

# rDVM QUARTERLY

VETERINARY COMMUNITY NEWS FROM AMC

FALL 2016



“Curiosity is  
insubordination in  
its purest form.”

– VLADIMIR NABOKOV



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Dear Colleagues,

It is my great pleasure to present you with another edition of our quarterly rDVM and alumni newsletter. In this edition, we chose to highlight some truly advanced applications of procedures that many of us use every day, for example, the medication piece by Dennis Slade or the special stain article that Ann Hohenhaus shared this month. How amazing is oral vitamin B12? I love that this platform allows us to bring these novel yet practical tips to you, not just to feature the work we do at AMC, but in the hope that we can share something that can be incorporated into another practice...something that helps our community shine brighter.

I would also like to devote a few words to One Health or the *One Medicine initiative*, as some are calling it. As veterinarians, we have always been very mindful of the similarities between human and veterinary medicine. We know that dogs and cats share 85% and 90% of their DNA with humans (respectively), and that many of the disease states, genetic or not, are the same, not including those that are zoonotic or other infectious diseases that affect all species. Historically though, it has always been unidirectional; veterinarians learning from the human experience, animals benefiting from human drugs and human technology, etc. The One Health concept is going to change that by showing everyone that both types of medicine can mutually benefit from collaboration, and that dogs and cats can be excellent models for human diseases. Changing public and human physician perceptions is a slow process, but a worthy one, and I'm pleased to share with you that we at the AMC are right in the thick of it! I currently serve on the scientific advisory boards of the One Health Commission and the Global Lyme Alliance, and AMC is a full partner in the Weill Cornell Medical School Clinical Research Consortium. We launched our first One Health conference last October and this year's conference on endocrinology will be held this November 5th. We are also actively participating in the inaugural Global One Health Day this November 3rd. Please visit [www.amcnny.org/onehealth](http://www.amcnny.org/onehealth) for more information on all of these exciting events.

The hard work is paying off – collaborations are growing, One Health is taught as part of the curriculum at several medical schools and we are all making a difference. Please let me know if you wish to become involved in the One Health movement. It truly takes a village.

As always, please feel free to contact me with any comments, questions or concerns about AMC. I look forward to hearing from you.

Richard



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To Our Valued Partners In Care,

As we welcome the change of season from summer to autumn, we also welcome continued expansion, renovation and growth at AMC. I hope that you will take a moment to read through this quarter's newsletter to learn more about our new dental and endoscopy suites, amongst other exciting news.

To those of you in our referral community that took the time to complete the recent survey about our staff, service and facility, I want to personally thank you for your evaluation. Your feedback is as important to us as the relationship that we share with you. Once again, we were extremely pleased with the response rate, and based on these results, we continue to learn how we may better serve you and improve your clients' experience at AMC.

Additionally, it gives me great pleasure to share that AMC has recently been approved as a Veterinary Emergency & Critical Care Society (VECCS)-Verified Veterinary Trauma Center. We join an elite group of nine existing verified practices across the country that provide total care for every aspect of the management of the small animal trauma patient – from emergency stabilization through definitive medical and surgical care as well as rehabilitation. AMC's membership to the VECCS-Verified Veterinary Trauma Center network further allows us to support one of our founding missions, by participating in evidence-based trauma research to help define and improve upon standards of care, reduce morbidities, and improve outcomes for severely injured patients.

As always, thank you for your support of AMC.

Sincerely,

Kate

**The Cancer Institute:** September 2016 marked the one year anniversary of the grand opening of AMC's Cancer Institute. Thanks to the generosity of Elaine and Kenneth G. Langone, the dedication of our oncology staff and the support of our referral network, we remain steadfast in our commitment to advance treatment, provide a better quality of life for pets with cancer and improve the odds. *Our work continues:*

## MEDICAL ONCOLOGY

### CLINICAL TRIALS

#### **ALVAC IL-2/Vaccination in Cats with Feline Fibrosarcoma:**

Study intended to use ALVAC IL-2 vaccine as an adjunct treatment for feline fibrosarcoma following surgical removal of tumor. Study intended to determine if this treatment is more effective and safer than other therapies and/or procedures currently used.

#### **RIBOSE-CYSTEINE /Study of safety and tolerability of a ribose-cysteine supplement in healthy canine patients:**

Evaluation includes changes in physical examination, standard laboratory values, as well as assessment of owner-noted side effects and any perceived changes in quality of life. To measure the effectiveness of the rib-cys supplement in increasing glutathione levels, we are measuring pre- and post-supplementation glutathione levels in serum and red blood cells.

Pending the results of this initial study, further investigation of the effects of supplementation on glutathione levels in oncology patients will be undertaken.

### RETROSPECTIVE STUDY

#### **Feline LSA:**

A retrospective evaluation of the prognostic significance of peripheral blood lymphocyte-to-monocyte ratio at diagnosis in cats with large-cell gastrointestinal lymphoma. This ratio has been shown to be an independent prognostic indicator in both humans and dogs.

### COLLABORATIVE CLINICAL BASIC SCIENCE RESEARCH

#### **Prognostic value of 25-Hydroxyvitamin D levels in canine patients with multicentric lymphoma currently treated with the chop based protocol (Cornell):**

An observational study intended to determine if serum Vitamin D levels in dogs with lymphoma, being treated with CHOP, have any prognostic implications or effects on response to treatment. Insufficient vitamin D level has been shown to be a negative prognostic indicator in human patients. Patients enrolled in the study will be monitored and evaluated to determine if trends develop in disease-free intervals, progression-free and overall survival correlated to patient vitamin D status.

#### **Tumor infiltration lymphocytes may harbor oncogenic mutations (MSKCC):**

Malignant transformation requires the interaction of cancer cells with their microenvironment, including infiltrating leukocytes. In veterinary medicine, mutational studies have largely focused on mutations solely within tumor cells - several of which have proven the presence of immune cells in the microenvironment of solid tumors in both dogs and cats. Canine tumors that have already been noted to cause local inflammatory reactions are of particular interest in this study - thus, the focus of this project is to study the DNA of inflammatory cells associated with solid tumors in the dog for possible mutations.

**Identified DNA mutations in solid tumors in dogs leading to effective toceranib (Palladia®) therapy (NYU):** Small molecule kinase inhibitors are increasingly used for the "precision therapy" of human cancer. There is a lack of investigation into the use of inhibitors in veterinary medicine. Toceranib is a veterinary-approved tyrosine kinase inhibitor (TKI) that targets the KIT mutation

present in a subset of mast cell tumors in dogs, and is currently FDA-approved for the treatment of grade II and III non-resectable mast cell tumors. However, this drug has also shown efficacy against several other tumor types. While some of these tumors have KIT mutations, others have been noted. To date, the majority of veterinary research in this area used retrospective data from biopsy samples that have been interrogated for the presence of a few select mutations. Clinical anecdotal data has supported the use of toceranib in patients with solid tumors. Further investigation of solid tumor DNA should lead to mutation discovery that supports an evidence-based approach to toceranib therapy. The present study is prospective, and designed to further investigate and characterize the mutational landscape present in canine solid tumors.

#### **Losartan immunotherapy in addition to standard of care doxorubicin chemotherapy in dogs with splenic hemangiosarcoma (Colorado State University Research Innovation Center):**

Hemangiosarcoma (HSA) is the most common malignant splenic tumor of dogs. Primary splenic hemangiosarcoma is typically characterized by a highly malignant disease course. Dogs often have a vague history of possible clinical signs at home for days to weeks prior to a crisis. Tumor rupture is common, leading to hemoabdomen and the recommendation for an

emergency splenectomy. Many dogs suffer from macroscopic metastasis at the time of initial evaluation and tumor spread to the liver, omentum, mesentery, and lungs is most common. Reported survival time is abbreviated with surgery alone at 1.6 months; the 1 year survival rate is only 10%. Chemotherapy in the adjuvant setting is aimed at combatting metastasis. Doxorubicin chemotherapy is the most efficacious agent. Chemotherapy modestly increases median survival time to 4-6 months.

Immunotherapy has emerged in human and veterinary oncology as a new approach to cancer therapy. In several human cancers, monocytes have been shown to play a role in cancerous metastasis. Recently, the metastatic lesions found in canine HSA where shown to have increased infiltration of monocytes. Immunotherapies aimed at preventing monocyte recruitment and/or mobilization may lead to prolonged survival times in this devastating disease by slowing metastasis. Losartan is a well-tolerated drug in dogs primary used for hypertension. However, at high doses, losartan that has been shown to decrease monocyte activation and thus losartan maybe a potential antimonocyte, antimetastatic therapy for canine HSA.

The Cancer Institute at the Animal Medical Center is currently enrolling canine splenic HSA patients into a clinical trial. All patients will receive standard of care chemotherapy

with doxorubicin. This study is a prospective, randomized, clinical trial with active control, intended to compare the effects of two drug therapies (doxorubicin paired with immunotherapy, vs. doxorubicin paired with placebo) on the progression free survival time of canine HSA patients after splenectomy. Progression free survival at the end of 4 months of doxorubicin chemotherapy will serve as the end point to this study. Morbidity and mortality will be compared between treatment groups.

Only the 40 dogs will be accepted for enrollment. To qualify, dogs must have a histopathologic diagnosis of splenic hemangiosarcoma. Biopsy reports of dogs to be considered for the study should be sent to the Animal Medical Center (Fax: 212-308-1017, Attn: Dr. Zseltvay or email directly to katherine.zseltvay@amcnyc.org) as soon as possible. Study patients will get prioritized appointments, with a goal of initial consult within 7 days of surgery. All enrolled dogs will have free clinical staging (thoracic radiographs and abdominal ultrasound) at the completion of the study as well as 75% of the total cost of chemotherapy visits. Dogs will be excluded if they have been treated with prior chemotherapeutics for HSA or suffer from any other malignancies.

If you have a patient who you would like to enroll, or if you are interested in learning more, please contact Dr. Katherine Zseltvay (katherine.zseltvay@amcnyc.org) or Dr. Ann Hohenhaus (ann.hohenhaus@amcnyc.org).





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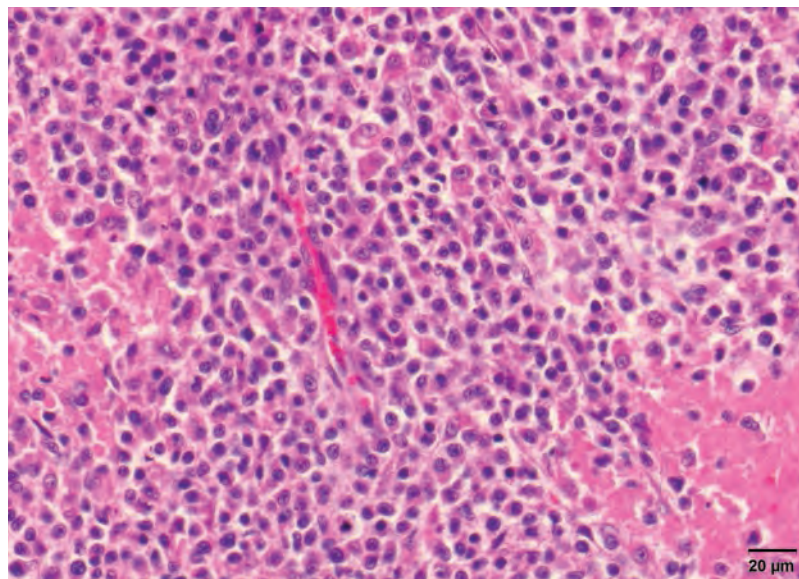
## Immunohistochemistry puts Muchacho on the road to recovery

At 13 years old, Muchacho, a male castrated shepherd mix, is no longer the mischievous young dog that earned him his name, but thanks to a team of surgeons, pathologists, and oncologists at the Animal Medical Center, he continues his happy life as a beloved grey-muzzled dog.

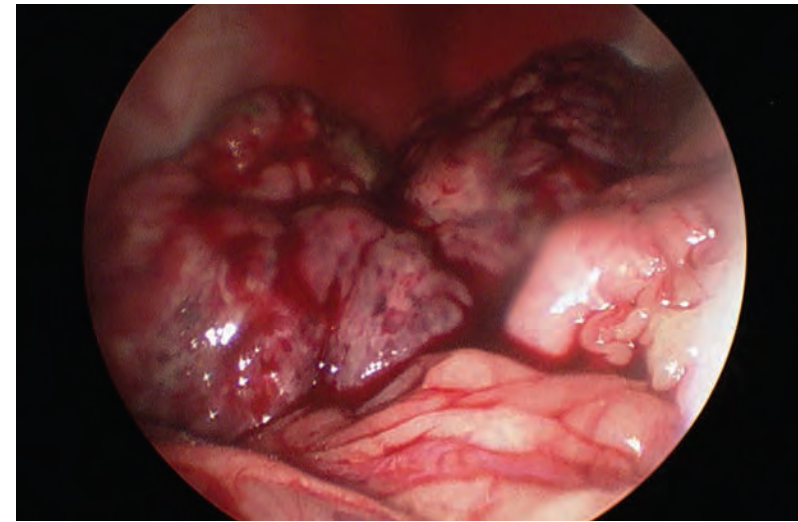
Muchacho saw his primary care veterinarian in March of 2016 because of polyuria and polydipsia. A thorough evaluation revealed a mild elevation in ALT and AST. (See the table *Selected clinical pathology results* for the exact values.) A urinalysis showed at 1.013 specific gravity with a quiet sediment and no bacterial growth. Because of the mild elevation in ALT and AST, Muchacho's primary care veterinarian recommended an abdominal ultrasound. The ultrasound identified three separate liver masses – a large mass in the right lobe and two smaller masses in the left lobe.

Muchacho's primary care veterinarian sent the results of the diagnostic evaluation to the Oncology Service care coordinator, Fazia Mangru. A quick review of the material by the Oncology Service veterinarians determined the Surgery Service should be Muchacho's first stop at AMC.

Dr. Dan Spector's surgical service was the first team of veterinarians to see Muchacho. After obtaining three view thoracic radiographs and a coagulation panel, both of which were normal, Muchacho was admitted with a plan for laparoscopic biopsies of the liver masses. Intraoperatively, laparoscopy was converted to an open laparotomy to allow surgical resection of the masses. Histopathology results gave two main differential diagnoses for the liver masses, either a malignant round cell tumor or a neuroendocrine carcinoma and recommended immunohistochemistry to differentiate the two possibilities.



Photomicrograph showing necrosis and infiltration of the liver with neoplastic cells. Cells are consistent with malignant round cell tumor or neuroendocrine carcinoma. (credit: Dr. Jamie Haddad, IDEXX Laboratories)



Laparoscopic view of one of the three liver masses prior to surgical resection.

Selecting the appropriate immunohistochemical stains can be daunting. These tests are commonly referred to by acronyms or abbreviations which make the tests seem somewhat enigmatic. Immunohistochemistry can be expensive which makes ordering exactly the right set of stains paramount. A quick visit to Dr. Jamie Haddad in her IDEXX-AMC office, determined an extended panel of stains was necessary in Muchacho's case. Deciphering the potential the malignant round cell tumor required stains for lymphoma, histiocytic sarcoma and plasma cell tumor. A separate set of stains was necessary to identify a possible neuroendocrine carcinoma. (See the table *Immunohistochemical stains used on Muchacho's malignant liver tumor* for details on stains and results.) During the oncology consultation, we encouraged Muchacho's family to pursue immunohistochemistry because the results would allow us to choose a chemotherapy protocol most appropriate for the tumor type. The positive staining for CD18 and CD3 confirmed an unusual diagnosis of hepatic T cell lymphoma.

Treatment with CHOP (cyclophosphamide, vincristine, doxorubicin and prednisone) chemotherapy was initiated the day after the immunohistochemistry results were released. The Oncology Service was extremely concerned about the rapid elevation of Muchacho's liver enzymes and total bilirubin over the three weeks since his primary care veterinarian had identified the mild elevations in ALT and AST. (See the table *Selected clinical pathology results* for the exact values.) The elevations were so severe, we were concerned about impending liver failure secondary to progressive lymphoma. Despite the worsening of Muchacho's liver enzymes during the first five weeks of chemotherapy, Muchacho showed an immediate clinical improvement, eating and drinking normally, once again going up and down stairs and even jumping into the car for his weekly trip to AMC. The only problematic episode so far during Muchacho's treatment has been a Grade III neutropenia one week following a chemotherapy treatment. This abnormality was discovered by his primary care veterinarian on a week when no chemotherapy was scheduled. A week of prophylactic antibiotics was all Muchacho needed and he resumed treatment the following week.

## Selected clinical pathology results - Muchacho

		CHEMOTHERAPY DOXORUBICIN	CHEMOTHERAPY DOXORUBICIN	CHEMOTHERAPY CYCLOPHOSPHAMIDE	ONCOLOGY CONSULTATION	RDVM EXAMINATION
	REFERENCE RANGE	6/24/16	5/17/16	4/26/16	4/12/16	3/20/16
ALT	18-121 U/L	201	2074	839	563	135
AST	16-55 U/L	26	276	103	96	128
SAP	5-160 U/L	206	1144	1472	1030	72
GGT	0-13 U/L	16	105	103	36	
T Bili	0-0.3 mg/dl	0.2	0.4	0.5	1.0	0.3
Albumen	2.7-3.9 g/dl	2.6	2.6	2.7	2.4	3.1

## Immunohistochemical stains used on Muchacho's malignant liver tumor

IMMUNOHISTOCHEMICAL STAIN	STAIN SPECIFICITY	RESULT
CD18	panleukocytic marker	neoplastic cells have diffuse strong perimembranous immunoreactivity
CD3	T lymphocyte marker	neoplastic cells have diffuse strong perimembranous/cytoplasmic immunoreactivity for CD3
CD79a	B lymphocyte marker	diffusely negative
Mum1	plasma cell marker	diffusely negative
AE1/AE3 cytokeratin	epithelial marker	diffusely negative
synaptophysin	neuroendocrine marker	diffusely negative
chromogranin A	neuroendocrine marker	diffusely negative



Muchacho's story highlights the teamwork required for a successful outcome in diagnosing and managing a complicated cancer patient. Because Muchacho's primary care veterinarian performed a complete diagnostic evaluation and shared those results with the Oncology Service, our care coordinators were able to prioritize a surgical consultation, streamlining the referral process. The presence of IDEXX-AMC's histopathology service on-site facilitated a discussion about the appropriate immunohistochemical stains that led to the final diagnosis. Throughout all this, Muchacho has been the model patient, cooperative and wonderful to care for. His excellent response to the chemotherapy protocol has been a gratifying experience for his family and his entire AMC team.

## Breakthrough in Cardiology Care: Effect of Pimobendan in Dogs with Preclinical Myxomatous Mitral Valve Disease and Cardiomegaly: The EPIC Study—A Randomized Clinical Trial

A medical breakthrough has been reported that will help extend the lives of asymptomatic dogs with advanced chronic degenerative mitral valve disease (MVD).

### What is the most common heart disease that afflicts dogs?

By the time a small breed dog reaches roughly 10 years of age, it has some degree of chronic MVD. In many cases, this will not interfere with general health, while others will develop heart failure and suffer a premature death.

### How have dogs with chronic mitral valve disease (MVD) been managed?

Until now, medical options have been limited and controversial. Some have advocated a wait and watch strategy – monitoring patient breathing for signs of heart failure and then treating when symptoms present. Others add an angiotensin converting enzyme inhibitor, but the benefit is modest, and some question its value.

### What are the results and clinical implications of the EPIC (Evaluation of Pimobendan In Cardiomegaly) study trial?

EPIC - a 5-year clinical trial - reports that pimobendan (Vetmedin®) given to dogs with severe mitral valve leakage, delayed the onset of congestive heart failure by an average of 15 months compared with placebo treated dogs.

Conducted by a large international group of cardiologists in 11 countries (AMC Cardiology among them), the study was concluded after interim analysis revealed significant benefit to dogs receiving this agent.

### How will this affect diagnosis and management of canine heart diseases?

In light of these findings, clinicians should change how they diagnose and manage MVD. Dogs with heart murmurs should be screened early, rather than wait for clinical signs of coughing or respiratory distress to develop. Assessment can be effectively made using history and physical examination along with the added benefit of chest radiography and/or echocardiography.

Dogs showing evidence of severe mitral valve disease and severe left atrial dilation may be considered as candidates to receive this therapy, which is intended to extend the asymptomatic period followed by long term medical monitoring.

*AMC Cardiologists are available 7 days/week to help you assess whether your patients may benefit from this therapy, and to help plan effective follow up and cardiac surveillance.*



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For more information on the EPIC study, read the publication:

Effect of Pimobendan in Dogs with Preclinical Myxomatous Mitral Valve Disease and Cardiomegaly: The EPIC Study—A Randomized Clinical Trial. Boswood A, Häggström J, Gordon SG, Wess G, Stepien RL, Oyama MA, Keene BW, Bonagura J, MacDonald KA, Patteson M, Smith S, Fox PR, Sanderson K, Woolley R, Szatmári V, Menaut P, Church WM, O'Sullivan ML, Jaudon JP, Kresken JG, Rush J, Barrett KA, Rosenthal SL, Saunders AB, Ljungvall I, Deinert M, Bomassi E, Estrada AH, Fernandez Del Palacio MJ, Moise NS, Abbott JA, Fujii Y, Spier A, Luethy MW, Santilli RA, Uechi M, Tidholm A, Watson P. *J Vet Intern Med.* 2016 Sep 28. doi: 10.1111/jvim.14586.

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## Novel Uses for Older Drugs

With the many drugs available in veterinary practice, new applications of existing medications may allow for innovative and creative medicine. Repurposing drugs can broaden utility and can guide a practical approach in stocking the clinic's dispensary or help with some challenging cases. Here are a few not-so-new drugs with uses above and beyond what you may be familiar with.

### **Cerenia**

**Novel uses: visceral analgesia, improved post-operative recovery, bronchitis, rhinitis**

Cerenia is the first veterinary-approved drug in the NK-1 receptor antagonists, commonly used to prevent vomiting (including secondary to motion sickness). However, neurokinin antagonism is being investigated for its effects and decreasing substance P production, which has roles in promoting visceral pain, inflammation, and histamine release. As such, the role of Cerenia in many treatment modalities is questioned and its potential benefits continue to be understood. Cerenia is routinely dosed in dogs at 2 mg/kg PO q24 orally (1 mg/kg SQ or IV can also be used); in cats 1 mg/kg PO, IV, SQ q24 is used.

**Visceral analgesia** – Studies showing less isoflurane to achieve MAC in canine patients receiving 1 mg/kg Cerenia during laparoscopic ovariohysterectomy suggest visceral analgesic effects (traction stimulation of the ovary and ovarian ligament performed); as such, it may have use as adjunctive therapy in pancreatitis, enteritis, and peritonitis patients. The author routinely uses Cerenia as long-term pulse therapy with feline chronic pancreatitis cases (1 mg/kg PO q24-78h).

**Improved post-operative recovery** – Canine patients given 1 mg/kg Cerenia prior to anesthesia for ovariohysterectomy experienced a significantly lower incidence of pre-anesthetic vomiting, post-anesthetic vomiting and faster recoveries, with lower visual assessment of nausea scores (opioid premedications used). Use of this drug may help improve post-anesthetic morbidities (esophagitis, aspiration pneumonia) and faster times to ambulation, which may more efficiently utilize hospital support staff.

**Bronchitis** – Substance P neuropeptide effects on sensitization of the cough reflex and airway leukocyte recruitment have been studied. Dogs diagnosed with chronic canine bronchitis who were treated with Cerenia (2 mg/kg, q48h for 14 days) we reported to have decreased cough frequency per client observation but failed to reduce airway inflammation via BAL significantly. While this drug cannot be currently recommended as a single agent treatment for bronchitis, its use as an adjunctive anti-tussive drug may be a valuable component of long-term control of clinical signs.

**Rhinitis** – Increased levels of substance P have been documented in BAL and nasal lavage fluids before and after allergen exposure of people with grass pollen allergy. In addition, after pollen allergen challenge, affected people exhibited decreased nasal airway resistance (secondary to inflammation), evidence of plasma leakage into secretions, and increased recruitment of eosinophils.

As such, the role of NK-1 receptor antagonists such as Cerenia may play a role in management of chronic rhinitis in veterinary patients. No reports of successful use of this drug for this condition has been published, and success of anecdotal usage varies. At this time, the use of Cerenia for rhinitis cannot be strongly supported but further studies may elaborate different outcomes.

### **Cyclosporine**

**Novel use: rhinitis**

Treating lymphoplasmacytic rhinitis in dogs is often frustrating and unrewarding given the lack of dependable therapeutic regimes. Given the assumption of underlying inflammatory and allergic etiologies, steroids are often used as part of multimodal therapy but may carry untoward longer-term side effects. Other immunomodulatory drugs – including cyclosporine – may provide added benefit in chronic management via T-helper cell downregulation. Although only limited case series exist, in some cohorts the use of concurrent longer-term cyclosporine with initial tapering doses of steroids provided more clinical control of rhinitis signs in comparison to treatment with steroid alone. Five mg/kg PO SID x 4 weeks with transition to every other day dosing long-term may be a consideration in conjunction to steroids and/or antibiotics.

### **Cobalamin**

**Novel use: oral supplementation**

Traditionally, correction of hypcobalaminemia was performed via parenteral administration, often with a protocol of weekly (transitioning to monthly) injections. Human studies have shown that approximately 1% of ingested free cobalamin may be absorbed passively, apart from intrinsic factor-related mechanisms. This same mechanism may be in part or wholly responsible to dogs as well. A cohort of 51 dogs with documented low B12 levels and concurrent chronic enteropathy treated with daily oral supplementation showed normalization of cobalamin (median 72 days). The benefits of oral supplementation may include improved owner compliance and reduced stress involved with injections. At this time, there is limited information on efficacy of oral cobalamin supplementation in cats and parenteral routes are recommended.

### **Sileo**

**Novel use: sedation for ultrasound, adjunctive use in collapsing trachea**

Sileo is an oromucosal dexmedetomidine gel which was recently released for use in noise aversion in dogs. It is too early on to see if off-label uses will emerge with this medication but in the future it may have a place for other applications - including potential use to facilitate patient compliance during ultrasound to use as adjunctive therapy in preemptive stress mitigation in collapsing trachea dogs.

### **Topiramate**

**Novel use: feline hyperaesthesia**

Topiramate (Topamax) is an anticonvulsant commonly used in the treatment of migraines in people and less commonly in dogs. The use of this drug for



other conditions is being explored and may have utility in the treatment of atypical seizures and/or migraine-like paroxysmal pain syndromes. Migraine-like pain was diagnosed in a Cocker Spaniel experiencing photophobia, phonophobia, nausea-like symptoms, low head carriage, and painful vocalization. Conventional drug trials were met with limited success after a robust diagnostic workup, but treatment with topiramate (10 mg/kg PO TID) resulted in marked clinical improvement. Similarly, topiramate was used to treat a cat with idiopathic ulcerative dermatosis (lesions dorsal midline of neck) with return of lesions when medication was stopped. Topiramate may be a consideration for similar neuropathic conditions but further research is warranted.

#### Trazodone

##### *Novel use: anxiolytic for transport/examination*

Trazodone, an antidepressant in the SARI (serotonin antagonist and reuptake inhibitor) class of drugs, has recently been gaining popularity for use as an anxiolytic and as a behavior modulator in dogs. A recent study demonstrated that the use of a single 50 mg tablet approximately 1 hour prior to a hospital visit resulted in superior tractability and decreased anxiety in feline patients. Use of this drug in known anxious or fractious cats may help facilitate less stressful appointments and increase owner satisfaction and compliance. The only side effect reported was sleepiness.

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## Gross Pathology: What's Your Morphologic Diagnosis?

**History:** A 15 year old, male castrated, Domestic Shorthair cat was presented for urinating and defecating outside of the litterbox for 3 weeks' duration. The owner did not note any straining to urinate or defecate, but perceived the abdomen to be swollen. At the last evaluation 9 months prior, elevated liver enzymes were interpreted to represent a flare-up of his previously diagnosed triaditis. Ultrasound evaluation revealed dilated, thickened biliary ducts and small intestinal thickening.

**Clinical findings:** Romeo was weak, cachectic, and dehydrated on exam, weighing one pound less than the previous examination. His abdomen was extremely distended in the cranial aspect, and felt firm. Romeo was admitted to the hospital for fluid therapy and supportive care. He was started on IV fluids and antibiotics. Bloodwork revealed anemia and mild kidney and liver disease. An ultrasound revealed significant common bile duct dilation. Supportive care was continued overnight, an injection of iron and darbepoetin were administered and the cat was discharged with treatments for triaditis and amino acid deficiencies. Due to continued decline at home, the patient was presented for euthanasia four days following discharge.

**Necropsy findings:** The following image includes the organs visible upon evaluation of the abdomen from the right side (lateral recumbency with left side down). Figure 1.

What's your morphologic diagnosis? Turn to page 13 for the gross summary and comments.



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FIG. 1



**Gross description:** Within the abdomen, there is a large, pale tan, fluctuant, fluid-containing cystic structure that measures 12 x 13.5 x 7.5 cm (Choledochal cyst). This structure communicates with the common bile duct and the hepatic ducts at two separate entrances. The sac also communicates with the duodenum via the intramural bile duct at the major duodenal papilla (Figures 2–4). This structure contains 450 mL of yellow to green, flocculent, bilious liquid, within which no calculi are found. No obvious cause of obstruction is evident. A red rubber tube can be easily passed from the major duodenal papilla into the sac, and from the common bile duct and hepatic ducts into the sac. The entrance from the common bile duct is small (approximately 2 mm in diameter). The gall bladder mucosa was severely, diffusely thickened by hyperplasia. The liver parenchyma is pale tan to light brown (pallor) and there is a diffusely enhanced reticular pattern

**Gross summary:**

Common bile duct: Choledochal cyst, severe with luminal bilious fluid

Gall bladder: Mucosal hyperplasia, diffuse, severe

Liver: Hepatopathy with parenchymal pallor and enhanced reticular pattern (histologically consistent with cholangiohepatitis)

Pancreas: Pancreatitis, chronic, diffuse with pancreatic duct ectasia, severe, diffuse and exocrine nodular hyperplasia

Small intestines: Enteropathy, diffuse with mural thickening (histologically consistent with enteritis)

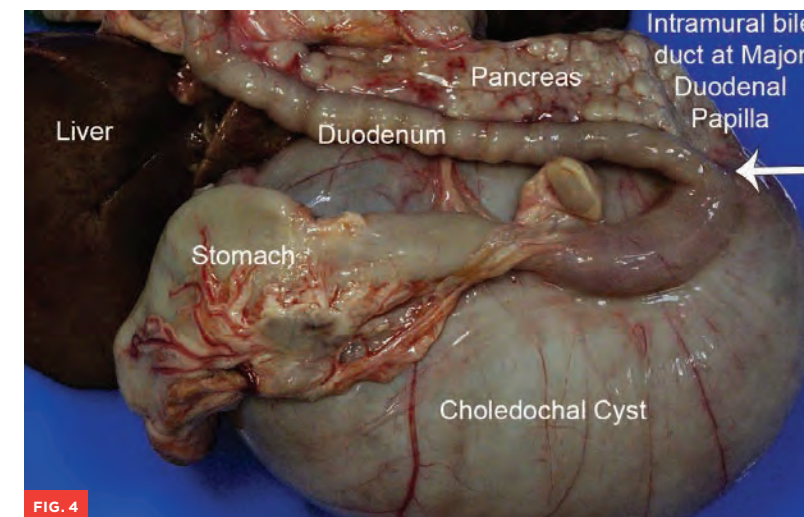
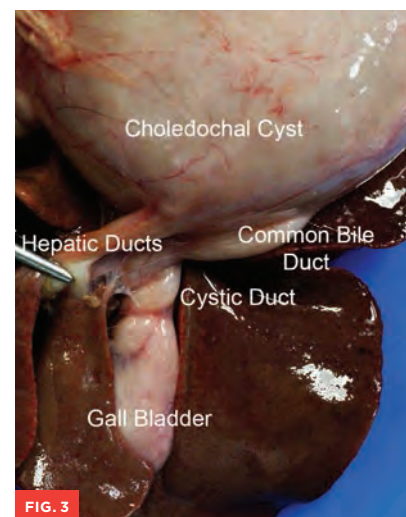
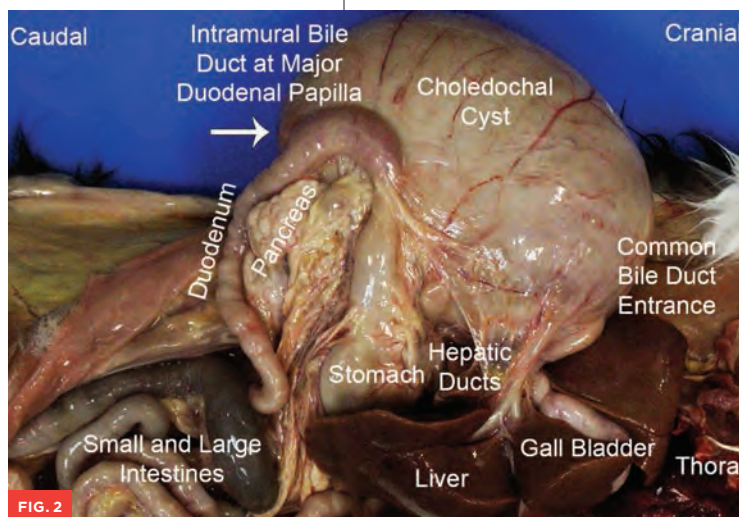
Stomach: Ulcerative gastritis, multifocal

**Comments:** The cystic dilation of the common bile duct is consistent with a choledochal cyst, which has been reported in cats,<sup>1,2</sup> and is the cause of the abdominal distension in this case. Cysts of the common bile duct are rare in humans (although observed more frequently in East Asian countries),<sup>3,4</sup> and

can be congenital or acquired.<sup>1-2,4</sup> There are five categories in humans under the modified Alonso-Ley classification, including type I (fusiform dilation of the extrahepatic bile duct), type II (a single extrahepatic diverticulum), type III (dilation of the intraduodenal portion of the bile duct), type IV (a combined intra and extrahepatic dilation of the bile duct), and type V (cystic dilation of the intrahepatic biliary system, also known as Caroli's disease).<sup>1-2,4</sup>

In this case, the cyst was more consistent with the type I classification, the most common type reported in people.<sup>4</sup> These cysts in humans contain bilious fluid, rich in pancreatic enzymes.<sup>1</sup> The majority are thought to be congenital, as they occur in infants and children, with about 20% of cases diagnosed in adults.<sup>1</sup> Reflux of pancreatic enzymes and increased pressures in a weakened common bile duct caused by an anomalous pancreaticobiliary junction (in which the pancreatic duct joins the common bile duct proximal to the sphincter of Oddi) has been hypothesized as a cause of late onset development of choledochal cysts.<sup>1,4</sup> Additional possibilities include gradual distention of a congenital dilation over time as well as dilation secondary to obstruction.<sup>1,4</sup> Underlying triaditis (as observed here) also cannot be ruled out as a cause of late onset cystic dilation. Stasis of bile within the cyst can result in bacterial growth and cholangitis,<sup>2</sup> and pancreatitis may also be related to reflux of pancreatic fluids caused by cyst compression.<sup>2</sup> The cat from one case report,<sup>1</sup> also had a history of inappropriate urination, hypothesized to be secondary to pressure applied upon the bladder due to the large size of the choledochal cyst. Malignant transformation of choledochal cysts have been reported in people,<sup>1-3</sup> and histologic evaluation of the cyst is required in order to rule out neoplasia.<sup>1,2</sup> Total excision of the cyst with reconstruction of the biliary tree is the preferred treatment in humans, as it mitigates the risk of neoplastic transformation.<sup>2,3</sup>

**Acknowledgements:** We would like to acknowledge Dr. John Cullen, Professor of Anatomic Pathology, North Carolina State University, for his expertise and comments on this case.



**References:**

1. Best EJ et al. Suspected choledochal cyst in a domestic short-hair cat. *J Fel Med Surg* 2010 Oct;12 (10):814-7.
2. Grand JG et al. Cyst of the common bile duct in a cat. *Aust Vet J* 2010 Jul;88(7):268-71.
3. Joseph VT and Raj PJ. A review of choledochal cyst in pediatric and adult patients. *J Hep Bil Pancr Surg* 1996 3:396-404.
4. Lipsett PA and Cameron JL. Choledochal cyst disease: a review. *J Hep Bil Pancr Surg* 1996 3:389-395.



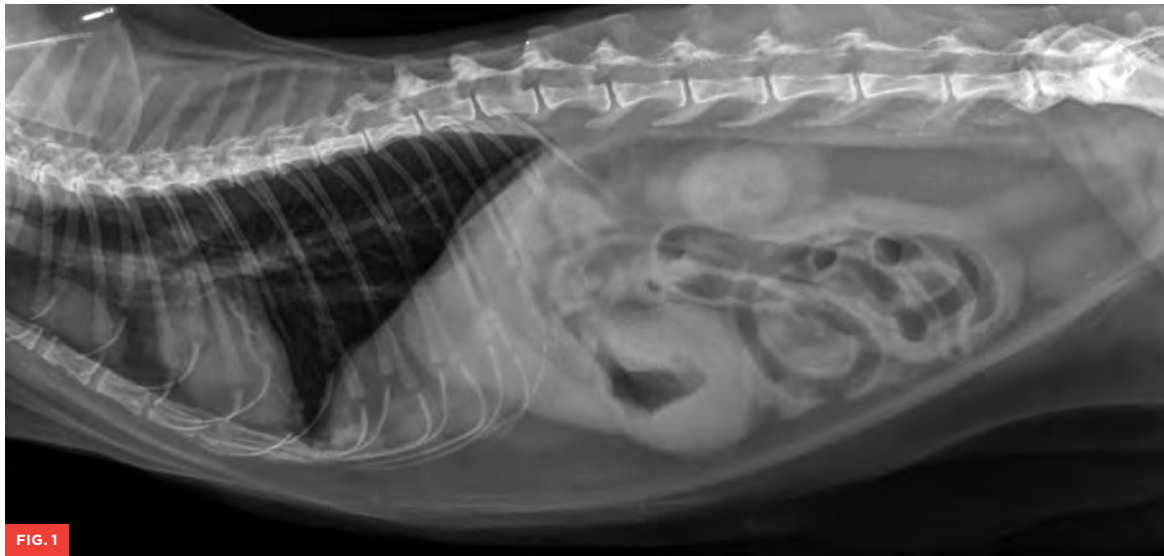


FIG. 1

FIGURES 1 & 2. Lateral and VD projections of the thorax/abdomen made by the referring veterinarian.



FIG. 2

## What's your diagnosis?

Anthony Fischetti, DVM, MS, DACVR  
*Head of Diagnostic Imaging*

**History:** 8 year old spayed female Domestic Shorthair cat with progressive vomiting and weight loss over the past two months.

Two views of the thorax/abdomen centered on the cranial abdomen and were submitted by the referring veterinarian. These images are provided. Make your radiographic diagnosis. What lesion is most responsible for vomiting?

*What's your diagnosis?*

Turn to page 22 for the diagnosis and case discussion.

## WHAT'S NEW

### DENTISTRY

We are proud to announce a new, fully equipped clinical dentistry suite that will employ the most advanced educational and patient care technologies available. Larger than our previous space, the new suite features state-of-the-art surgical, restorative and endodontic treatment areas; iM3 CR 7 Vet Advanced Digital X Ray Imaging and the most advanced anesthesia and patient monitoring equipment. Our dedicated staff is committed to providing the highest quality dental care for our patients and yours. Thank you for your confidence and the opportunity to serve the veterinary community. For more information, please call 212-329-8678.

Routine procedures performed at AMC include:

- Dental cleaning
- Endodontic therapy
- Jaw fracture repair
- Medical and surgical treatments for feline stomatitis
- Oral cancer surgery
- Orthodontics
- Restorations
- Root canal
- Surgical extractions
- Treatment for tooth resorption
- Treatment of periodontal disease





## ENDOSCOPY

AMC is pleased to announce that our expanded endoscopy suite provides state-of-the-art equipment and procedures, including concurrent and independent fluoroscopy studies and controlled ventilation anesthesia, to better serve you and your patients. Services provided include:

- Respiratory tract endoscopy
- Upper GI tract endoscopy
- Lower GI tract endoscopy
- Urinary and genital tract endoscopy
- Abdominal endoscopy

For an appointment or consultation, please call 212-329-7053.



## VECCS VETERINARY TRAUMA CENTER DESIGNATION FOR AMC

We are pleased to announce that the Veterinary Emergency & Critical Care Society (VECCS), along with the Veterinary Committee on Trauma (VetCOT) have approved the Animal Medical Center as an VECCS-Verified Veterinary Trauma Center — making us one of only 10 veterinary hospitals across the U.S. who share this designation.

As the only recognized VECCS-verified Veterinary Trauma Center in New York, AMC provides total care for every aspect of the management of the small animal trauma patient from emergency stabilization through definitive medical and surgical care and rehabilitation. Moreover, board certified specialists in the field of emergency and critical care, surgery, and radiology are on staff and available for consultation 24 hours a day, 7 days a week.

## ONE HEALTH

Registration is open for AMC's second annual One Health Conference: *Connecting Human and Veterinary Medicine, A Comparative Approach to Endocrine Disease*

November 5, 2016

8:00 am–6:00 pm

Weill Cornell Medical College  
Belfer Research Building  
413 East 69th Street, NYC

Leading experts across human and veterinary medicine will share case information and explore a collaborative approach to diseases and disorders of the endocrine system, in order to help advance treatment, prevention, and patient care. There

is no cost to attend and RACE credits will be awarded to veterinary professionals. For updated information and registration, visit [amcn.org/onehealth](http://amcn.org/onehealth)

## STAFF UPDATES

After completing a specialty internship in AMC's Integrative & Rehabilitative Medicine Service, we are pleased to welcome Barry Chernov, DVM, to our full-time staff.

## CLINICAL TRIALS/ CURRENT STUDIES

### Cardiology

Assessment of safety and effectiveness of Lasix administered by IV bolus compared with constant rate infusion to treat dogs with first time congestive heart failure

### Dentistry

Comparison of treating early canine periodontal disease with closed root planing alone versus concurrent use of doxycycline hyclate gel or clindamycin hydrochloride hydrogel

### Internal Medicine

Comparison of constant rate intravenous infusion and intermittent intramuscular administration of regular insulin in cats with diabetic ketoacidosis

### Interventional Radiology & Interventional Endoscopy

Allogeneic stem cell delivery for cats with chronic kidney disease. Phase I: Safety  
Autogenous stem cell delivery for chronic kidney disease. Phase II: Efficacy

Treatment of extrahepatic biliary duct obstruction (EHBDO) in dogs and cats by endoscopic retrograde cholangiopancreatography (ERCP) with biliary stent placement or the use of a rescue Subcutaneous Intestinal Biliary Bypass Device (SIBB)

Drug-eluting bead chemoembolization for non-resectable hepatocellular carcinoma (HCC) in dogs

### Radiation Oncology

Stereotactic Body Radiation Therapy (SBRT) for the treatment of nasal adenocarcinoma in the canine

### Surgery

Evaluation of preoperative CT imaging to predict surgical resection of liver tumors in dogs and cats

For additional details and contact information for these studies, please visit [amcn.org/clinicaltrials](http://amcn.org/clinicaltrials).

## CONTINUING EDUCATION LECTURE SERIES

The AMC events listed are open to all area veterinarians and technicians and are FREE of charge. All lectures are held at AMC from 8:00–9:00 am, unless otherwise noted. AMC lecture topics are subject to change. Please visit [amcn.org/lectures](http://amcn.org/lectures) or email [education@amcn.org](mailto:education@amcn.org) for up-to-date information. You may also sign up to receive email updates. All Partners In Practice lectures are free and CE accredited, but require registration. Visit our Partners In Practice page to register today at [amcn.org/pipseminars](http://amcn.org/pipseminars), as these events fill up quickly.



## Upcoming Lectures

November 3, 2016

### Soft Tissue Surgery

Presented by Dr. Birchard (outside speaker)

November 4, 2016

### Intro to Dermatology

Presented by Dr. Macina

November 7, 2016

### Upper Airway Disease

Presented by Dr. Palma

November 8, 2016

### Exotic Anesthesia

Presented by Dr. Quesenberry

November 10, 2016

### Feline Cardiomyopathy

Presented by Dr. Trafny

November 11, 2016

### Minimally Invasive Surgery

Presented by Dr. Spector

November 14, 2016

### Toxicities

Presented by Dr. Prittie

November 17, 2016

### Intro to Interventional Endoscopy

Presented by Dr. Berent

November 18, 2016

### Congestive Heart Failure

Presented by Dr. Fox

November 21, 2016

### Transfusion Medicine

Presented by Dr. Appleman

November 22, 2016

### Hypercoagulation

Presented by Dr. Buriko

November 28, 2016

### Fracture Management

Presented by Dr. Kalafut

November 29, 2016

### Pharmacology of

### Emergency Drugs

Presented by Dr. Lefman

## PIP COMPREHENSIVE CLINICAL CONFERENCES

Partners In Practice Comprehensive Clinical Conferences are intended to provide several hours of comprehensive review and updates of important and contemporary topics in veterinary medicine. Upon completion, participants should gain enhanced knowledge of the selected topic. Conferences are held at AMC on Sundays from 9:00 am–3:00 pm and are both RACE and NYSED approved.

Sunday, November 6

### LVT Conference: Dentistry Review and Update

## PIP PRACTICAL CLINICAL WORKSHOPS

Partners In Practice Practical Clinical Workshops are designed to promote sound diagnosis and effective therapies. Participants are encouraged to bring and share case materials, if they wish. Participate in our time honored teaching rounds and small group interactive workshops. Space is limited to 15 participants, so register today. These PIP Workshops are held at AMC on Tuesday evenings from 7:00–8:30 pm and are NYSED approved.

November 8, 2016

### GI Disease

Presented by Dr. Doug Palma

December 6, 2016

### Anemia

Presented by Dr. Beth Appleman

## PIP VETERINARY TECHNICIAN LECTURES

We also offer free New York State accredited CE for veterinary technicians as part of our Partners In Practice program. This CE is open to all local LVTs.

Lectures will be held the week of the VMA of NYC meeting on either a Monday, Tuesday or Thursday, and will run from 6:00–7:00 pm. These lectures are NYSED approved.

December 6, 2016

### Introduction to Interventional Radiology

Presented by Dr. Chick Weisse

If you need additional information or have questions about our PIP lectures, please contact Dr. Phil Fox at philip.fox@amcny.org or call 212-329-8606.

## RESEARCH HIGHLIGHTS

### Anesthesia

Dr. Fischer has published two seminal textbook chapters that describe safe and effective anesthetic techniques for the critically ill patient, and for pets with endocrine disease. The new information describes methods for anesthetic induction that should be considered for animals in shock, with hemodynamic compromise, respiratory difficulties, and in geriatric patients. This information is a must-read for practitioners looking to learn new and effective methods to safely anesthetize animals with these common conditions.

Fischer, Berit. Induction Techniques for the Really Sick Patient; Anesthetic Considerations for Endocrine Disease. In: Smith, Lesley J., *Questions and Answers in Small Animal Anesthesia*, Ames, Iowa : John Wiley and Sons, Inc., 2016.

### Cardiology

Drs. Fox and Schober published a comprehensive update on feline hypertrophic cardiomyopathy, the most common form

of heart disease in cats. While the majority of affected cats are asymptomatic, a proportion is at risk to develop CHF, arterial thromboembolism, and cardiac death. Clinical evaluation to discover prognostic indicators helps identify high risk patients. Current management focuses upon identifying risk factors, individualizing therapy, and focused monitoring. Treatments include drugs intended to reduce the risk of blood clots in cases with severe LA dilation, drugs to reverse LV remodeling, or medications to improve systolic or diastolic dysfunction.

Fox PR, Schober KA. Management of asymptomatic (occult) feline cardiomyopathy: Challenges and realities. *J Vet Cardiol* 2015;17 Suppl 1:S150-8.

In dogs and cats, assessing cardiac biomarkers can add objective data to the clinical assessment of heart disease. Dr. Fox and colleagues studied the utility of NT-proBNP to discriminate cardiac from non-cardiac respiratory distress and evaluate heart disease severity. A cut-off >2,447 pmol/L discriminated CHF from noncardiac respiratory distress (81.1% sensitivity; 73.1% specificity. A model including LA to aortic ratio, heart rate, LV diameter, and ACVIM heart disease scheme most accurately associated average plasma [NT-proBNP] with heart disease severity.

Fox PR, Oyama MA, Hezzell MJ, et al. Relationship of plasma N-terminal pro-brain natriuretic peptide concentrations to heart failure classification and cause of respiratory distress in dogs using a 2nd generation ELISA assay. *J Vet Intern Med.* 2015;29:171-9.

### Emergency and Critical Care

Drs. Olan and Prittie studied the

safety and suitability of Procalamine as a viable option for short-term parenteral nutrition in ill and injured dogs. Serial monitoring of blood parameters was advocated due to the potential for acid base, electrolyte, and blood glucose alterations.

Olan N, Prittie J. Retrospective evaluation of Procalamine administration in a population of hospitalized dogs: 36 cases (2010-2013). *J Vet Emerg Crit Care* 2015;25:405-415.

Drs. Cazzolli and Prittie wrote a comprehensive literature review evaluating the benefits of resuscitation fluids to treat critically ill pets. Clinical data from human patients did not reveal advantages associated with colloidal fluid resuscitation. In addition, hydroxyethyl starch solutions used in critically ill humans may be associated with significant adverse effects. Whether these agents can be successfully used in sick animals awaits further study.

Cazzolli D, Prittie J. The crystalloid-colloid debate: Consequences of resuscitation fluid selection in veterinary critical care. *J Vet Emerg Crit Care* 2015;25:6-19.

### Internal Medicine

Dr. White and colleagues studied whether hypercoagulability in proteinuric dogs was related to the degree of proteinuria, presence of systemic arterial hypertension, presence of hypoalbuminemia, or reduced antithrombin activity. Hypercoagulability was prevalent in dogs with PLN, but could not be predicted based upon the presence or degree of proteinuria, systemic arterial hypertension, hypoalbuminemia, or low AT activity. Thromboembolism was uncommon in these cases.

White CR, Langston C, Hohenhaus AE, Lamb K, Hackner S, Fox PR. Evaluation of the relationship between clinical variables and thromboelastographic findings in dogs with protein-losing nephropathy. *J Vet Emerg Crit Care* (San Antonio). Epub 2015 Oct 12.

### Interventional Radiology

Interventional radiology uses fluoroscopy to assist in the delivery of therapeutic materials to organ systems, vessels, and body systems. In this article, Dr. Chick Weisse summarizes the growing subspecialty of interventional oncology. These interventions are used to re-establish patency in states of malignant obstructions, deliver local chemotherapy, stop hemorrhage via transarterial embolization or chemoembolization, and administer cancer therapies to patients without other safe options.

Weisse C. Veterinary interventional oncology: from concept to clinic. *The Veterinary Journal*;205(2):198-203, 2015.

Veterinary Image-Guided Interventions, a seminal veterinary textbook, was edited by Drs. Chick Weisse and Allyson Berent — leaders in the emerging field of minimally invasive technology. The handbook provides invaluable reference to this specialty by demonstrating indications and procedures that utilize stents, balloons, and other devices to treat cancer, cardiovascular disease, GI, urinary tract, and other body systems.

*Veterinary Image-Guided Interventions*, First Edition. Edited by Chick Weisse and Allyson Berent. © 2015 John Wiley & Sons, Inc. Published 2015 by John Wiley & Sons, Inc.: 978-1-118-37828-1.

### Interventional Endoscopy

Bile duct obstruction can result in serious health consequences in dogs. Dr. Allyson Berent and colleagues describe techniques for endoscopic retrograde cholangiography and endoscopic retrograde biliary stenting of the common bile duct. Their findings demonstrate that these techniques for minimally invasive treatment of extrahepatic bile duct obstruction are feasible. Further application requires wider study.

Berent A, Weisse C, Schattner M, et al. Initial experience with endoscopic retrograde biliary stenting for treatment of extrahepatic bile duct obstruction in dogs. *Journal Am Vet Med Assoc* 2015;246:436-446.

### ABOUT THIS NEWSLETTER

This newsletter is distributed quarterly to AMC's network of referring veterinarians and others who opt-in to receive this publication. If you have questions regarding this newsletter or would like to sign up to be included in our distribution, please email [info@amcny.org](mailto:info@amcny.org).

To receive our current staff directory, email [info@amcny.org](mailto:info@amcny.org).

For access to the AMC Patient Referral Form, visit [amcny.org/referralform](http://amcny.org/referralform).

Cover photo courtesy of Corey Towers

Designed by Anthony Coombs



## AMC Dedicated Phone Numbers for Referring Veterinarians

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9 am – 5 pm

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**Dr. Betsy Bond**  
**Dr. Dennis Trafny**  
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Monday – Sunday  
9 am – 5 pm

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**Dr. Stephen Riback**  
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9 am – 5 pm

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**Dr. Allyson Berent**  
212-329-8700  
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9 am – 5 pm

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**Dr. John McCue**  
**Dr. Abbie Lebowitz**  
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212-329-8797  
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9 am – 5 pm

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212-329-8813  
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Tuesday 10 am – 5 pm  
Thursday 2 pm – 9 pm  
Friday 9 am – 3 pm

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Monday – Friday  
9 am – 5 pm

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**Dr. Barry Chernob**  
212-329-8860  
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9 am – 5 pm

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212-329-8863  
Wednesday – Saturday  
9 am – 5 pm

### SURGERY SERVICE 3

**Dr. Pamela Schwartz**  
212-329-8867  
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9 am – 5 pm

### SURGERY SERVICE 4

**Dr. Rob Hart**  
212-329-8674  
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### A.M.C. PORTAL

[amcny.org/referral-portal-login](http://amcny.org/referral-portal-login)

### DR. RICHARD GOLDSTEIN, CMO

347-733-7338  
[richard.goldstein@amcny.org](mailto:richard.goldstein@amcny.org)

### PRIORITY EMERGENCY/CRITICAL CARE HOTLINE

212-329-8616 or  
646-556-6411 (fax)

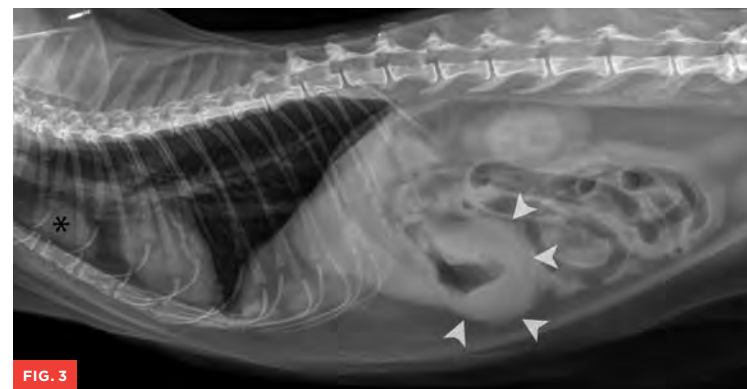


FIG. 3



FIG. 4

## What's your diagnosis?

**Radiographic findings:** The stomach is large and irregular on both views. On the lateral, the pyloric antrum and body are rounded and thick with an irregular gas-filled lumen (white arrowheads). On the VD view, the body and pylorus of the stomach are thickened and irregular (white arrowheads). The right kidney is irregular in shape (white asterisk). A rounded soft tissue mass is cranial to the heart on the lateral view and focally widens the cranial mediastinum on the VD view (black asterisk).

### Radiographic diagnosis:

1. Moderate to severe eccentric wall thickening of the stomach.
2. Soft tissue mass, cranial mediastinum.
3. Irregularly shaped kidney as a sign of chronic renal disease.

**Conclusions:** The normal cat's stomach is usually a tear-drop shape on the lateral view and generally does not extend far caudally on the VD view unless there is a large amount of recently ingested food in it. Making the diagnosis of gastric wall thickening or mass is certainly possible from abdominal radiographs. This cat went on to CT (additional images with arrows denoting the gastric mass) and ultrasound-guided fine needle aspirates of the gastric wall mass. The final diagnosis was gastric lymphoma with sternal lymphadenopathy (cranial mediastinal mass) also consistent with lymphoma. The cat received chemotherapy and the gastric mass decreased in size by 90%. The vomiting is most likely attributed to the large gastric mass as these clinical signs resolved as the mass shrank.

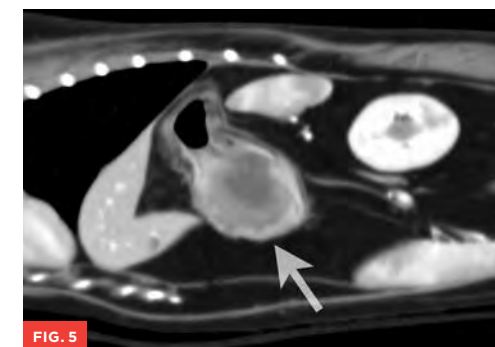


FIG. 5

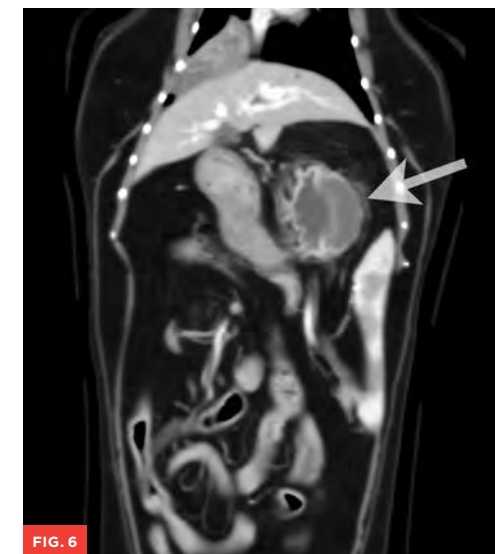


FIG. 6

**FIGURES 3 & 4.** Same as Figures 1 and 2 but with arrowheads outlining an abnormally large and irregular stomach. Notice the irregular centrally located gas in the lumen of a thick walled stomach on both views.

**FIGURES 5 & 6.** Sagittal and dorsal reformatted CT images of the cat's abdomen. Notice the eccentric thickening of the body of the pylorus on the sagittal image (arrow) and the fundus of the stomach on the dorsal (arrow). Also notice how the normal undulating mucosal wall of the stomach abruptly is lost at the site of the tumor.



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