 year of age can be increased outside of the reference interval and should be cautiously interpreted in this age group. (continued on next page)

Consultant Corner - continued

Are there any other indications for submitting a TLI other than exocrine pancreatitis insufficiency?

Pancreatitis can lead to the release of trypsinogen and trypsin into the vascular space resulting in increased serum TLI concentrations. Serum TLI is only increased in approximately 30-40% of cats and dogs with pancreatitis. Thus a PLI test should be performed in patients with suspected pancreatitis. Clinical suspicion of exocrine pancreatic insufficiency is the indication for submission of a sample for TLI testing and even though an elevated TLI above 50.0 µg/L (dogs) or 100.0 µg/L (cats) is consistent with acute or chronic pancreatitis it is also not as specific for pancreatitis as is PLI.

Does renal disease affect the result of the PLI?

In dogs and cats with experimentally induced kidney disease serum PLI concentration was not clinically significantly increased. However, it should be noted that renal failure can be a complication of severe pancreatitis and pancreatitis can be a complication of renal failure.

Do you have any dietary recommendations for patients with pancreatitis?

In dogs with pancreatitis an ultra low-fat diet (a diet containing less than 20 g/fat per 1000 kcal) is recommended for most patients. In cats with pancreatitis feeding a low-fat diet is not as important and usually a diet that is easily digestible and slightly lower in fat is often chosen. Also, high fat diets, such as low-carb and renal diets should be avoided in cats with pancreatitis.

Can measurement of fecal alpha1-proteinase inhibitor be used to monitor response to therapy in dogs with protein losing enteropathy?

The main role of measurement of fecal alpha1-proteinase inhibitor concentrations is the diagnosis of protein losing enteropathy and a study has shown that an increase in fecal alpha1-PI concentration may precede a decrease in serum albumin concentrations in dogs with gastrointestinal disease. The role of fecal alpha1-PI concentration in disease monitoring is currently being evaluated, but it is currently unknown whether values normalize with treatment and how they are affected by various treatment modalities.

What is the role of canine C Reactive Protein in gastrointestinal disease?

C–reactive protein (not to be confused with protein c, which is used to differentiate between portosystemic vascular anomalies and microvascular dysplasia in dogs) has been shown to be increased in cases of inflammatory bowel disease and to correlate with clinical and histologic markers of gastrointestinal inflammation. Furthermore, it has been shown to normalize with disease resolution and thus may be useful for monitoring for gastrointestinal disease remission and therapeutic efficacy. However, C-reactive protein is not specific for intestinal inflammation and inflammatory diseases of various organs can cause increases.

Is testing for Clostridium difficile Toxin A and B and Clostridium perfringens enterotoxin useful in diagnosing clostridial disease in dogs and cats?

Clostridial bacteria are present in the healthy gastrointestinal tract of both dogs and cats, which can make it difficult to determine if they are the cause of clinical signs in diseased animals. Therefore, testing for clostridial toxins in cases of hemorrhagic gastroenteritis is recommended to increase the specificity for identifying cases where the bacteria are not only present but producing toxins that may contribute to clinical disease.

GI Lab Web site updates

We are constantly looking for ways to improve our service. Recently we have implemented two new features on our website http://vetmed.tamu.edu/gilab for our clients.

Preprinted Clinic Information on Submission Forms

After logging into our website using their clinic username and password, clinics will be able to generate a personalized submission form that contains their specific clinic information as well as our most recent tests and prices. Select one of the options listed under *Submission Forms*. Clinic staff won't need to complete the clinic information, it will already be done!

If address, phone or email information needs updating, please notify us and we will be happy to assist you. By using this prefilled form you can be assured that the clinic information entered into our data base will be correct. We have several clinics with names that are very similar and sometimes handwritten forms are difficult to read. This will help us to better serve you.

Credit Card Payments can be made on-line

We have recently added a new option for clients to make credit card payments on-line. You will enter the invoice from the billing statement you receive in the mail.

After you log in with your clinic username and password, select *GI Lab Invoice Payment*. You will be directed to a secure page within the Texas A&M system to make payments quickly and easily. The first time you access the credit card system you can choose to register (which then would store your information for future visits) or not. If you choose to register, you can also choose to register using the same log in info as the GI site or something completely different that may be easier for you to remember.

The important part to know is that this is a completely different system than the GI website, so the Texas A&M credit card payment system doesn't recognize your GI Lab information unless that is what you use if you choose to register for the first time.

An analogy that may help explain this better is to think of the GI website as two different databases. You can use the same log in and password if you choose, but either way you have to register on both websites as one does not have interaction with the other. I hope this explains the new process. Please let us know if you have any questions.

If you have forgotten your clinic username, password or have other questions please email us at or call 979-862-2861 and we will be happy to assist you.

VETERINARY MEDICINE & BIOMEDICAL SCIENCES
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