BEST OF ACVIM 2015

GI Focus

I. Pharyngeal and Esophageal Dysphagia in Dogs (Stan Marks and Diane Shelton-UCDAVIS)

A. Breed predispositions for pharyngeal disease:

Bulldog, French bulldog-sliding hiatal hernias
Dachsunds: Cricopharyngeal achalasia
Golden retrievers: Cricopharyngeal dyssynchrony
Cockers and Springers: Cricopharyngeal dysphagia
Bouviers and CKSC: muscular dystrophy
Boxers: Inflammatory myopathies

B. Breed predispositions for esophageal dysfunction:

German Shepherd, Great Dane, Irish Setter, labs (also laryngeal paralysis). Inherited in wire haired fox terriers and miniature schnauzers.

C. History and PE/visualization

Keep in mind 4 phases of swallowing: preparatory, oral, pharyngeal and esophageal phases. Not everything is esophageal. Important to try to characterize where problem seems to be. Typical signs are dropping food, repetitive attempts to swallow, gagging and retching or coughing while eating/drinking or recurrent pneumonias. Inquire about recent anaesthesia, progression of signs and drug history. Observing feeding/drinking-**owner video extremely important**. PE with a good oral and neuro exam (neuromuscular disease).

D. Diagnostics:

Routine lab screening-Electrolytes, CK can be especially important-**DO NOT IGNORE EVEN MILD INCREASES IN CK!** Consider thyroid testing, hypoadrenocorticism, lead, myasthenia gravis (remember to repeat testing if disease is progressive-especially if initially testing is borderline).

Cervical and thoracic radiographs.

Refer for fluoroscopy, esophagoscopy, EMG/NCV, muscle biopsies, CT/MR, manometry, esophageal pH testing.

(Shelton GD. Vet Clin Pathol. 2010; 39: 278-295 Routine and specialized laboratory testing for the diagnosis of neuromuscular diseases in dogs and cats)

E. Specific Cases

1. Inflammatory myopathies: CK frequently increased. Consider muscle biopsy.
2. Dachsund case-UES disease with cp muscle hypertrophy-cricopharyngeal achalasia. Diagnosed by contrast fluoroscopy. Surgery possible.
3. GR puppy- cricopharyngeal dyssynchrony. UES opens but incoordinated timing. Likely due to denervation. Also diagnosed with fluoroscopy. Usually not correctable, work on food consistency or tube feeding.
4. Extremely high CKs with muscular dystrophy

F. Megaesophagus
   1. Idiopathic
      Congenital forms-with appropriate feeding can resolve on occasion (delay in maturation of esophageal neuromuscularsystem?) No focal ME with congenital myasthenia gravis.

   2. Marks retrospective: Acquired-MG-50% of MG only have esophageal signs

   3. Other causes: PRAA, hypothyroid?, hypoadrenocortcism, lead, polymyopathies and neuropathies, toxins, neoplasia, other immune disease, strictures
   4. Need to rule out causes before deeming idiopathic
G. Esophagitis and GERD with or without stricture
H. Other: neoplasia, parasites, FB
I. Characterization of Dysphagia (UCDAVIS-Bonadio)

Retrospective, 742 dogs. Labs, goldens and GS most common breeds. ME most common disease (38.3%), GER (8.9%), foreign body (8.5%), sliding hiatal hernia (7.3%), cricopharyngeal dysphagia (4.6%) and unknown (17.7%). 26% had no fluoroscopy.

A. Rational Use of Antacids in the Dog and Cat (Marks -UCDAVIS and Tolbert-TENN)
Goal of Treatment: Gastric pH > 4 for 67% of day and >3 for 75% of day (extrapolated from human studies).
   1. Acute vs chronic control?
      Proton pump inhibitors are the most potent inhibitors of gastric acid secretion and very effective at treating all acid related disorders, but H2RAs are faster to some effect than PPIs. Makes no sense to give PPI intermittently. Ranitidine not good at reaching higher pH. Famotidine best of H2RAs (0.5 mg/kg BID IV or 1 mg/kg BID PO) No benefit to TID dosing.
   2. Most canine and feline studies use Bravo capsules-placed endoscopically and monitor pH.
      Good evidence for twice daily use of omeprazole at 1mg/kg, efficacious when split enteric coated and gastrogard paste also efficacious (Tolbert-dogs and Parkinson cats) Downside is all studies in healthy animals.

B. Should we use H2RA with PPI for first few days?
   1. PPIs accumulate in the very acidic secretory canaliculus of parietal cells thus they need acidic environment to effectively start working. Best given after a fast and before eating due to highest acid content in parietal cell.
   2. One study (12 beagles) showed no difference in pantoprazole with famotidine vs pantoprazole alone in time appropriate pH was achieved.
   3. Some evidence in humans for using famotidine at night in addition to PPIs to control nocturnal acid break through.
   4. Bottom line-I did not get a clear answer as this still seems to be unresolved.

C. What about prevention?
   1. EVERYTHING at NCSU gets PPIs! Is this a good practice?
   2. Less information presented on prevention. One study of PPI use in anaesthetic cases (ortho cases) may protect from reflux esophagitis and stricture by decreasing pH.
   3. Specific uses: GI ulcers, Stress (sled dog papers), hepatic disease, GI neoplasia, MCT, critical illness, spinal cord disease, reflux esophagitis.
   4. 4. Misoprostel (prostaglandin analog) for NSAID toxicity
   5. Another study (Whittemore-TENN) looked at erosion and ulcer formation in 9 research dogs being treated with 2 mg/kg/d/ prednisone/placebo, prednisone and 1 mg/kg/d aspirin and prednisone and aspirin with 1mg/kg/d omeprazole . Documented increased formation of erosions and ulcers in all groups with no difference between groups. Need more studies and BID dosing of omeprazole, but good documentation of mucosal lesions with prednisone.

II. Additional GI research abstracts

A. Evaluation of a one stage esophageal balloon dilation feeding tube for esophageal strictures (Weisse and Berent, AMC)

Feeding tube with a balloon incorporated. Owner can do balloon dilation at home instead of multiple anaesthesias and dilations. Just starting-4 dogs, 2 with very good response. (Likely more data now)

B. Ultrasonographic evaluation of antiemetic drugs on antral motility and gastric emptying in healthy dogs (Bogard and Gaschen)

Prokinetic effects of metoclopramide, dolasetron, maropitant, saline (SQ) and cisapride (oral) in 14 healthy dogs (randomized, blinded, crossover study). Motility index (MI) calculated. Metoclopramide caused the most pronounced and sustained MI of all drugs tested-has highest prokinetic activity in the gastric antrum-most pronounced post prandially)

C. The effect of the probiotic Sivoy™ (mix of strains of lactic acid bacteria and bifidobacteris-also called VSL#3) on clinical and histopathological parameters in cats with chronic idiopathic constipation and megacolon. (Rossi, Italy)

In humans, probiotics have been investigated in colonic motility disorders. This study used 10 client owned cats with idiopathic constipation (ICC) or idiopathic megacolon (IMC). No antibiotics within a month and poor response to medical management. 90 day trial with Sivoy. Significant clinical and histopathological improvement seen in cats treated with probiotic. Needs more study, but an interesting possibility.

Also IBD canine study (Rossi) with VSL#3 treatment compared to prednisone (1mg/kg/day) plus metronidazole (20 mg/kg BID) showed a protective effect of VSL#3 strains was observed in dogs with IBD, with a significant decrease in clinical and histological scores and a decrease in CD3+ T-cell infiltration.

D. Prognostic factors for ST (<6 mo) and LT (> 6 mo) Survival in Dogs with PLE (Gianella, Italy)

Clinical signs and clinical pathological findings at time of diagnosis do not predict ST vs LT survival. CIBDAI (canine inflammatory bowel disease activity index) scores and cholesterol at 1 month are the best predictors.

(See CIBDAI sheet)

E. Prolonged Administration of Prednisolone (high dose) alone or in combination with azathioprine alters serum cPLI (Spec cPLI) in dogs. (Ohta, Japan)

Oral prednisolone alone given in immune mediated disease was documented to increase Spec cPLI numbers. Concurrent administration of azathioprine had no additional effect in increasing cPLI.

F. Effects of an oral supplement based on Chondroitin Sulfate, Resistant Starch and prebiotics in Dogs with histologically confirmed IBD. (Segarra, Spain)

1. CS inhibits NF-KB and may decrease inflammation. Large bowel fermentation of certain resistant starches increases butyrate which helps maintain intestinal barrier integrity. Prebiotics can promote growth of beneficial gut flora.
2. 12 IBD dogs given placebo along with standard treatment and 10 dogs given supplement with standard treatment. 6 month trial.
3. No SE noted from supplement. Clinical improvement seen sooner in supplements group and histo scores better in supplemented group.
4. Not available yet?

III. Biliary Abstracts

A. Natural History of biliary sludge in dogs (DeMonaco, Vg-Md)

1. AUS performed on 74 healthy dogs. 57% had biliary sludge and were followed for 1 year with serial AUS and biochemistry.
2. Biochemistry unchanged over 1 year. “No significant difference” in sludge over time and no progression to mucocoeles. None resolved. Did become less gravity dependent. All remained asymptomatic.
3. Need cat study.

B. Possible Association of GB mucocoeles (GBM) with selected preventative drug use in dogs: Matched case control study (Gookin, NCSU)

1. 77 GBM dogs and 154 controls at NCSU from 2001-2011. Detailed history of all drugs given.
2. Shelties, Cocker and Chihuahuas overrepresented.
3. GBM dogs: 2.6 times more likely to be on thyroid supplementation or being treated for HAC. Also 2.079 times as likely to be on a product containing imidacloprid.

4. Due to the unique drug metabolism in shelties (ABCB1 mutation), Shelties were separated out and compared to all other dogs. Once separated, Shelties with GBM were 8.2 times more likely to have been given a product containing imidacloprid than control dogs. Other GBM dogs had no association with imidocloprid and GBM.
5. Suggest a possible association between imidacloprid drug use and GBM in Shelties. (Use caution in interpreting as a high confidence interval and marginal p value, but interesting to consider and needs larger studies).

C. Association between biliary cytology and microbiology in dogs and cats: 52 cases (2004-2014) (Pashmakova, TAMU)
    1. Bactobilia in 17/52 (33%) and positive culture in 11/52 (21%). One negative cytology resulted in a positive culture. Poor agreement between inflammation and positive culture.
    2. Most common bacteria were Enterococcus (7/11) and E coli (5/11)

IV. Endocrine Abstracts

A. Evaluation of canine TSH (cTSH) as a diagnostic test for hyperthyroidism in cats- Peterson (786 cats)
    1. Can cTSH be used to help diagnose HT (hyperthyroid) and/or distinguish between HT cats and normal cats?
    2. T4 had a 94 % sensitivity with a 93% specificity. fT4 had a 96% sensitivity with an 82% specificity.
    3. cTSH is very suppressed to undetectable (<0.3 ng/ml) in hyperthyroid cats. 98.2% of HT cats had nondetectable cTSH. Cats with detectable cTSH had mild or moderate disease and numbers were directly correlated with severity. TSH was detectable in 59% of normal cats and 86% of cats suspected of being HT but were not. Overall cTSH had a 98.2% sensitivity (cTSH will be suppressed) and just a 49.3% specificity (many euthyroid cats had indetectable cTSH).
    4. cTSH seems unlikely to be of great use in diagnosing HT and distinguishing from non HT cats.

B. Assessment of renal function in HT cats managed with Y/D diet. (Vaske, Hills, Kansas)
    1. Previous studies demonstrating GFR declines with any HT treatment. Y/D has yet to be evaluated in terms of GFR.
    2. 15 client owned cats. GFR, standard renal function testing including SDMA and epaxial muscle diameter determined pretreatment and 6 months into treatment.
    3. T4 significantly decreased along with creatinine. No change over 6 months in GFR, SDMA or emd. SDMA correlated better with GFR.
    4. Although not all cats became or remained euthyroid, TT4 was decreased in all cats without decreasing GFR. SDMA may be better at helping determine renal function pre and post HT treatment.

C. T.Y. Hui, D.S. Bruyette, G.E. Moore, and J.C. Scott-Moncrief. Effect of Feeding an Iodine-Restricted Diet in Cats with Spontaneous Hyperthyroidism. J Vet Intern Med 2015;29:1063–1068

A retrospective case series of 49 client owned hyperthyroid cats exclusively fed Y/D diet was recently published. Serum total T4 (TT4) normalized in 20/48 cats (42%) at day 21-60 and 39/47 cats (83%) at 61–180 days. Cats in which the TT4 concentrations were still above reference range at 21–60 days had a significantly higher starting TT4 than those that normalized their TT4 levels during the same time period (P = .038). Overall, restricted-iodine diets were effective at maintaining serum TT4 concentrations within reference ranges for a majority of cats with hyperthyroidism over 1 year, although not all clinical signs of hyperthyroidism improved.

D. Safety and Efficacy of a GLP-1 (glucagon like peptide)agonist: Glargine combination for feline DM
   1. Human type 2 DM as a model for feline disease.
   2. In humans, targeting the incretin system has become an important therapeutic approach for treating type 2 diabetes. Two drug classes have been developed: glucagon-like peptide (GLP)-1 receptor agonists (exenatide and liraglutide) and dipeptidyl peptidase 4 (DPP-4) inhibitors. Clinical data have revealed that these therapies improve glycemic control while reducing body weight (GLP-1 receptor agonists, specifically) and systolic blood pressure (SBP) in patients with type 2 diabetes.
   3. The incretin effect is responsible for 50–70% of total insulin secretion after oral glucose administration. There are two naturally occurring incretin hormones that play a role in the maintenance of glycemic control: glucose-dependent insulinotropic polypeptide and GLP-1, both of which have a short half-life because of their rapid inactivation by DPP-4. In patients with type 2 diabetes, the incretin effect is reduced or, in some cases, absent. In particular, the insulinoptropic action of glucose-dependent insulinotropic polypeptide is lost in patients with type 2 diabetes. However, it has been shown that, after administration of pharmacological levels of GLP-1, the insulin secretory function can be restored in this population, and thus GLP-1 has become an important target for research into new therapies for type 2 diabetes.

      GLP-1 has multiple physiological effects that make it an attractive candidate for type 2 diabetes therapy. It increases insulin secretion while inhibiting glucagon release, but only when glucose levels are elevated, thus offering the potential to lower plasma glucose while reducing the likelihood of hypoglycemia. Furthermore, gastric emptying is delayed and food intake is decreased after GLP-1 administration. Indeed, in a 6-week study investigating continuous GLP-1 infusion, patients (human) with type 2 diabetes achieved a significant weight loss of 1.9 kg and a reduction in appetite from baseline compared with patients receiving placebo, where there was no significant change in weight or appetite. Preclinical studies reveal other potential benefits of GLP-1 receptor agonist treatment in individuals with type 2 diabetes, which include the promotion of β-cell proliferation and reduced β-cell apoptosis. These preclinical results indicate that GLP-1 could be beneficial in treating patients with type 2 diabetes. However, because native GLP-1 is rapidly inactivated and degraded by the enzyme DPP-4 and has a very short half-life of 1.5 min, to achieve the clinical potential for native GLP-1, patients would require 24-h administration of native GLP-1. Because this is impractical as a therapeutic option for type 2 diabetes, it was necessary to develop longer-acting derivatives of GLP-1.

4. Studies with exenatide have been initiated in small animals in the last 2-3 years.
5. A double bind, placebo controlled x-over design with 8 DM cats (BCS>4) was conducted. Group A was treated with glargine and exenatide and group B with glargine only. All cats had previously been on glargine. 2 cats in group A became anorexic and 1 cat had clinical hypoglycemia necessitating a decrease in dose. Cats in both groups had asymptomatic hypoglycemia documented on a 12 hour BG curve. 3 cats in group A had a decrease in insulin requirements and 1 in group B. 87.5% of cats in group A had a decrease in weight and 5 cats in group B gained weight. (Although due to low numbers, no true significance was noted)
6. Weight loss could be a significant benefit with exenatide. Likely to be seeing more work in this area in future.

E. Update on insulin treatments for dogs and cats: insulin dosing pens and more (Thompson, Australia) (To follow soon)

See notes: Comprehensive review of products and treatment recommendations. Nice to have!

F. Day to day variation of serial BG curves in DM dogs treated with BID NPH and detemir insulins in well controlled dogs. (DeMarco, Ohio)
    1. 5 dogs on NPH and 3 dogs on detemir had 4 BGC conducted at home.
    2. Analysis of curves for mean and SD of fasting, nadirs, and maximums showed less variation in the detemir group. This suggests overall less day to day variation in insulin action and greater confidence when interpreting BG curves.

G. Efficacy of Prozinc^{R} insulin in naïve and insulin established cats using continuous interstitial glucose monitoring (CIG). (Ward, GA)
    1. 10 naïve cats and 10 cats stable on prozinc. CIG monitoring over years.
    2. Established Prozinc was effective at controlling BGs and clinical signs in cats for the 4 year period. Onset and duration of action indicate BID therapy for most cats, but some cats can tolerate once daily dosing
    3. Lots more information in abstract.

H. Diagnosis of Canine HAC is associated with gender, age, breed and co-morbid conditions. (Lourenco, GA)
    1. 1519 dogs evaluated over 20 years
    2. Main points of interest: HAC is significantly associated with co-morbid conditions and that HAC is NOT a significant cause of mortality in dogs.

I. Effect on Glucosuria on urine specific gravity (Behrend, Auburn and Ohio)
    1. A commonly held belief is that concentrated urine in a DM patient is from excess glucose and true concentrating ability by the kidneys cannot be evaluated.
    2. Canine urine samples without glucose were used to serial add varying concentrations of glucose. Bottom line was the changes in USG created by adding glucose were small and clinically insignificant. Thus, Even in the face of glucosuria, an accurate estimation of renal concentrating ability can be determined.

V. Miscellaneous

A. Effect of hematuria on UP:C in cats (Vientos-Plotts and Behrend, Auburn, Ohio)
   1. Previously established that hematuria in canines must be visible to affect protein in urine . This study used cat urine and a series of additions of RBCs in increasing amounts. In contrast to canine study, this study showed that in cats, hematuria, even when not visible, does significantly impact UP:C. Sediment examination results need to be considered when evaluating cat UP:Cs.

B. Individual and Combined Effect of Long Chain N-3 Polyunsturated Fatty Acids (PUFAs) and Low Dose Aspirin on Platelet Function in Healthy Dogs
   1. Thromboembolic events are relatively common and can be catastrophic complications in a variety of diseases. Antiplatelet therapies can be ineffective some cases. As n-3 PUFAs can inhibit platelet function and enhance anti platelet efficacy, this study was done to compare the anti-platelet effects (in healthy dogs) of low dose aspirin (1mg/kg/day) alone, n-3 PUFAs (100 mg/kg/day) alone and the combination of the above treatments. Platelet function was measured with platelet function analyzer closer time and aggregometry. Flow cytometry was also used for platelet activation (P-selectin). No change was seen in platelet function with PUFAs alone, aspirin alone did demonstrate decreased platelet function and the combination therapy decreased platelet function significantly more than aspirin alone. No changes were seen in any group with platelet activation. More studies are needed, but combination therapy has the potential to increase the efficacy of anti-latelet therapy in dogs.

(patient label)

NC State Veterinary Hospital

Clinical Evaluation of Canine Chronic Enteropathy

Date: _____

History: _____

_____

_____

Previous diet trial If yes, which diet and for how long? Did it help?

_____

Previous antibiotic trial (State dose and length of therapy)? Did it help?

___Tylosin ___Metronidazole ___Other/none (specify)

_____

Deworming trial (State dose and length of therapy)? Did it help?

___Fenbendazole ___Praziquantel ___Pyrantel ___Other/none(specify)

_____

Other medications prescribed: _____

Current medications: _____

MODIFIED CIBDAI CRITERIA: (circle what applies)

A. Attitude/Activity:	0=normal	1=slightly decreased	2=moderately decreased	3=severely decreased
B. Appetite:	0=normal	1=slightly decreased	2=moderately decreased	3=severely decreased
C. Vomiting:	0=none	1= 1x/week	2= 2-3x/week	3= >3x/week
D. Stool consistency:	0=normal	1=soft feces	2=very soft feces	3=watery diarrhea
E. Stool frequency:	0=normal	1= 2-3x/day	2= 3-5x/day	3= >5x/day
F. Weight loss:	0=none	1=mild (<5% loss)	Presence of fresh blood	Presence of mucus
G. Colitis*:	no colitis	Straining		

* THERE ARE NO POINTS FOR COLITIS

2=moderate (5-10% loss) 3=severe (>10% loss)

Summation of values - Total Composite CIBDAI Score: _____

0-3 points	4-5 points	6-8 points	9 or greater
Clinically insignificant disease	Mild IBD	Moderate IBD	Severe IBD

Endoscopy: (Performed today) Upper GI Lower GI Both Neither

Lab tests (Performed today): CBC CHEM UA FECAL A&M panel Abdominal rads/AUS Other (Specify in comments)

Diagnosis: _____

Treatment: _____

Comments: _____

Clinician Signature: _____

NC State Veterinary Hospital

Clinical Evaluation of Feline Chronic Enteropathy

(patient label)

Date: _____

History: _____

_____

_____

Previous diet trial? If yes, which diet and for how long? Did it help?

_____

Previous antibiotic trial (state dose and length of therapy)?

___Tylosin ___Metronidazole ___other/none (specifiy)

_____

Deworming trial (state dose and length of therapy)?

___Fenbendazole ___Praziquantel ___Pyrantel ___other/none (specify)

_____

Other medications prescribed: _____

Current medications: _____

FCEAI CRITERIA: (circle what applies)

A. Attitude/Activity	0=normal	1=slightly decreased	2=moderately decreased	3=severely decreased
B. Appetite	0=normal	1=slightly decreased	2=moderately decreased	3=severely decreased
C. Vomiting	0=none	1= 1x/week	2= 2-3x/week	3= >3x/week
D. Diarrhea	0=normal	1=soft feces	2=very soft feces	3=watery diarrhea
E. Weight loss	0=none	1= mild (<5% loss)	2=moderate (5-10% loss)	3=Severe (>10% less)
F. Total Protein	0=normal	1=increased		
G. ALT/ALP	0=normal	1=increased		
H. Phosphorus	0=normal	1=decreased		
G. Endoscopic lesions	0=absent/not performed		1=present	

Summation of values - Total FCEAI Score: _____

Endoscopy: (Performed today) Upper GI Lower GI Both Neither

Lab tests (Performed today) CBC CHEM UA FECAL A&M panel Abdominal rads/AUS Other (specify)

Diagnosis: _____

Treatment: _____

Comments: _____

Clinician Signature: _____