November 2013 Abstracts

Journal of the American Animal Hospital Association (Nov/Dec)

Intermittent Single-Agent Doxorubicin for the Treatment of Canine B-Cell Lymphoma
Mary Lynn Higginbotham, Dudley L. McCaw, James K. Roush, Jerome C. Nietfeld, Melinda J. Wilkerson, Kimberly Reeds, Diana Burr
Canine B-cell lymphoma is a highly treatable disease, but cost and logistical factors may hamper an owner’s ability to pursue treatment of their pet with this disease. The authors evaluated the use of single-agent doxorubicin in an intermittent fashion for efficacy in the treatment of this disease. Morphologic and clinical data were analyzed for prognostic significance. Eighteen dogs with B-cell lymphoma, all with multicentric disease, were enrolled. The overall complete response (CR) rate was 78%, median total doxorubicin remission time (TDR) was 80.5 days, and median overall survival (OS) was 169.5 days. The median number of doxorubicin doses administered was 4.5. First remission times were significantly affected by clinical stage and substage of disease. Outcome for the dogs in this study were similar to those previously reported for single-agent doxorubicin treatment. Additionally, the intermittent nature of the treatments made the described protocol more feasible for the owners who enrolled their pets in this study. Intermittent single-agent doxorubicin is not a substitute for multiagent chemotherapy protocols in the treatment of canine lymphoma; however, it is a reasonable alternative if the cost and time commitments are limiting factors for an owner.

A Prospective Evaluation of CT in Acutely Paraparetic Chondrodystrophic Dogs
Jennifer Deck Bibevski, Mark Daye, Todd D. Henrickson, Todd W. Axlund
The clinical usefulness of computed tomography (CT) as a sole diagnostic modality in identifying disc lesion(s) in chondrodystrophic breeds presenting with acute signs of intervertebral disc disease (IVDD) is incompletely characterized. CT was used prospectively to determine the validity of this tool. Neurologic examinations and CT scans were performed on all dogs at presentation. Surgical decompression was based on those findings. Clinical follow-up examinations were performed on days 1 and 14 postsurgically. CT detected a lesion consistent with clinical findings in 63 of 69 cases (91%). All 63 dogs with Hansen type I IVDD lesions were identified on CT alone. The surgeon and radiologist agreed on lesion level in 72 of 78 lesions (92%) and lateralization in 71 of 78 lesions (91%). Improvement in neurologic grade was documented in 60 of 69 dogs (87%) by 14 days. CT imaging can be used as a single imaging modality in chondrodystrophic dogs presenting with acute paresis. CT used in this manner is a reliable and noninvasive tool for detecting spinal compression secondary to IVDD in chondrodystrophic dogs.

Hypercalcemia of Malignancy Associated with Renal Cell Carcinoma in a Dog
Christine H. Merrick, Stephanie E. Schleis, Annette N. Smith, Courtney L. Mallett, Emily C. Graff, Calvin Johnson
A 10 yr old castrated male Siberian husky was evaluated for polyuria, polydipsia, a retroperitoneal mass, and urolithiasis. A marked elevation in Ca was noted on initial blood work, and results of additional testing were consistent with hypercalcemia of malignancy, including an elevated parathyroid hormone-related peptide (PTHrp) value. Based on clinical signs, blood work, diagnostic imaging, and cytology results, unilateral renal neoplasia was suspected. Following a complete right nephrectomy and cystotomy, histopathologic examination confirmed a diagnosis of renal cell carcinoma (RCC). Five days postoperatively, the hypercalcemia had nearly resolved and the PTHrp was zero. This is the first reported case of hypercalcemia of malignancy associated with RCC in a dog.

Chronic Compressive Myelopathy and Progressive Neurologic Signs Associated with Melarsomine Dihydrochloride Administration in a Dog
Sarah A. Moore, Christopher L. Mariani, Arnaud Van Wettere, Luke B. Borst
A 7 yr old castrated male Great Dane presented with a history of progressive myelopathy following the intramuscular injection of melarsomine dihydrochloride 8wk previously. MRI revealed paraspinal and epidural abscesses at the 13th thoracic (T13) and first lumbar (L1) disc space. The dog’s condition worsened despite medical management, necessitating surgical decompression. Surgical decompression resulted in rapid improvement of the patient’s clinical signs. Histopathologic evaluation of the lesions revealed pyogranulomatous inflammation. Cultures of fluid and tissue within the lesions were negative for bacterial growth, and no infectious organisms were visualized histologically. Melarsomine-associated neurologic signs can be chronic and progressive in nature, presumably secondary to ongoing sterile inflammation that may result in spinal cord compression.

Canine Vaginal Leiomyoma Diagnosed by CT Vaginourethrography
A 13 yr old female spayed Labrador retriever presented for vulvar bleeding. Abdominal radiographs revealed a soft tissue mass in the ventral pelvic canal. A computed tomography (CT) exam and a CT vaginourethrogram localized the mass to the vagina, helped further characterize the mass, and aided in surgical planning. A total vaginectomy was performed and the histologic diagnosis was leiomyoma. Vaginal tumors make up 1.9–3% of all tumors. Seventy-three percent of vaginal tumors are benign, and 83% of those are leiomyomas. Leiomyomas often have a good long-term prognosis with surgical resection. The diagnostic investigation of this case report utilized a multimodal imaging approach to determine the extent and respectability of the vaginal mass. To the best of the authors’ knowledge, this is the first report describing a CT vaginourethrogram.

**Cardiac MRI Findings in a Dog with a Diffuse Pericardial Mesothelioma and Pericardial Effusion**

Ricardo Guillem Gallach, Wilfried Mai

Veterinary cardiac MRI (cMRI) is a relatively new technique. A dog with recurrent pericardial effusion and a questionable right atrial mass lesion on echocardiography underwent cMRI. cMRI provided excellent anatomic information about the heart and surrounding structures and helped to rule out the presence of a focal mass. A diffuse thickening and enhancement of the pericardium was detected. Pericardiectomy was performed and histopathology revealed a diffuse pericardial mesothelioma. This case illustrates the potential of cMRI in the management of patients with pericardial effusion when echocardiographic findings are equivocal and illustrates cMRI findings in a case of diffuse pericardial mesothelioma.

**Pituitary Metastasis of Pancreatic Origin in a Dog Presenting with Acute-Onset Blindness**

Rodrigo Gutierrez-Quintana, Inc’s Carrera, Melanie Dobromylskij, Janet Patterson-Kane, Maria Ortega, Annette Wessmann

Pituitary metastases have rarely been recorded in dogs, and to date, none of those reported have been of pancreatic origin. MRI findings are available for only one of those cases. Herein the authors present an 11 yr old English springer spaniel diagnosed with pituitary metastasis of pancreatic origin with a 24 hr history of blindness and only a single lesion on MRI. Neurologic and ophthalmologic examinations localized the lesion to the optic nerves, optic tracts, or optic chiasm. MRI showed a single lesion characterized by a well-circumscribed pituitary mass with extrasellar extension, causing compression of the optic chiasm. Signal intensity was unusual as enhancement could not be appreciated after contrast administration. The dog was euthanized without further diagnostic tests. Histopathologic examination revealed a poorly differentiated exocrine pancreatic carcinoma with widespread metastasis involving the pituitary gland. To the authors’ knowledge, this is the first such case reported in a dog. Pituitary metastases should be included as a differential diagnosis for dogs presenting with acute-onset blindness and for single brain masses affecting the pituitary gland.

**GH Deficiency in a Dalmatian Puppy with Megaesophagus**

Kyu-Deok Cho, Ji-Houn Kang, Sung-Jun Noh, Dongwoo Chang, Ki-Jeong Na, Eui-Bae Jeung, Mhan-Pyo Yang

An 8 wk old female Dalmatian weighing .56 kg presented with growth retardation. The puppy exhibited no abnormalities during physical examination other than significantly reduced growth compared with her littermates. Endocrine results suggested pituitary dwarfism. Two wk later, the puppy returned due to the onset of megaesophagus, but the puppy unfortunately died the following morning. This case report describes the diagnosis of dwarfism in a Dalmatian puppy that was caused by growth hormone (GH) deficiency and describes its early clinical manifestations.

**Clinicopathologic and MRI Characteristics of Presumptive Hypertensive Encephalopathy in Two Cats and Two Dogs**

Jeremy O’Neill, Marc Kent, Eric N. Glass, Simon R. Platt

Two dogs and two cats were evaluated for the acute-onset of abnormal mentation, recumbency, and blindness. All cases had systemic hypertension, ranging from 180 mm Hg to 260 mm Hg. MRI of the brain disclosed noncontrast-enhancing, ill-defined, T2-weighted (T2W) hyperintensities in the white matter of the cerebrum in the areas of the frontal, parietal, temporal, and occipital lobes. Lesions were also observed in the caudate nuclei and thalamus (n ¼ 1 in each). Intracranial hemorrhage was observed in one animal. Diffusion-weighted imaging (DWI) was consistent with vasogenic edema in two animals. Retinal lesions were observed in three animals. Hypertension was secondary to renal disease in three animals. A primary underlying disorder was not identified in one animal. Normalization of blood pressure was achieved with amiodipine either alone or in combination with enalapril. In one cat, hypertension spontaneously resolved. In three cases, neurologic improvement occurred within 24–48 hr of normalization of blood pressure. The presumptive diagnosis of hypertensive encephalopathy was supported by the MRI findings and neurologic dysfunction coincident with systemic hypertension in which the neurologic dysfunction improved with treatment of hypertension. The prognosis...
appears good for the resolution of neurologic deficits with normalization of blood pressure in animals with hypertensive encephalopathy.

**Iatrogenic Pneumothorax Associated with Inadvertent Intrapleural NGT Misplacement in Two Dogs**
Juliet Gladden

This case report presents two cases of inadvertent intrapleural nasogastric tube (NGT) misplacement with consequent creation of a bronchopleural fistula and the development of an iatrogenic pneumothorax in dogs. Due to the simplicity and relative ease of NGT placement and the lack of reported life-threatening complications in the veterinary literature, the serious risks associated with this procedure are often overlooked. Although pulmonary complications with NGT misplacement have been previously reported in the human literature, serious and potentially fatal complications have not been currently described in veterinary patients. Both of the cases described herein were medically managed with successful outcomes; however, one case was associated with significant morbidity.

**Veterinary Clinics of North America (Nov/Dec)**

**Clinical Approach to Advanced Renal Function Testing in Dogs and Cats**
Barrak M. Pressler

**KEY POINTS**
- Advanced renal function tests may allow earlier detection of reduced renal functional mass and localization of damage to a particular nephron segment, and are required for diagnosis or exclusion of some causes of kidney injury.
- Measurement of glomerular filtration rate (GFR) allows for precise quantitative assessment of remaining filtration and excretion ability by the kidneys.
- Spot samples of simultaneously collected urine and plasma provide clinically reasonable approximations of total daily urine electrolyte excretion.
- The majority of plasma albumin is size and charge excluded from the ultrafiltrate; glomerular damage results in increased filtration of albumin and excretion into the urine. Microalbuminuria may be detected prior to positive reactions on standard urine protein dipstick pads, and before the urine protein:creatinine (UPC) ratio increases above reference range.
- Urinary N-acetyl-b-D-glucosaminidase (NAG):creatinine ratio is increased in dogs with chronic kidney disease, pyelonephritis, uncontrolled diabetes mellitus, pyometra, or X-linked hereditary nephropathy but does not differ before versus after control of hyperadrenocorticism with trilostane or transphenoidal hypophysectomy.

**A Laboratory Diagnostic Approach to Hepatobiliary Disease in Small Animals**
Seth E. Chapman, Roger A. Hostutler

**KEY POINTS**
- Liver enzymes can be classified as leakage or induction enzymes; although they are sensitive indicators for detection of disease and/or cholestasis, they often are not specific for a primary cause.
- Increased serum enzyme activities can occur in clinically normal animals, and in animals with hepatic and nonhepatic disease.
- Serum bile acids and ammonia can be measured to evaluate hepatic function.
- Detection of other biochemical abnormalities, such as hypoproteinemia, hypoglycemia, or hypocholesterolemia, may be useful. However, these analytes are often not sensitive indicators of liver disease.

**Diagnosis of Small Intestinal Disorders in Dogs and Cats**
Karin Allenspach

**KEY POINTS**
- A serum albumin concentration of less than 2 g/L is an indicator of poor prognosis in dogs with inflammatory bowel disease (IBD).
- Cobalamin should be supplemented in all cases with decreased serum cobalamin concentrations.
- Increased canine pancreatic lipase in dogs with IBD is associated with a worse outcome.
- In cases of suspected intestinal lymphoma, polymerase chain reaction for antigen receptor rearrangements and immunophenotyping by flow cytometry or immunohistochemistry should be used in conjunction with clinical signs to help establish a diagnosis.
- Evaluation of intestinal biopsies for expression of CD11c using immunofluorescence may be a helpful diagnostic test for IBD in dogs.
- Genetic testing for mutations in innate immunity receptors is available for German Shepherd dogs, and could become a useful test for other breeds of dogs in the future.
**Practical Interpretation and Application of Exocrine Pancreatic Testing in Small Animals**

Caroline Mansfield

**KEY POINTS**
- A positive specific canine pancreatic lipase (spec-cPL) or SNAP-cPL in dogs should be considered in conjunction with other clinical signs and diagnostic imaging to ensure acute pancreatitis is the main cause of the clinical presentation.
- A negative spec-cPL or SNAP-cPL result means acute pancreatitis is unlikely to be the cause of the dog’s presenting signs.
- Serum canine pancreatic elastase-1 (cPE-1) has a high specificity (92%) for the diagnosis of pancreatitis; increases in serum cPE-1 are more likely to be seen in severe acute pancreatitis.
- Feline acute pancreatitis is best diagnosed by a combination of clinical signs, feline pancreatic lipase immunoreactivity, and abdominal ultrasound.
- Close evaluation of cats with pancreatitis for concurrent disease is essential.
- Chronic pancreatitis is difficult to diagnose with laboratory testing.
- Pancreatic cytology may be of benefit in diagnosing pancreatic neoplasia.

**Using Cardiac Biomarkers in Veterinary Practice**

Mark A. Oyama

**KEY POINTS**
- Blood-based assays for cardiac biomarkers can assist in the diagnosis of heart disease in dogs and cats.
- The most established applications are differentiation of cardiac versus noncardiac causes of respiratory signs and the detection of preclinical cardiomyopathy.
- Cardiac biomarkers are best used as part of the overall clinical cardiac workup that includes the medical history, physical examination, electrocardiogram, thoracic radiographs, and echocardiography.
- The selection of proper patient populations in which to test is key to obtaining reliable results.
- Future applications might include the use of cardiac biomarkers to help guide therapy and improve patient outcomes.

**Practical Acid-Base in Veterinary Patients**

Andrea A. Monnig

**KEY POINTS**
- Acid-base assessment can be quickly and easily performed in veterinary patients.
- Rapid recognition of acid-base disorders can aid clinicians in developing a diagnostic and therapeutic plan, as well as monitor response to therapy.
- Four primary acid-base disturbances exist when using traditional means of acid-base interpretation: metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis.
- Compensation for a primary acid-base disturbance is expected within a set time frame.
- Mixed disturbances may be present if PCO2 and HCO3 are moving in opposite directions, pH is normal despite abnormalities in PCO2 or HCO3, the pH change is more significant than what is predicted for the primary disturbance, or the patient fails to mount the expected compensatory response.

**Use of Lactate in Small Animal Clinical Practice**

Leslie C. Sharkey

**KEY POINTS**
- Lactate concentration is used as an indicator of tissue hypoperfusion and hypoxia, particularly in critical care or perioperative settings.
- Lactate concentration is used to determine the severity of an underlying disorder, assess response to therapy, and predict outcome, especially if serial lactate levels are measured.
- Decreasing levels of lactate suggest improvement, whereas prolonged increases in lactate concentration imply deterioration with a poor prognosis.
- Repeated lactate concentrations should be determined on the same instrument with close attention to sample collection and processing and adherence to recommendations for instrument quality control.

**Hypocalcemia of Critical Illness in Dogs and Cats**

Marie K. Holowaychuk

**KEY POINTS**
- Hypocalcemia is an important electrolyte disturbance in critically ill dogs and cats best detected by measuring ionized calcium, the biologically active form, rather than total or adjusted calcium.
Hypocalcemia is associated with certain medications and treatments commonly administered to critically ill patients, as well as with various underlying diseases such as acute kidney disease, pancreatitis, parathyroid disease, sepsis, and trauma.

Suggested underlying mechanisms include hypovitaminosis D, acquired or relative hypoparathyroidism, or hypomagnesemia, as well as alterations in the ionized fraction of calcium caused by changes in chelated or protein-bound calcium.

If severe or acute, hypocalcemia can cause obvious clinical signs of hyperexcitability, including tremors, twitching, spasms, or seizures, or more subtle signs related to cardiovascular collapse.

Emergency treatment with calcium gluconate is recommended when clinical signs are present or if there is moderate to severe ionized hypocalcemia.

**Diagnosis of Disorders of Iron Metabolism in Dogs and Cats**

Andrea A. Bohn

**KEY POINTS**

- Serum iron concentration is often not an accurate reflection of body iron stores.
- Serum iron concentration decreases with inflammation and iron deficiency.
- Ferritin is currently the best assay for body iron stores.
- Low ferritin indicates iron deficiency; normal ferritin does not rule it out.
- Care must be taken when interpreting levels of ferritin and transferrin because they are acute-phase proteins and inflammation can affect results.
- On a hemogram, MCVretic and CHretic may indicate iron deficiency before MCV and mean cell hemoglobin concentration.

**Making Sense of Lymphoma Diagnostics in Small Animal Patients**

Mary Jo Burkhard, Dorothee Bienzle

**KEY POINTS**

- Cytologic assessment is diagnostic in most cases of diffuse large B-cell and diffuse lymphoblastic lymphoma in dogs.
- The cytologic diagnosis of lymphoma is more challenging in cats than in dogs.
- Although cytology is useful for staging lymphoma, histopathology is necessary for classification and grading.
- Immunophenotyping by flow cytometry allows evaluation of lymphocyte populations using a panel of antibodies, and serves as an adjunctive tool for both diagnosis and prognosis.
- Polymerase chain reaction (PCR) to detect clonal antigen receptor gene rearrangement (PARR) is a relatively new test in veterinary medicine that has strong potential for supporting the diagnosis of lymphoma. However, false-positive and false-negative results may confound the diagnosis, and PARR is less sensitive in cats than in dogs.
- Immunohistochemistry and immunocytochemistry should not be used as stand-alone diagnostic techniques, nor should an interpretation be based on a single antibody label.

**Current Diagnostic Trends in Coagulation Disorders Among Dogs and Cats**

Marjory B. Brooks, James L. Catalfamo

**KEY POINTS**

- Include hemostatic defects in the initial differential diagnosis of patients with signs of hemorrhage.
- Collect appropriate samples for platelet count and coagulation panel early in the diagnostic workup. Remember that sample quality is critical for valid results.
- Use results of initial screening tests and patient response to guide further testing.
- New techniques such as flow cytometry, thrombin-generation assays, thrombelastography, and anticoagulant drug monitoring are under investigation for veterinary patients; however, their ability to improve diagnosis or treatment requires further study in clinical trials.

**Molecular Diagnostics for Infectious Disease in Small Animal Medicine: An Overview from the Laboratory**

Joshua B. Daniels

**KEY POINTS**

- The term “molecular diagnostics” refers to tests that detect nucleic acid (DNA/RNA).
- Real-time polymerase chain reaction (PCR) (ie, quantitative PCR) allows increased sensitivity and specificity compared with conventional PCR.
- Knowing the conditions under which tests are clinically validated has implications for choosing sample types and selecting transport media in which to convey the sample to the laboratory.
The core pedigree (16 diabetic cats) was 0.049, and mean unaffected parents sometimes produced always skipped at of fully or genes causing diabetes are autosomal ra

Males (n = 14) and females (n = 5) were both affected, suggesting that the gene or genes causing diabetes are autosomal rather than sexlinked. Examination of the pedigree revealed few signs of fully penetrant dominant gene action: diabetes was ostensibly rarely seen in sequential generations and nearly always skipped at least one and often more generations; apparently unaffected offspring of apparently unaffected parents sometimes produced affected progeny. The mean relatedness of the affected animals within the core pedigree (16 diabetic cats) was 0.049, and mean inbreeding 0.033. Based on 100,000 permutations of the trait values, the expected relatedness of a random sample of 16 animals taken from the phenotyped animals

Using Cytology to Increase Small Animal Practice Revenue
Joanne Hodges

KEY POINTS
- Cytology is a readily available, practical test for use in general and specialty practice.
- Most tissues are amenable to routine sampling methods.
- Knowledge about specific tissue-sampling or lesion-sampling methods can improve specimen quality for cytology interpretation.
- Cytology generates revenue whether performed in-house or sent to reference laboratory for expert evaluation.
- Clear client communication about goals, expectations, and plans for using cytology in the diagnosis and treatment of each patient is important.
- Microscopic review of each cytology specimen should be performed in an organized fashion with assessment for cellularity, quality, and any potential artifacts.

The New Zealand Veterinary Journal (Nov/Dec)

Effects of tramadol or morphine in dogs undergoing castration on intraoperative electroencephalogram responses and post-operative pain
K Kongara, JP Chambers, CB Johnson and VSR Dukkipati

AIM: To compare the effects of pre-operatively administered tramadol with those of morphine on electroencephalographic responses to surgery and post-operative pain in dogs undergoing castration.

METHODS: Dogs undergoing castration were treated with either pre-operative morphine (0.5 mg/kg S/C, n = 8) or tramadol (3 mg/kg S/C, n = 8). All dogs also received 0.05mg/kg acepromazine and 0.04 mg/kg atropine S/C in addition to the test analgesic. Anaesthesia was induced with thiopentone administered I/V to effect and maintained with halothane in oxygen. Respiratory rate, heart rate, end-tidal halothane tension (EtHal) and end-tidal CO2 tension (EtCO2) were monitored throughout surgery. Electroencephalograms (EEG) were recorded continuously using a three electrode montage. Median frequency (F50), total power (Ptot) and 95% spectral edge frequency (F95) derived from EEG power spectra recorded before skin incision (baseline) were compared with those recorded during ligation of the spermatic cords of both testicles. Post-operatively, pain was assessed after 1, 3, 6 and 9 h using the short form of the Glasgow composite measure pain scale (CMPS-SF). RESULTS: Dogs premedicated with tramadol had higher mean F50 (12.2 (SD 0.2) Hz) and lower Ptot (130.39 (SD 12.1) µv2) compared with those premedicated with morphine (11.5 (SD 0.2) Hz and 161.8 (SD 15.1) µv2, respectively; p<0.05) during ligation of testicle 1. There were no differences in EEG responses between the two treatment groups during ligation of testicle 2 (p>0.05). The F95 of the EEG did not differ between the two groups during the ligation of either testicle (p > 0.05). Post-operatively, no significant differences in the CMPS-SF score were found between animals premedicated with tramadol and morphine at any time during the postoperative period. No dog required rescue analgesia. CONCLUSION AND CLINICAL RELEVANCE: Tramadol and morphine administered pre-operatively provided a similar degree of post-operative analgesia in male dogs at the doses tested.

Investigation of diabetes mellitus in Burmese cats as an inherited trait: a preliminary study
CA O’Leary, DL Duffy, MA Gething, C McGuckin and JS Rand

AIM: To investigate, in a pilot study, a possible genetic component to type 2 diabetes mellitus (T2D) in Burmese cats in New Zealand by analysing pedigree data. METHODS: Pedigrees were obtained for 305 Burmese cats living in New Zealand; diabetes was diagnosed in 19 of these due to presence of polyuria and polydipsia, persistent concentrations of glucose in plasma >16 mmol/L and glucosuria prior to insulin treatment. Pedigrees were also submitted for 16 cats with no clinical signs of T2D. The remaining 270 cats were unobserved relatives of these individuals. Inbreeding coefficients and heritability were calculated, and a single major locus model segregation analysis was conducted using pedigree analysis software. RESULTS: Nineteen cats were diagnosed with T2D. Males (n = 14) and females (n = 5) were both affected, suggesting that the gene or genes causing diabetes are autosomal rather than sexlinked. Examination of the pedigree revealed few signs of fully penetrant dominant gene action: diabetes was ostensibly rarely seen in sequential generations and nearly always skipped at least one and often more generations; apparently unaffected offspring of apparently unaffected parents sometimes produced affected progeny. The mean relatedness of the affected animals within the core pedigree (16 diabetic cats) was 0.049, and mean inbreeding 0.033. Based on 100,000 permutations of the trait values, the expected relatedness of a random sample of 16 animals taken from the phenotyped animals.
would be 0.013 (SD 0.007) (permutation p = 0.0009). The observed inbreeding was also significant (permutation p = 0.02). Heritability was estimated to be 9 (95% CI = 0–57)% assuming all animals with unknown status were unaffected. The best fitting genetic model was a major gene model with dominant expression with the risk allele frequency at 15% with 60% penetrance.

Sarcomatoid renal cell carcinoma with scant epithelial components in an Angora cat
MY Gulbahar, HH Arslan, A Gacar, MO Karayigit, O Nisbet, H Albayrak and YB Kabak
CASE HISTORY: A 6-year-old, neutered, female Angora cat presented with a history of lethargy and anorexia for 2 months and a clinically palpable and gradually enlarging, solid mass in the abdominal cavity extending from the last costal arch to the pelvic cavity. CLINICAL FINDINGS: Examination of the cat revealed jaundice, dehydration and hypothermia. Haematological manifestations included lymphopenia and substantial decrease in haematocrit value. Biochemical analysis of the blood revealed hypoglycaemia, three-fold elevated blood urea nitrogen values, increased level of serum aspartate aminotransferase and increased total bilirubin while the creatinine level was normal. Ultrasonographic examination of the abdomen showed a disrupted and large hypoechoic area around the left kidney. The cat was anaesthetised and the left kidney was removed, but the cat died following surgery. PATHOLOGICAL FINDINGS: On post-mortem examination, the left kidney was markedly enlarged and both the cortical and medullary parenchyma were replaced by confluent, multilobulated, pale tan-white, firm nodular masses protruding above the capsular surface. Metastasis was not observed. Cytological examination revealed a population of spindleshaped cells of variable size, with abundant coarse chromatin and occasionally prominent nucleoli. Initial sections of the kidney were indicative of undifferentiated sarcoma confirmed by immunohistochemistry revealing vimentin-positive and cytokeratin-negative results in all tumour tissues. Additional sections showed very small amounts of both cytokeratinpositive and vimentin-positive areas. DIAGNOSIS: Sarcomatoid renal cell carcinoma (SRCC) with scant epithelial components originating from left kidney.

Journal of Feline Medicine and Surgery

Introduction to endoscopy in the cat: Where to start? What to buy?
Elise Robertson and Philip Lhermette
Practical relevance: For many years, endoscopy and minimally invasive surgery have been considered ‘standard’ in human healthcare. With the expansion of the used medical equipment market, and the falling cost of new equipment, veterinary practitioners are now starting to appreciate first-hand the benefits of performing endoscopic procedures: for example, vastly improved visualisation of the surgical site, reduced tissue trauma, minimal postoperative pain and faster recovery times, especially in feline patients. In addition, clients almost always choose a less invasive procedure if the capabilities are present, and will often consent to these procedures sooner than they would to conventional surgery. Aim: This article aims to guide the general feline practitioner towards a basic understanding of endoscopic and ancillary equipment, and in the direction of appropriate training required to perform routine endoscopic procedures. Evidence base: The authors draw on information provided in a combination of published texts, articles, reviews and their own clinical experience to provide a practical information guide for the clinician interested in feline endoscopy.

Gastrointestinal Endoscopy In The Cat: Equipment, techniques and normal findings
Christiane Stengel, Elise Robertson, and Reto Neiger
Practical relevance: Feline gastrointestinal (GI) endoscopy is in high demand, particularly by cat owners already aware of the clinical benefits and availability of this procedure within the human healthcare system. This article will provide a basic introduction to GI flexible endoscopy, covering important aspects of endoscope selection, clinical indications, and basic techniques required to perform a thorough and diagnostically meaningful examination in the cat. Clinical challenges: Challenges associated with implementing endoscopy in GI tract investigations can include lack of appropriate/suitable-sized equipment to perform a thorough examination in the cat, insufficient operator training/understanding in how to ‘drive the scope’ through the GI tract, and/or lack of confidence in differentiating normal from abnormal. Audience: This article is intended to familiarize and motivate the feline practitioner to develop basic endoscopic skills. Clinical proficiency can only be obtained through use of appropriate equipment, formal training and hours of practice indistinguishin normal from abnormal. Evidence base: The guidance contained in this article is based on a combination of the published literature, the authors’ personal experience and the experience of colleagues.

Gastrointestinal endoscopy in the cat: Diagnostics and therapeutics
Reto Neiger, Elise Robertson, and Christiane Stengel
Practical relevance: Endoscopic examination of the feline gastrointestinal (GI) tract is a minimally invasive method for obtaining biopsy samples of the GI mucosa, which is often necessary for a diagnosis of chronic GI...
diseases. In addition endoscopy has several therapeutic indications including foreign body retrieval, oesophageal stricture dilation and placement of a percutaneous gastrostomy tube. Clinical challenges: Initially, practitioners must learn the subtle manipulations necessary to efficiently guide the endoscope through the GI tract to obtain biopsy samples of high diagnostic quality, and develop skills for implementing interventional procedures (eg, foreign body removal). Another challenge in mastering GI endoscopy is the ability to recognise normal from abnormal, which requires many years of practice and experience. Endoscopy is a diagnostic and interventional procedure that should be performed only in conjunction with a thorough history, physical examination, appropriate laboratory evaluation, and radiographic and/or ultrasonographic imaging. Audience: This review is intended to familiarize both the general and referral practitioner with GI endoscopy as a minimally invasive diagnostic and therapeutic intervention for the feline patient. Evidence base: The guidance contained within this article is based on a combination of the published literature, the authors’ personal experience and the experience of colleagues.

Upper Respiratory Tract Endoscopy in the Cat: A minimally invasive approach to diagnostics and therapeutics
David S Sobel
Clinical challenges: Endoscopy of the feline upper respiratory tract has always taken a bit of a back seat to exploration of the canine nose and paranasal sinuses, pharynx and trachea, due to some anatomic limitations and lack of availability of appropriate-sized equipment. Practical relevance: With proper training, however, even the inexperienced endoscopist can find that endoscopy and endoscopic surgery can be of tremendous utility in feline practice. What had previously been largely off-limits sites, in terms of direct visualization and surgical intervention, the feline rhinarium, paranasal sinuses, pharynx and trachea are now anatomic areas that can be effectively visualized in most clinical scenarios. Moreover, endoscopic surgery is now an area gaining significant appreciation for its diagnostic and therapeutic benefits. Audience: This article will not serve as a complete treatise on disease processes of the upper respiratory tract in cats, but rather is intended as a technical and instructional reference point on upper airway endoscopy for veterinary surgeons, both in first opinion as well as referral small animal practice.

Lower respiratory tract endoscopy in the cat: Diagnostic approach to bronchial disease
Jonathan D Dear and Lynelle R Johnson
Practical relevance: Respiratory endoscopy is a useful diagnostic tool to evaluate the airways for the presence of mass lesions or foreign material while allowing for sample collection for cytologic and microbiologic assessment. While bronchial disease (eosinophilic or neutrophilic) is the most common lower respiratory disease identified in cats, infectious, anomalous and neoplastic conditions can clinically mimic inflammatory bronchial disease. Diagnostic imaging is unable to define the etiology for clinical signs of cough, tachypnea or respiratory difficulty, necessitating visual evaluation and collection of airway samples. Endoscopy allows intervention that can be life-saving and also confirmation of disease, which is important given that life-long medication is likely to be required for management of inflammatory airway disease. Patient group: Cats with either airway or pulmonary disease benefit from laryngoscopy, tracheoscopy and bronchoscopy to determine an etiologic diagnosis. In the best situation, animals that require these procedures present early in the course of disease before clinical decompensation precludes anesthetic intervention. However, in some instances, these tests must be performed in unstable cats, which heightens the risk of the procedure. Cats that do not respond to empiric medical therapy can also benefit from bronchoscopic evaluation. Clinical challenges: Due to the small size of feline airways and the tendency for cats to develop laryngospasm, passage of endoscopic equipment can be difficult. Bronchoconstriction can lead to hemoglobin desaturation with oxygen and respiratory compromise. Evidence base: This article reviews published studies and case reports pertaining to the diagnostic approach to feline respiratory disease, focusing specifically on endoscopic examination of the lower airways in cats. It also discusses appropriate case selection, equipment, endoscopic techniques and visual findings based primarily on the authors’ experiences.

American Journal of Veterinary Research
Evaluation of a rapid pressor response test in healthy cats.
Objective—To evaluate angiotensin I and angiotensin II rapid pressor response tests in healthy cats. Animals—6 purpose-bred sexually intact male cats. Procedures—Telemetric blood pressure (BP) implants were placed in all cats. After 2 weeks, cats were anesthetized for challenge with exogenous angiotensin I or angiotensin II. Continuous direct arterial BP was recorded during and immediately after IV administration of boluses of angiotensin I or angiotensin II at
increasing doses. Blood pressure responses were evaluated for change in systolic BP (SBP), change in diastolic BP (DBP), and rate of increase of SBP by 4 observers.

Results—Following IV angiotensin I and angiotensin II administration, transient, dose-dependent increases in BP (mean ± SEM change in SBP, 25.7 ± 5.2 and 45.0 ± 9.1; change in DBP, 23.4 ± 4.7 mm Hg and 36.4 ± 7.8 mm Hg; for 100 ng of angiotensin I/kg and angiotensin II/kg, respectively) and rate of increase of SBP were detected. At angiotensin I and II doses < 2.0 ng/kg, minimal responses were detected, with greater responses at doses ranging from 20 to 1,000 ng/kg. A significant effect of observer was not found. No adverse effects were observed. Conclusions and Clinical Relevance—The rapid pressor response test elicited dose-dependent, transient increases in SBP and DBP. The test has potential as a means of objectively evaluating the efficacy of various modifiers of the renin-angiotensin-aldosterone system in cats. Ranges of response values are provided for reference in future studies.

Association between subcutaneous fat thickness measured on thoracic radiographs and body condition score in dogs.
Deborah E. Linder, Lisa M. Freeman, James Sutherland-Smith.
Objective—To determine whether subcutaneous fat thickness measured on thoracic radiographs was associated with body condition score (BCS) in dogs.
Animals—87 client-owned dogs (41 males and 46 females) with a median age of 10.0 years (range, 1 to 16 years) and median weight of 20.3 kg (range, 3.1 to 58.0 kg).
Procedures—Age, sex, body weight, and breed were recorded. Body condition scores (scale from 1 to 9) and muscle condition scores were assigned by a single investigator. Subcutaneous fat thickness was measured at the level of the eighth rib head on a dorsoventral or ventrodorsal radiographic view of the thorax by a single investigator. Ratios of subcutaneous fat thickness to the width of the midbody of T8 on the ventrodorsal or dorsoventral radiographic view (T8 ratio) and to the length of the midbody of T4 on a right lateral radiographic view (T4 ratio) were calculated and compared with BCS by means of the Spearman correlation method.
Results—Median BCS was 6 (range, 1 to 9), and all muscle condition scores were represented. There were significant correlations between BCS and T4 ratio ($r = 0.86$) and between BCS and T8 ratio ($r = 0.84$).
Conclusions and Clinical Relevance—Results indicated that in this population, there was a significant association between BCS and subcutaneous fat thickness measured on thoracic radiographs. Findings suggested that measuring subcutaneous fat thickness could aid in the retrospective assignment of BCS in studies involving dogs in which BCS was not recorded in the medical record.

Effect of dexamethasone or synthetic ACTH administration on endogenous ACTH concentrations in healthy dogs.
Andrew C. Bugbee, Jo R. Smith, Cynthia R. Ward.
Objective—To determine the effects of dexamethasone or synthetic ACTH administration on endogenous ACTH concentrations in healthy dogs.
Animals—10 healthy neutered dogs. Procedures—Each dog received dexamethasone (0.01 mg/kg), synthetic ACTH (5 µg/kg), or saline (0.9% NaCl) solution (0.5 mL) IV at intervals of ≥ 30 days. Plasma endogenous ACTH concentrations were measured before (baseline; time 0) and 1, 8, 12, and 24 hours after drug administration; serum cortisol concentrations were measured before and 1 hour after synthetic ACTH and saline solution administration and 8 hours after dexamethasone administration.
Results—Analysis of serum cortisol concentrations confirmed effects of drug administration. Dexamethasone significantly decreased the endogenous ACTH concentration from the baseline value at both 8 and 12 hours. Synthetic ACTH administration significantly decreased the endogenous ACTH concentration from the baseline value at 8 hours. Saline solution administration had no significant effect on endogenous ACTH concentration. Conclusions and Clinical Relevance—Dexamethasone and synthetic ACTH administered IV at doses used routinely during testing for hyperadrenocorticism caused significant but transient reductions of endogenous ACTH concentrations in healthy dogs. Thus, a 2-hour washout period following ACTH stimulation testing before collection of samples for measurement of the endogenous ACTH concentration may be insufficient. Although this effect has not been verified in dogs with hyperadrenocorticism, these data suggested that samples for measurement of endogenous ACTH concentrations should be obtained before or > 8 hours after initiation of an ACTH stimulation test or before or > 12 hours after the start of a low-dose dexamethasone suppression test.

Pharmacokinetics, bioavailability, and hemodynamic effects of trazodone after intravenous and oral administration of a single dose to dogs.
Ariane R. Jay, Ursula Krotscheck, Elizabeth Parsley; Lisa Benson; Ariel Kravitz; Abby Mulligan; Jharon Silva, Hussni Mohammed, Wayne S. Schwark.
Objective—To determine the pharmacokinetics and hemodynamic effects of trazodone after IV and oral administration in dogs and bioavailability after oral administration. Animals—6 adult Beagles. Procedures—
Dogs received trazodone HCl (8 mg/kg) orally and IV in a randomized controlled crossover design. Blood samples were collected at various times after administration. Heart rates and indirectly measured blood pressures of dogs and plasma concentrations and pharmacokinetics of trazodone were determined. Results—Following IV administration, the mean ± SD elimination half-life, apparent volume of distribution, and plasma total body clearance were 169 ± 53 minutes, 2.53 ± 0.47 L/kg, and 11.15 ± 3.56 mL/min/kg, respectively. Following oral administration, the mean ± SD elimination half-life and absolute bioavailability were 166 ± 47 minutes and 84.6 ± 13.2%, respectively. Maximum plasma concentration following oral administration was 1.3 ± 0.5 µg/mL, and time to maximum plasma concentration was 445 ± 271 minutes. After IV administration, all dogs immediately developed transient tachycardia (184.3 ± 8.0 beats/min), and 3 of 6 dogs developed aggression. Increase in heart rate was significantly associated with increase in plasma drug concentration following IV administration. Conclusions and Clinical Relevance—Results of this study indicated oral administration of trazodone resulted in acceptable absolute bioavailability, with substantial variability in time to maximum plasma concentration. Individualized approaches in dosing intervals may be necessary for dogs receiving oral trazodone. An orally administered dose of 8 mg/kg was well tolerated in dogs; IV administration of a dose of 8 mg/kg caused substantial adverse effects, including tachycardia and behavior disinhibition.

Journal of Small Animal Practice

Thoracoscopic pericardial window for management of pericardial effusion in 15 dogs.
S. Atencia, R. S. Doyle and N. T. Whiteley
Objectives; To report short-term complications and long-term outcomes of thoracoscopic pericardial window for management of pericardial effusion in dogs.
Methods; Retrospective study of dogs in which thoracoscopic pericardial window was performed using a three-cannula technique. Surgery time, complications, postoperative management, area of resected pericardium, histopathology results and outcome were evaluated. Results; Diagnoses included dogs with idiopathic pericardial effusion (n=10), cardiac mass (n=4) and mesothelioma (n=1). One case required conversion to sternotomy. Median thoracoscopic surgery time was 52 ± 5 (range, 45-80) minutes. Complications occurred in four (26%) cases. Median time to discharge was one (range, 1-6) day. Of dogs with idiopathic pericardial effusion, one is alive at 150 days, one was lost to follow-up at 180 days while eight were euthanased of which five were for unrelated reasons. All dogs with neoplastic causes died or were euthanased because of their illness. Median survival time for dogs with idiopathic pericardial effusion (635 days; range, 70-1165) was significantly longer than that for dogs with neoplasia (30 days; range, 1-107). Clinical Significance; Thoracoscopic pericardial window is of low morbidity with short surgery and hospitalisation times. It provides good long-term control of idiopathic pericardial effusion but short-term palliation of clinical signs in dogs with neoplastic disease.

Associations between obesity and physical activity in dogs: a preliminary investigation.
R. Morrison, V. Penpraze, A. Beber, J. J. Reilly and P. S. Yam
Objectives; To assess whether obesity has any association with objectively measured physical activity levels in dogs. Methods; Thirty-nine dogs wore Actigraph GT3X accelerometers (Actigraph) for 7 consecutive days. Each dog was classified as ideal weight, overweight or obese using the 5-point body condition scoring system. Total volume of physical activity and time spent in sedentary behaviour, light-moderate intensity physical activity and vigorous intensity physical activity were compared between body condition categories. Results; Valid accelerometer data were returned for 35 of 39 dogs recruited. Eighteen dogs were classed as ideal weight, 9 as overweight and the remaining 8 as obese. All dogs spent a significant proportion of the day sedentary and obese dogs spent significantly less time in vigorous intensity physical activity than ideal weight dogs (7 ±3 minute/day versus 21 ±15 minute/day, P=0.01). Clinical Significance; Obesity is associated with lower vigorous intensity physical activity in dogs, as is also thought to occur in humans. These preliminary findings will help inform a future, larger study and may also improve our understanding of the associations between obesity and physical activity in dogs.

Screening diagnostics to identify triggers in 21 cases of steroid-responsive meningitis-arteritis.
J. H. Rose and T. R. Harcourt-Brown
Objectives; To evaluate whether screening tests used to identify infectious and neoplastic triggers for immune-mediated haemolytic anaemia, in particular a complete blood count and differential, serum biochemistry profile, urine analysis (including culture), abdominal ultrasound and thoracic radiographs, can identify triggers for steroid-responsive meningitis-arteritis. Methods; Retrospective descriptive review. Results; Twenty-one steroid-responsive meningitis-arteritis cases were identified in which all screening tests had been performed. All cases had changes in complete blood count (including neutrophilia, monocytosis, lymphocytosis, eosinopenia or anaemia); 19 had changes in biochemistry (including hypoalbuminaemia,
hyperglobulinaemia, increased alkaline phosphatase activity, hyperphosphataemia, increased total calcium concentration, hypercholesterolaemia, hyperkalaemia, increased urea concentration and increased alanine aminotransferase activity); two cases had an elevated urine protein to creatinine ratio but none had positive urine culture results; no cases had abnormalities on orthogonal radiographs of the thorax; four cases had abnormalities identified on abdominal ultrasound, which following cytological examination suggested inflammation in the absence of pathological organisms. Clinical Significance; Screening tests used to identify infectious and neoplastic triggers in immune-mediated haemolytic anaemia did not isolate triggers for steroid-responsive meningoitis-arteritis in the population of dogs under investigation.

**Comparison of surgical duration of canine ovarioectomy and ovariohysterectomy in a veterinary teaching hospital.**

K. P. Harris, V. J. Adams, P. Fordyce and J. Ladlow.

Objective; To prospectively evaluate ovarioectomy and ovariohysterectomy via midline coeliotomy when being employed by supervised final year veterinary students for the purpose of routine canine neutering. Methods; One hundred and eight female dogs of various breeds, presented to a veterinary teaching hospital for neutering, were randomly allocated to one of two surgery groups, ovarioectomy or ovariohysterectomy. The specified procedure was performed by a supervised final year veterinary student. If the duration of surgery exceeded 2 hours or if major surgical or anaesthetic complications occurred, the supervising surgeon intervened to complete the procedure. Results; Data analysed included age, weight, time from first incision to start of closure, duration of closure, total surgical time and length of incision. Fifty-four dogs underwent each procedure. There was no significant difference between the two surgery groups for any of the measured variables. Clinical Significance; Ovarioectomy is not associated with shorter surgical times or smaller abdominal incisions than ovariohysterectomy when employed by inexperienced surgeons. As no major complications novel to ovarioectomy occurred in this cohort of dogs, this study adds support to the existing literature indicating that ovarioectomy is an acceptable alternative to ovariohysterectomy for canine neutering.

**Investigation of prognostic indicators for human uveal melanoma as biomarkers of canine uveal melanoma metastasis.**


Objective; To evaluate if 14 genes that discriminate metastasising and non-metastasising human uveal melanomas can differentiate metastasising and non-metastasising uveal melanomas in dogs. Methods; Nineteen archival biopsies of eyes with a histopathological classification of primary benign (n = 9) and malignant (n = 10) uveal melanoma were selected. Thoracic and/or abdominal metastases confirmed metastatic spread of the primary tumour in seven dogs during the follow-up period. Gene expression was assayed by Reverse Transcription-quantitative Polymerase Chain Reaction. Genes displaying statistically significant differences in expression between the metastasising and non-metastasising tumours were identified. Results; Four genes (HTR2B, FXR1, LTA4H and CDH1) demonstrated increased expression in the metastasising uveal melanomas. Clinical Significance; This preliminary study illustrates the potential utility of gene expression markers for predicting canine uveal melanoma metastasis. The genes displaying elevated expression in the metastasising tumours are part of a 12-discriminating gene set used in a routine assay, performed on fine needle aspirate biopsies collected without enucleation, for predicting human uveal melanoma metastasis. Further work is required to validate the results.

**Intraoperative identification of canine hepatocellular carcinoma with indocyanine green fluorescent imaging.**


Objectives; To evaluate the feasibility of high-sensitivity near-infrared fluorescence imaging with indocyanine green for intraoperative identification of hepatocellular carcinoma in dogs. Methods; Twelve hepatic nodules were surgically resected from six dogs. In each dog, 0.5 mg/kg indocyanine green was intravenously injected for 12 to 18 hours preoperatively. The hepatic nodules were investigated under laparotomy using a near-infrared fluorescence imaging light camera system prior to resection. Resected nodules were histopathologically diagnosed and their fluorescence images were evaluated. Results; Of the 12 hepatic nodules, 6 were diagnosed as hepatocellular carcinoma and 6 as nodular hyperplasia. Indocyanine green-fluorescence was observed in four large hepatocellular carcinoma nodules and one case of nodular hyperplasia, whereas it was absent in the remaining nodules. The sensitivity and positive predictive values of indocyanine green fluorescent imaging for hepatocellular carcinoma was 71.4% and 80.0%, respectively. Complete resection of the hepatic masses was achieved in all dogs. Clinical Significance; Near-infrared fluorescence imaging may be feasible for intraoperative mapping of hepatocellular carcinomas in hepatic lobes and may help increase the chance of complete resection of hepatocellular carcinoma in dogs.
Generalised peripheral oedema associated with amlodipine therapy in two dogs.
K. E. Creevy, M. A. Scuderi and A. E. Ellis
This report details two cases of adverse drug reactions to amlodipine. The first case presented with diffuse peripheral oedema and a history of amlodipine therapy. Haematology, clinical chemistry, endocrine testing, thoracic, abdominal and cardiac imaging revealed no cause for oedema. Amlodipine therapy was discontinued and oedema diminished markedly within 72 hours. The second case presented for bilateral retinal detachments secondary to systemic hypertension. Haematology, clinical chemistry, thoracic and abdominal imaging were unremarkable and amlodipine therapy was begun. Within 72 hours, diffuse peripheral oedema developed that was unresponsive to therapy and the dog was euthanised. Veterinarians should be aware of the potential serious adverse events associated with commonly used drugs; severe, diffuse oedema is a possible adverse drug event in dogs treated with amlodipine.

Traumatic tympanic bulla fracture.
J. A. Rubin, S. E. Kim and N. J. Bacon
A Pekingese dog was presented for evaluation of head trauma with ventral head and neck swelling, puncture wounds, palpable mandibular fractures, and loss of menace, severe miosis, and loss of palpebral reflex of the right eye. Computed tomography confirmed multiple mandibular and zygomatic fractures, a right ear canal avulsion, and a complete right tympanic bulla fracture with ventral displacement. The tympanic bulla fracture was managed conservatively. Topical lubrication and antibiotic ointment was prescribed for the right eye. A subtotal hemimandibulectomy was performed to address the mandibular fractures. A temporary oesophagostomy feeding tube was placed. No short-term complications developed as a result of the fractured bulla and avulsed ear canal being left in situ, and no complications were reported 18 months after the injury. To the authors’ knowledge this is the first report of a traumatic tympanic bulla fracture in the dog.

Journal of Veterinary Internal Medicine (Nov/Dec)

Diagnosis of Spontaneous Canine Hyperadrenocorticism: 2012 ACVIM Consensus Statement (Small Animal)
This report offers a consensus opinion on the diagnosis of spontaneous canine hyperadrenocorticism. The possibility that a patient has hyperadrenocorticism is based on the history and physical examination. Endocrine tests should be performed only when clinical signs consistent with HAC are present. None of the biochemical screening or differentiating tests for hyperadrenocorticism are perfect. Imaging can also play a role. Awareness of hyperadrenocorticism has heightened over time. Thus, case presentation is more subtle. Due to the changes in manifestations as well as test technology the Panel believes that references ranges should be reestablished. The role of cortisol precursors and sex hormones in causing a syndrome of occult hyperadrenocorticism remains unclear.

Evidence-Based Medicine: The Design and Interpretation of Noninferiority Clinical Trials in Veterinary Medicine
K.J. Freise, T.-L. Lin, T.M. Fan, V. Recta, and T.P. Clark
Noninferiority trials are clinical studies designed to demonstrate that an investigational drug is at least as effective as an established treatment within a predetermined margin. They are conducted, in part, because of ethical concerns of administering a placebo to veterinary patients when an established effective treatment exists. The use of noninferiority trial designs has become more common in veterinary medicine with the increasing number of established veterinary therapeutics and the desire to eliminate potential pain or distress in a placebo-controlled study. Selecting the appropriate active control and an a priori noninferiority margin between the investigational and active control drug are unique and critical design factors for noninferiority studies. Without reliable historical knowledge of the disease response in the absence of treatment and of the response to the selected active control drug, proper design and interpretation of a noninferiority trial is not possible. Despite the appeal of conducting noninferiority trials to eliminate ethical concerns of placebo-controlled studies, there are real limitations and possible ethical conundrums associated with noninferiority trials. The consequences of incorrect study conclusions because of poor noninferiority trial design need careful attention. Alternative trial designs to typical noninferiority studies exist, but these too have limitations and must also be carefully considered.

Intervertebral Disk Degeneration in Dogs: Consequences, Diagnosis, Treatment, and Future Directions
N.D. Jeffery, J.M. Levine, N.J. Olby, and V.M. Stein
Evidence of intervertebral disk degeneration (IVDD) is extremely common in dogs, and its prevalence increases with age. It has many important consequences because degeneration of the intervertebral disks often is a prelude
to disk herniation, which can injure the spinal cord, spinal nerves, or both. This review summarizes the advances in diagnosis and treatment of IVDD that have been made since the 1950s when the first detailed description of the degenerative changes was published. It also discusses new approaches to treatment of the associated spinal cord injury and new methods by which to classify injury severity that are currently under development.

Splenosystemic Shunts in Cats: A Retrospective of 33 Cases (2004–2011)
J-S. Palerme, J.C. Brown, S.L. Marks, and A.J. Birkenheuer
Background: Portosystemic shunts are uncommonly reported in cats. The majority of reports describe congenital shunts in young cats originating from the left gastric vein. Although they are only rarely reported, acquired portosystemic shunts in cats appear to be more variable in their anatomic location.
Hypothesis/Objective: To describe the signalment and disease conditions found in cats with splenosystemic shunts. Animals: Thirty-three client-owned cats with documented splenosystemic shunts.
Materials and Methods: Retrospective study. All cats with vascular communications between the splenic and left renal veins or the splenic vein and caudal vena cava diagnosed ultrasonographically between 2004 and 2011 were included. Collected data included age, breed, sex, presenting complaints, clinicopathologic data, as well as clinical diagnosis when available. Results: Splenosystemic shunts were identified in 1.3% of the cats that had an abdominal ultrasound performed during the study period. Older, spayed female cats were found to be significantly overrepresented when compared with the total population of cats having undergone ultrasound over the same time period. A large proportion of cats (42%) had a hepatopathy with the potential for associated portal hypertension. Conclusions and Clinical Importance: Neither the signalment of cats in this report nor the anatomy of their portovascular anomalies shared similarities with those cats previously identified with single-vessel shunts. The relevance and etiology of these newly described splenosystemic shunts remain elusive and warrants further investigation.

The Effect of Feeding a Renal Diet on Plasma Fibroblast Growth Factor 23 Concentrations in Cats with Stable Azotemic Chronic Kidney Disease
R.F. Geddes, J. Elliott, and H.M. Syme
Background: Fibroblast growth factor 23 (FGF-23) is a phosphatonin, which is increased in cats with azotemic CKD. Dietary phosphate restriction decreases FGF-23 concentrations in humans and rodents, but this relationship has not previously been examined in the cat. Objectives: To investigate the effect of feeding renal diet on plasma FGF-23 concentrations in cats with stable azotemic CKD. Animals: Azotemic, client-owned cats (≥9 years); 33 cats ate renal diet (RD group) and 11 cats did not eat renal diet (comparator group) over 28–56 days. Methods: Retrospective longitudinal study: Plasma FGF-23, PTH, and phosphate concentrations were measured at baseline and after 28–56 days. Cats in the RD group were classified as hyperphosphatemic (HP) or normophosphatemic (NP) based on the International Renal Interest Society targets for plasma phosphate concentration. Nonparametric tests were performed.
Results: In the HP group (n = 15), feeding renal diet was associated with a significant decrease in plasma phosphate (P = .001), PTH (P = .007), and FGF-23 (P = .008), but not creatinine concentrations (P = .91). In the NP group (n = 18), feeding renal diet was associated with a significant decrease in plasma FGF-23 (P = .006), but not phosphate (P = .48), PTH (P = .35), or creatinine concentrations (P = .10). No significant changes were seen in any parameters in the comparator group during the study period. Conclusions and Clinical Importance: Feeding renal diet is associated with reductions in plasma FGF-23 concentrations in hyper- and normophosphatemic cats with stable azotemic CKD, suggesting that dietary phosphate restriction may enable cats with CKD to maintain normal plasma phosphate concentrations in association with lower plasma FGF-23 concentrations.

Evaluation of Neutrophil Gelatinase-Associated Lipocalin as a Marker of Kidney Injury in Dogs
G. Segev, C. Palm, B. LeRoy, L.D. Cowgill, and J.L. Westropp
Background: Acute kidney injury (AKI) is a common and often fatal disorder in dogs. Hypothesis: Urine neutrophil gelatinase-associated lipocalin (NGAL)/creatinine ratio is a sensitive and specific biomarker of AKI in dogs. Animals: Ninety-four dogs.
Methods: Prospective study. Dogs were classified as follows: (1) healthy dogs, (2) dogs with lower urinary tract disorders, (3) dogs with chronic kidney disease (CKD), (4) dogs with azotemic International Renal Interest Society (IRIS) AKI Grades II–V, and (5) dogs with IRIS AKI Grade I (nonazotemic). Urinary NGAL was quantitated in each dog using an ELISA assay and concentrations were expressed as a ratio to urinary creatinine concentration from the same specimen, and designated the urinary NGAL/creatinine ratio (UNCR). Results: There was a significant difference in UNCR among the study groups (P < .001). Both the azotemic and nonazotemic AKI groups had higher UNCR when compared with all other groups (P < .001 for all pairs). There was a statistically significant difference in UNCR between dogs diagnosed with CKD compared with dogs with lower urinary tract diseases (P = .005) as well as between dogs with CKD and healthy dogs (P = .001). Receiver
operator characteristics (ROC) analysis of UNCR as an indicator of azotemic and nonazotemic AKI had an area under the ROC curve of 0.94 and 0.96, respectively. Conclusions and Clinical Relevance: NGAL/creatinine ratio is a sensitive and specific marker of AKI. It can be used to screen patients at risk for AKI and can be utilized to diagnose milder forms of AKI potentially earlier in the course of the disease.

**The Effect of an Oral Probiotic Containing Lactobacillus, Bifidobacterium, and Bacillus Species on the Vaginal Microbiota of Spayed Female Dogs**


**Background:** Recurrent urinary tract infections (UTIs) are often difficult to treat. Vaginal colonization with lactic acid producing bacteria (LAB) is associated with reduced frequency of recurrent UTIs in women. Oral probiotics might help increase the prevalence of vaginal LAB and decrease the frequency of recurrent UTIs in dogs. Hypothesis: Administration of an oral probiotic supplement containing Lactobacillus, Bifidobacterium, and Bacillus species will increase the prevalence of LAB in the vagina of dogs. Animals: Thirty-five healthy, spayed female dogs without history of recurrent UTIs. Methods: Prospective, controlled study. Enrolled dogs received an oral probiotic supplement for 14 or 28 days. A vaginal tract culture was obtained from each dog before and after oral probiotic administration. Twenty-three dogs received the oral probiotic supplement daily for a period of 14 days and 12 dogs received the oral probiotic supplement daily for a period of 28 days. Results: Lactic acid-producing bacteria were isolated from 7 of 35 dogs prior to probiotic administration. After the treatment course, 6 of 35 dogs had LAB isolated. Only one of these dogs had LAB Enterococcus caninesterini) isolated for the first time. Enterococcus caninesterini was the most common LAB isolated from all dogs in this study, although it was not included in the probiotic supplement. Conclusions and Clinical Importance: Lactic acid-producing bacteria are not a common isolate from the vaginal vault of dogs. Administration of this oral probiotic supplement for a 2- or 4-week period did not increase the prevalence of vaginal LAB in dogs.

**In Vivo Confocal Endomicroscopy of Small Intestinal Mucosal Morphology in Dogs**

M.J. Sharman, B. Bacci, T. Whittet, and C.S. Mansfield

**Background:** Confocal endomicroscopy (CEM) is an endoscopic technology that permits in vivo cellular and subcellular imaging of the gastrointestinal mucosa. Objective: To determine the feasibility of CEM to evaluate small intestinal mucosal topologic morphology in dogs and to characterize the appearance in healthy dogs. Animals: Fourteen clinically healthy research colony dogs. Methods: Experimental study. Dogs were anesthetized for standard endoscopic evaluation of the small intestine followed by CEM. Two fluorophores were used to provide contrast: fluorescein (10% solution, 15 mg/kg IV) before administration of topical acriflavine (0.05% solution) via an endoscopy spray catheter. A minimum of 5 sites within the small intestine were assessed and at each location, sequential adjustment of imaging depth allowed collection of a three-dimensional volume equivalent to an ‘optical biopsy’ CEM-guided pinch biopsies were obtained for histologic examination. Results: CEM provided high-quality in vivo cellular and subcellular images. Intravenous administration of fluorescein provided sufficient contrast to allow assessment of the vasculature, cellular cytoplasmic features and goblet cell numbers, and distribution. Topical application of acriflavine preferentially stained cellular nucleic acids, allowing evaluation of nuclear morphology. Quality of captured images was occasionally affected by motion artifact, but improved with operator experience. Conclusion and Clinical Importance: CEM provides in vivo images that allow for cellular and subcellular assessment of intestinal mucosal morphology during endoscopy. This has implications for aiding in vivo diagnosis of gastrointestinal disease.

**Evaluation of a Catalase-Based Urine Test for the Detection of Urinary Tract Infection in Dogs and Cats**


**Background:** Bacterial infection of the urinary tract is a common disorder in dogs and cats. Although microscopic examination of urine sediment is routinely used to screen for infection, this test can lack sensitivity or require expertise. A reliable in-clinic screening test would be a useful adjunct for the identification of dogs and cats with bacterial urinary tract infection (UTI). Hypothesis: That a catalase-based urine test (Accutest UriscринTM) is more sensitive screening test for UTI in dogs and cats than urine microscopic sediment examination. Animals: One hundred and sixty client-owned dogs and cats. Methods: Surplus urine from animals presented to a veterinary teaching hospital was used in this prospective observational study. A routine urinalysis, aerobic bacterial culture, and the Uriscрин test were performed on cystocentesis samples. Sensitivity and specificity with 95% confidence intervals and positive and negative likelihood ratios were calculated for Uriscрин and microscopic sediment examination using culture results as the gold standard. Results: Bacterial culture was positive in 27/165 (16.4%) samples. The sensitivity, specificity, and positive and negative likelihood ratios for the Uriscрин were 89%, 71%, 3.0, and 0.15, respectively. Sensitivity, specificity, and positive and negative likelihood ratios for urine sediment microscopic examination were 78%, 90%, 7.8, and 0.24, respectively. Conclusions and Clinical Importance: The Uriscрин is a more sensitive screening test for UTI in dogs and cats than sediment
Randomized, Controlled Trial of Budesonide and Prednisone for the Treatment of Idiopathic Inflammatory Bowel Disease in Dogs

T.L. Dye, K.J. Diehl, S.L. Wheeler, and D.S. Westfall

Background: Budesonide has been used to treat inflammatory bowel disease (IBD) in dogs, but no controlled studies have been performed to evaluate efficacy of this treatment. Objective: To compare budesonide and prednisone for induction therapy of IBD in dogs by using IBD activity index scores and evaluating frequency and severity of owner-reported adverse effects. Animals: Forty client-owned dogs with newly diagnosed idiopathic IBD were enrolled between April 2001 and January 2004; 34 dogs completed the 6 week study.

Methods: Double-blinded, randomized controlled trial. Dogs were randomized to receive either pure powder-based budesonide (1–7 kg: 2 mg PO q24h, 7.1–15 kg: 3 mg PO q24h, 15.1–30 kg: 5 mg PO q24h) or prednisone (1 mg/kg PO q12h 9 3 weeks then 0.5 mg/kg PO q12h 9 3 weeks). IBD activity index (IBDAI) scores were determined at diagnosis and after 6 weeks of treatment. Pet owners completed weekly questionnaires regarding clinical signs and incidence and severity of adverse effects. Results: Significant differences in remission rates (>75% decrease in IBDAI scores) were not observed with a remission rate of 78% in the budesonide group and 69% in the prednisone group (P = .70). Frequency of adverse effects was similar between the 2 groups. Conclusions and Clinical Importance: There was no demonstrable difference in remission rates or incidence of adverse effects between prednisone and budesonide for induction therapy of IBD in dogs.

Using Syndromic Surveillance to Estimate Baseline Rates for Healthcare-Associated Infections in Critical Care Units of Small Animal Referral Hospitals


Background: Expected rates of healthcare-associated infections (HCAI) have not been established in veterinary hospitals. Baseline rates are critically needed as benchmarks for quality animal care.

Objective: To estimate the occurrence of events related to HCAI identified using a standardized syndromic surveillance system in small animals in critical care cases at referral hospitals. Animals: Weaned dogs and cats (n = 1,951) that were hospitalized in the critical care unit of referral teaching hospitals during a 12-week period.

Methods: Multicenter, prospective longitudinal study. A survey was completed for all enrolled animals to record demographics, information about procedures and treatments that animals received, and to document the occurrence of defined nosocomial syndromes. Data were analyzed to identify risk factors associated with the occurrence of these nosocomial syndromes.

Results: Controlling for hospital of admission, 16.3% of dogs (95% confidence intervals [CI], 14.3–18.5) and 12% of cats (95% CI, 9.3–15.5) were reported to have had ≥1 nosocomial syndrome occur during hospitalization. Risk factors found to have a positive association with the development of a nosocomial syndrome were longer hospital stays, placement of a urinary catheter, surgical procedures being performed, and the administration of antulcer medications and antimicrobial drugs excluding those given perioperatively.

Conclusions and Clinical Importance: Syndromic surveillance systems can be successfully standardized for use across multiple hospitals to effectively collect data pertinent to HCAI rates and risk factors for occurrence.

SLC3A1 and SLC7A9 Mutations in Autosomal Recessive or Dominant Canine Cystinuria: A New Classification System


Background: Cystinuria, one of the first recognized inborn errors of metabolism, has been reported in many dog breeds.

Hypothesis/Objectives: To determine urinary cystine concentrations, inheritance, and mutations in the SLC3A1 and SLC7A9 genes associated with cystinuria in 3 breeds. Animals: Mixed and purebred Labrador Retrievers (n = 6), Australian Cattle Dogs (6), Miniature Pinschers (4), and 1 mixed breed dog with cystine urolithiasis, relatives and control dogs. Methods: Urinary cystinuria and aminoaciduria was assessed and exons of the SLC3A1 and SLC7A9 genes were sequenced from genomic DNA. Results: In each breed, male and female dogs, independent of neuter status, were found to form calculi. A frameshift mutation in SLC3A1 (c.350delG) resulting in a premature stop codon was identified in autosomal-recessive (AR) cystinuria in Labrador Retrievers and mixed breed dogs. A 6 bp deletion (c.1095_1100del) removing 2 threonines in SLC3A1 was found in autosomal-dominant (AD) cystinuria with a more severe phenotype in homozygous than in heterozygous Australian Cattle Dogs. A missense mutation in SLC7A9 (c.964G>A) was discovered in AD cystinuria in Miniature Pinschers with only heterozygous affected dogs observed to date. Breed-specific DNA tests were developed, but the prevalence of each mutation remains unknown. Conclusions and clinical importance: These studies describe the first AD inheritance and the first putative SLC7A9 mutation to cause cystinuria.
cystinuria in dogs and expand our understanding of this phenotypically and genetically heterogeneous disease, leading to a new classification system for canine cystinuria and better therapeutic management and genetic control in these breeds.

**Upper Airway Obstruction in Norwich Terriers: 16 Cases**


**Background:** Norwich Terriers have grown increasingly popular as show animals and pets, and awareness of respiratory problems within the breed is growing.

**Objective:** To describe components of obstructive upper airway syndrome in a nonbrachycephalic terrier breed.

**Animals:** Sixteen Norwich Terriers; 12 with and 4 without clinical signs of respiratory disease.

**Methods:** Prospective case series. Physical and laryngoscopic examinations were performed by 1 investigator in all dogs. Medical and surgical interventions were summarized and results of follow-up examination or owner reports were recorded.

**Results:** The study population was comprised of 9 females (6 intact) and 7 males (5 intact). Median age was 3.0 years (range, 0.5–11 years). Of 12 dogs presented for a respiratory complaint, physical examination was normal in 4 dogs. Laryngoscopic examination was abnormal in 11/12 dogs with redundant supra-arytenoid folds, laryngeal collapse, everted laryngeal saccules, and a narrowed laryngeal opening in most. Of 4 dogs lacking clinical signs, all had normal physical examination; however, 3/4 dogs had similar appearance of the larynx to dogs with clinical signs. Response to surgical intervention was minimal to moderate in all dogs.

**Conclusions and Clinical Importance:** Norwich Terriers suffer from an upper airway obstructive syndrome that differs from that encountered in brachycephalic breeds. Affected dogs are difficult to identify without laryngoscopic examination because of the lack of clinical signs and abnormalities in physical examination findings, despite severe airway obstruction. Care is warranted when anesthetizing Norwich Terriers because of the small size of the laryngeal opening.

**Doppler Echocardiographic Evaluation of Midventricular Obstruction in Cats with Hypertrophic Cardiomyopathy**

H.B. MacLea, J.A. Boon, and J.M. Bright

**Background:** Hypertrophic cardiomyopathy (HCM) is heterogeneous in both people and cats, with variability in the distribution of hypertrophy, hemodynamic characteristics, and Doppler echocardiographic findings.

**Objectives:** To document the Doppler echocardiographic characteristics of midventricular obstruction in some cats with HCM.

**Animals:** Eight cats with hypertrophic cardiomyopathy. Materials and Methods: Retrospective case series. The medical records of cats presenting to the cardiology service at Colorado State University between February 2009 and January 2012 were reviewed. All cats had a physical examination; Doppler systolic blood pressure measurement; and transthoracic two-dimensional (2D), M-mode, and Doppler echocardiography were performed. A more thorough evaluation of the echocardiographic images and measurements was performed. Cats included in this study had echocardiograms of adequate quality to confirm the diagnosis of midventricular obstruction by documentation of left midventricular concentric hypertrophy; a midventricular turbulent Doppler color flow pattern; and high velocity, late-peeking flow at the area of turbulence. Cats with evidence of systemic hypertension defined as a systolic Doppler blood pressure of greater than 170 mmHg were excluded. Results: All 8 cats had left ventricular hypertrophy at the level of the papillary muscles; left, midventricular hypertrophy; and in 4/8 cats there was apical hypertrophy or basilar hypertrophy of the interventricular septum. Color flow Doppler revealed turbulent flow in 8/8 cats and spectral Doppler (continuous and pulsed wave) revealed increased flow velocities and late-peeking flow profiles at the level of the left midventricle. Two of 8 cats had a bifid midventricular flow profile in which there was a midysystolic decline in left ventricular velocities with elevated velocities extending into early diastole. The peak left ventricular outflow velocity in all 8 cats was normal.

**Conclusions and Clinical Importance:** A variant of HCM characterized by hypertrophy at the level of the papillary muscles with midventricular obstruction is present in some cats. Recognition of this variant of feline HCM allows identification of HCM in cats with murmurs where the more classic features of HCM are not present.

**Effects of a Sustained-Release Form of Isosorbide Dinitrate on Left Atrial Pressure in Dogs with Experimentally Induced Mitral Valve Regurgitation**


**Background:** The effects of isosorbide dinitrate (ISDN) have not been sufficiently investigated in conscious dogs with mitral valve regurgitation (MR). Objective: The objective was to investigate the effects of a sustained-release form of ISDN (sr-ISDN) on hemodynamics and the autonomic nervous system in dogs with MR.

**Animals:** Six healthy Beagles weighing 11.2–2.2 kg (2 years of age; 2 males and 4 females) were used.
Methods: Experimental, crossover, and interventional study. Dogs with experimentally induced MR were administered placebo, 2, 5, and 10 mg/kg sr-ISDN PO on separate days with a 7-day washout period between randomized dosings. Left atrial pressure (LAP) had been recorded continuously from 30 minutes before administration of sr-ISDN to 12 hours after administration. Results: LAP was significantly decreased after administration in the 5 and 10 mg/kg groups. Significant decrease was observed at 3 and 4 hours after administration in the 5 mg/kg group. In the 10 mg/kg group, significant decrease was observed at 2, 3, 4, 5, 6, 7, 10, and 11 hours after administration. The lowest value was observed at 4 hours after administration in the 5 and 10 mg/kg groups (20.9 ± 4.2 to 15.9 ± 3.9 mmHg, P < .01, and 21.3 ± 4.0 to 13.6 ± 4.2 mmHg, P < .001).

Conclusions and Clinical Importance: Sustained-release form of ISDN showed significant decrease of LAP in the 5 mg/kg and 10 mg/kg groups, and duration of effect was dose related.

Prognostic Indicators in Cats with Hypertrophic Cardiomyopathy

Background: Left atrial (LA) enlargement, congestive heart failure (CHF), and aortic thromboembolism (ATE) are associated with decreased survival in cats with hypertrophic cardiomyopathy (HCM), but the prognostic value of echocardiographic variables has not been well characterized. Hypothesis/Objectives: We hypothesized that LA echocardiographic variables and assessment of left ventricular (LV) diastolic and systolic function would have prognostic value in cats with HCM. Animals: Two hundred eighty-two cats diagnosed with HCM. Methods: Clinical and echocardiographic records of affected cats seen at the Royal Veterinary College from 2004 to 2009 were retrospectively analyzed. Only cats with echocardiographic confirmation of LV diastolic wall thickness ≥26 mm were included. Outcomes were obtained from clinical records or referring veterinarians and owners. Results: Deaths occurred in 164 cats, of which 107 were believed to have been cardiac deaths. Univariable predictors of an increased risk of cardiac death included older age, absence of a murmur, presence of a gallop sound or arrhythmia, presentation with either CHF or ATE, extreme LV hypertrophy (≥9.0 mm), LV fractional shortening (FS%) ≤30%, regional wall hypokinesis, increased left atrial size, decreased left atrial function, spontaneous echo-contrast/thrombus or both, absence of left ventricular outflow tract obstruction, and a restrictive diastolic filling pattern. Cox’s proportional hazard analysis identified LA dysfunction, low LV systolic function, and extreme LV hypertrophy as independent predictors of decreased cardiac survival time. Conclusions and Clinical Importance: Echocardiographic measurement of LA function, extreme LV hypertrophy, and LV systolic function provides important prognostic information in cats with HCM.

Association of Dilated Cardiomyopathy with the Striatin Mutation Genotype in Boxer Dogs

Background: Myocardial disease in the Boxer dog is characterized by 1 of 2 clinical presentations, dilated cardiomyopathy (DCM) characterized by ventricular systolic dysfunction, dilatation and tachyarrhythmias, and arrhythmogenic right ventricular cardiomyopathy (ARVC) characterized by ventricular tachyarrhythmias, syncope, and sudden death. Boxer ARVC has been associated with a deletion in the striatin gene in some families. Hypothesis/Objectives: We hypothesized that both presentations represent a single disease, and the development of DCM in the Boxer is associated with the striatin deletion. Animals: Thirty-three adult Boxer dogs with DCM, 29 adult Boxer dogs with the striatin deletion and ARVC, and 16 Boxers without cardiac disease. Methods: DNA samples were evaluated for the striatin deletion. Association of the deletion with the DCM phenotype was tested by a Fisher’s exact test. T-tests were used to evaluate potential differences between the positive heterozygous and positive homozygous groups with DCM with regard to age, LVIDDD, LVIDS, and FS%. Results: Thirty of 33 dogs with DCM were positive for the striatin deletion. The striatin mutation and the positive heterozygous and positive homozygous groups with DCM with regard to age, and echocardiographic measurements. Conclusions and Clinical Importance: This study demonstrates an association between DCM in the Boxer dog and the striatin mutation, particularly with the homozygous genotype. The observation that 3/33 dogs developed DCM and lacked the striatin mutation suggests that there is at least 1 other cause of DCM in the Boxer dog.

Longitudinal Analysis of Quality of Life, Clinical, Radiographic, Echocardiographic, and Laboratory Variables in Dogs with Myxomatous Mitral Valve Disease Receiving Pimobendan or Benazepril: The QUEST Study

Background: Myxomatous mitral valve disease (MMVD) is an important cause of morbidity and mortality in dogs. Objectives: To compare, throughout the period of follow-up of dogs that had not yet reached the primary endpoint, the longitudinal effects of pimobendan versus benazepril hydrochloride treatment on quality-of-life (QoL) variables, concomitant congestive heart failure (CHF) treatment, and other outcome variables in dogs suffering from CHF secondary to MMVD. Animals: A total of 260 dogs in CHF because of MMVD.

Methods: A prospective single-blinded study with dogs randomized to receive pimobendan (0.4–0.6 mg/kg/day) or benazepril hydrochloride (0.25–1.0 mg/kg/day). Differences in outcome variables and time to intensification of CHF treatment were compared. Results: A total of 124 dogs were randomized to pimobendan and 128 to benazepril. No difference was found between groups in QoL variables during the trial. Time from inclusion to 1st intensification of CHF treatment was longer in the pimobendan group (pimobendan 98 days, IQR 30–276 days versus benazepril 59 days, IQR 11–121 days; P = .0005). Postinclusion, dogs in the pimobendan group had smaller heart size based on VHS score (P = .013) and left ventricular diastolic (P = .035) and systolic (P = .0044) dimensions, higher body temperature (P = .030), serum sodium (P = .0027), and total protein (P = .0003) concentrations, and packed cell volume (P = .030). Incidence of arrhythmias was similar in treatment groups. Conclusions and Clinical Importance: Pimobendan versus benazepril resulted in similar QoL during the study, but conferred increased time before intensification of CHF treatment. Pimobendan treatment resulted in smaller heart size, higher body temperature, and less retention of free water.

Short-Term Hemodynamic and Neuroendocrine Effects of Pimobendan and Benazapril in Dogs with Myxomatous Mitral Valve Disease and Congestive Heart Failure


Background: Pimobendan and benazepril are frequently used with diuretics to treat dogs in congestive heart failure (CHF) caused by myxomatous mitral valve disease (MMVD). Aim: To compare the short-term effects of pimobendan versus benazepril on pump function, heart size, and neuroendocrine profile in dogs with CHF caused by MMVD.

Animals: Sixteen client-owned dogs. Material and methods: Seven-day prospective single-blinded study of dogs stabilized on furosemide monotherapy, randomized to pimobendan (0.4–0.6 mg/kg/day) or benazepril (0.25–1.0 mg/kg/day). Dogs had first-pass radionuclide angiocardiography, and heart size was measured by radiography and echocardiography. Circulating neuroendocrine hormones were measured.

Results: Baseline variables did not differ between treatment groups. Greater decreases in the pimobendan than in the benazepril group were found for heart rate (P = .001), heart rate-normalized pulmonary transit time (P = .02), left atrial size (P = .03), and systolic and diastolic left ventricular diameters (P < .001 and P = .03, respectively) and volumes (P < .001 and P = .02, respectively), whereas ejection fraction increased more (P = .02) in the pimobendan group. Of the neuroendocrine hormones, only N-terminal proatrial natriuretic peptide (NT-proANP) differed (P = .04) between groups. Within groups, plasma aldosterone increased (P = .01), and NT-proANP (P = .01) and NT-proB-type (P = .02) natriuretic peptide decreased in the pimobendan group, and NT-proANP (P = .02) and plasma vasopressin (P = .01) decreased in the benazepril group. Conclusions and Clinical Importance: Pimobendan improves short-term cardiac function more than benazepril in dogs with CHF caused by MMVD. Pimobendan treatment enables the heart to work at smaller end-systolic and diastolic dimensions while maintaining adequate forward stroke volume. Some of the treatment responses found in neuroendocrine profile might have therapeutic relevance.

Transesophageal Echocardiography Guided Patent Ductus Arteriosus Occlusion with a Duct Occluder

J. Silva, O. Domenech, A. Mavropoulou, P. Oliveira, C. Locatelli, and C. Bussadori

Background: Angiography and fluoroscopy are the standard methods to guide transcatheter occlusion of patent ductus arteriosus (PDA). The use of iodinated contrast agents and radiation exposure pose risks of animals and staff. Objectives: To assess feasibility of transesophageal echocardiography (TEE) for device size selection and procedure monitoring for PDA occlusion with a duct occluder (DO) without the use of angiography. Animals: Eighty client-owned dogs with left-to-right PDA. Methods: Prospective study. Dogs with left-to-right PDA undergoing transcatheter occlusion were included. Procedures were performed without angiography and device size selection was based on TEE measurements. Procedures were monitored with simultaneous TEE and fluoroscopy and both methods were compared. Visualization of the ductus and dimensions obtained by TEE and trans thoracic echocardiography (TTE) were compared. Results: Complete PDA occlusion was achieved in 79/80 cases. TEE was consistently superior to TTE for PDA visualization and the latter showed higher values for ductal dimensions when compared to the former. TEE provided adequate procedure monitoring in 73 cases (91%). Fluoroscopy exposure time (2.77 _ 1.2 minutes (mean, SD)) was lower than previously reported for the same procedure.
Conclusions and Clinical Importance: TEE is a useful and efficient tool for device size selection and can be used for procedure monitoring in most cases. Fluoroscopy exposure time can be reduced and the use of contrast agents can be avoided. However, fluoroscopy is required in a minority of cases when TEE monitoring is not feasible or incomplete and should be available for this procedure.

**Trilostane Therapy for Treatment of Spontaneous Hyperadrenocorticism in Cats: 15 Cases (2004–2012)**
A.M. Mellett Keith, D. Bruyette, and S. Stanley

Background: Medical treatment with trilostane improves clinical signs, causes unclear insulin requirement changes, and variable survival times in cats.

Objectives/Hypothesis: To characterize the long-term efficacy of trilostane in treating cats with hyperadrenocorticism (HAC). Animals: Fifteen client-owned cats with spontaneous HAC. Methods: Multicenter descriptive retrospective study with a search performed on all medical records for cats diagnosed with spontaneous HAC. Results: Clinical signs (13 of 15 cats) and ACTH stimulation testing results (13 of 15) improved with trilostane therapy. Diabetes mellitus was reported in 9/15 cases. Insulin requirements decreased by 36% within 2 months in 6/9 diabetic cats. Median survival time was 617 days for all cats (range 80–1,278 days). Complications included weight loss, urinary tract infections, chronic kidney disease, seizures, and recurrent pancreatitis. Hypocortisolemia was documented in 1 case. Cause of death occurred as a result of nonadrenal or nondiabetic illnesses (renal failure, seizures [caused by hypoglycemia or unknown]), or lymphoma. Conclusions and Clinical Importance: Trilostane ameliorates clinical signs of HAC in cats, is tolerated well in the long term, and can lead to improved regulation of diabetes.

**Evaluation of 2 Trilostane Protocols for the Treatment of Canine Pituitary-Dependent Hyperadrenocorticism: Twice Daily versus Once Daily**
C. Arenas, C. Meli_an, and M.D. P_erez-Alenza

Background: Trilostane is the drug of choice to treat pituitary-dependent hyperadrenocorticism (PDH) in dogs, but there is still controversy about which protocol best controls the clinical signs and results of adrenal functioning test. Objectives: To compare the efficacy of twice daily (BID) versus once daily (SID) trilostane administration and to compare the safety of both protocols in the treatment of dogs with PDH. Animals: Thirty-two client-owned dogs diagnosed with PDH between 2008 and 2010 and treated with trilostane either BID or SID. Methods: In this prospective randomized study, 2 trilostane protocols were evaluated on the basis of the owner’s perception of clinical signs, on the results of laboratory tests, and on the results of the ACTH stimulation test in dogs with PDH. Dogs were followed up for a period of 1 year. Results: During the study, more dogs in the BID group had complete clinical recovery than in the SID group. However, there was no significant difference in the mean post-ACTH cortisol concentration between groups. Basal cortisol concentration at 6 months was higher in animals treated SID compared with animals treated BID. Mean total daily doses of trilostane used to control PDH, as well as adverse effects observed in the course of the study, in both groups were not statistically different. Conclusion and Clinical Importance: Adverse effects were mild using either protocol of treatment. Using trilostane BID might increase the number of dogs with a good clinical response compared with using trilostane SID.

**Activating Mutations of GNAS in Canine Cortisol-Secreting Adrenocortical Tumors**
M.M.J. Kool, S. Galac, C.G. Spandauw, H.S. Kooistra, and J.A. Mol

Background: Cushing’s syndrome or hypercortisolism is a common endocrinopathy in dogs. In approximately 15% of cases, the disorder is caused by adrenocorticotropin (ACTH)-independent hypersecretion of cortisol by an adrenocortical tumor (AT). Without other explanation, the cortisol hypersecretion has been referred to as autonomous.

Objectives: To investigate whether ACTH-independent hypersecretion of cortisol may be associated with aberrant activation of the melanocortin 2 receptor (MC2R)-cyclic AMP (cAMP)-protein kinase A (PKA) pathway. Animals: All analyses were performed on 44 cortisol-secreting ATs (14 adenomas and 30 carcinomas) derived from dogs diagnosed with ACTH-independent hypercortisolism. Methods: Mutation analysis was performed of genes encoding the stimulatory G protein alpha subunit (GNAS), MC2R, and PKA regulatory subunit 1A (PRKAR1A) in all ATs. Results: Approximately one-third of all ATs harbored an activating mutation of GNAS. Missense mutations, known to result in constitutive activation, were present in codon 201 in 11 ATs, in codon 203 (1 AT), and in codon 227 (3 ATs). No functional mutations were found in MC2R and PRKAR1A. Conclusions and Clinical Importance: Activation of cAMP signaling is a frequent event in canine cortisol-secreting ATs and may play a crucial role in both ACTH-independent cortisol production and tumor formation. To the best of our knowledge, this is the first report of potentially causative mutations in canine cortisol-secreting ATs.
Evaluation of the Oral Fludrocortisone Suppression Test for Diagnosing Primary Hyperaldosteronism in Cats
Background: Primary hyperaldosteronism (PHA) in cats is suggested by clinical signs and an elevated plasma aldosterone-to-renin ratio (ARR), but a test to confirm the diagnosis is lacking. Hypothesis: Fludrocortisone does not suppress urinary aldosterone excretion in cats with PHA, but does so in cats with arterial hypertension because of other causes. Animals: Nineteen client-owned cats with arterial hypertension because of PHA (n = 9) or other causes (n = 10). Methods: Prospective clinical study. The urinary aldosterone-to-creatinine ratio (UACR) was evaluated in morning urine before, during, and after 4 days of oral fludrocortisone administration in a dose of 0.05 mg/kg q12h. Arterial blood pressure and plasma potassium concentration were measured before and after fludrocortisone administration. Results: A basal UACR above 46.5 9 10^-9, the upper limit of the reference range, was found in 3 cats with PHA. All PHA cats had basal UACRs >7.5 9 10^-9. In all non-PHA cats with a basal UACR >7.5 9 10^-9, fludrocortisone administration induced >50% suppression. In contrast, fludrocortisone administration resulted in <50% suppression in 6 of the 9 PHA cats. Neither basal UACR, nor UACR after suppression testing, correlated with the etiology of PHA (adenoma, adenocarcinoma, or suspected bilateral hyperplasia of the zona glomerulosa). Fludrocortisone induced hypokalemia in 7 cats, but did not induce or exacerbate arterial hypertension. Conclusions and Clinical Importance: Measuring the UACR before and after 4 days of administering fludrocortisone is a practical method of confirming most cases of PHA in cats, and of substantiating the absence of PHA in cats having an ARR within the reference range.

T.E. Pancotto, J.H. Rossmesl Jr., K. Zimmerman, J.L. Robertson, and S.R. Were
Background: Intramedullary neoplasms of the canine spinal cord are infrequently reported. Objective: To describe distribution, clinicopathologic characteristics, radiographic findings, and clinical features of canine intramedullary spinal tumors. Methods: Retrospective series of histologically confirmed canine intramedullary spinal tumors. Contingency tables were generated for categorical variables (breed, sex, treatment, pain, chief complaint, localization, histology, imaging, and site). Associations were assessed by Fisher’s exact, Wilcoxon rank sum test, t-test, and one-way ANOVA.
Results: Intramedullary spinal cord tumors comprised 16% (53/331) of all tumors of the spinal cord. Primary tumors were diagnosed in 66% (35/53) of cases, with neuroepithelial-origin tumors comprising 51% (18/35) of all primary neoplasms. Intraparenchymal metastases of transitional cell carcinoma and hemangiosarcoma accounted for 66% (6/18 each) of all secondary tumors. Primary tumors were more likely to affect younger dogs. Dogs with intramedullary metastases were most commonly presented for primary myelopathic signs (8/18, 44%). The majority of all tumors (52.8%) occurred in the T3-L3 spinal cord segments. All dogs with cervical neurolocalization had primary tumors. Dogs with metastatic lesions had a shorter duration of clinical signs before presentation, but there was no difference in survival time between dogs with primary as compared with secondary tumors. Conclusions: Intramedullary spinal cord tumors are uncommon. Primary intramedullary spinal cord tumors are more common than secondary intramedullary spinal cord tumors and tend to occur in the cervical spinal cord of younger dogs. Intramedullary metastases occur in older dogs, are rarely asymptomatic, and neurologic dysfunction is a common clinical presentation. Dogs with primary tumors may have a protracted clinical course compared with those with intramedullary metastases.

Lymphoma Immunophenotype of Dogs Determined by Immunohistochemistry, Flow Cytometry, and Polymerase Chain Reaction for Antigen Receptor Rearrangements
L. Thalheim, L.E. Williams, L.B. Borst, J.E. Fogle, and S.E. Suter
Background: Immunohistochemistry (IHC), flow cytometry (FC), and PCR for antigen receptor rearrangements (PARR) are 3 widely utilized tests to determine immunophenotype in dogs with lymphoma (LSA). Objectives: This study evaluated the ability of FC and PARR to correctly predict immunophenotype as defined by IHC and to determine the level of agreement among the 3 tests. Animals: Sixty-two dogs with lymphoma. Methods: Retrospective study. Medical records were searched to identify dogs with LSA that had concurrent IHC, FC, and PARR performed. Immunophenotype results were categorized as B-cell, T-cell, dual immunophenotype (B- and T-cell), or indeterminate. The results of FC and PARR were evaluated for correctly classifying B- and T-cell LSA as compared with IHC. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated in addition to concordance between each test. Results: The sensitivity of FC was significantly higher than PARR for both B-cell (91% versus 67%; P < 0.0072) and T-cell (100% versus 75%; P < 0.0312) LSA. The percent agreement between FC and IHC was 94%, between PARR and IHC was 69%, between FC and PARR was 63%, and among all 3 tests was 63%. Conclusions and Clinical Importance: Flow cytometry is superior to PARR in correctly predicting immunophenotype when evaluating lymph nodes.
from dogs already diagnosed with B- or T-cell LSA. If fresh samples are not available for FC, PARR is an acceptable assay for determination of immunophenotype given its high specificity.

**The Prognostic Utility of Degenerative Left Shifts in Dogs**
A.G. Burton, L.A. Harris, S.D. Owens, and K.E. Jandrey

**Background:** A degenerative left shift (DLS) in dogs is reported to be a poor prognostic indicator, but no studies have been reported to verify this claim. **Hypothesis/Objectives:** To characterize the canine population affected by DLS and to determine if the presence and severity of the DLS are associated with increased risk of euthanasia or death. **Animals:** Three-hundred and nineteen dogs with DLS (cases) and 918 dogs without DLS (controls) presented to the University of California, Davis Veterinary Medical Teaching Hospital between April 1, 1995 and April 1, 2010. **Methods:** Retrospective case-control study. All cases had a CBC performed within 24 hours of presentation that showed an immature neutrophil count higher than the mature neutrophil count.

Controls were matched by year of presentation and primary diagnosis. Survival analysis was used to determine the risk of death or euthanasia associated with DLS and other potential predictors. **Results:** Half of cases versus 76% of controls were alive at discharge. Median in-hospital survival time was 7 days for cases and 13 days for controls. DLS was a significant predictor of death or euthanasia in both univariate and multivariate analysis (hazard ratio, HR, 1.9; 95% CI 1.54–2.34). **Conclusions and Clinical Importance:** DLS in dogs is associated with an increased risk of death or euthanasia. This finding, however, varies with disease diagnosis and should be interpreted in light of the individual patient.

**Masitinib-Associated Minimal Change Disease with Acute Tubular Necrosis Resulting in Acute Kidney Injury in a Dog**

**Efficacy of AST-120 in Dogs with Chronic Idiopathic Enteropathies**
M. Volkmann, N.C. Wirtherle, G.F. Beddies, and B. Kohl

**Background:** Chronic idiopathic enteropathies (CIE) in dogs are complex diseases of unknown origin. **AST-120 is a spherical carbon adsorbent preparation with a high adsorption ability for low molecular substances. Objectives:** Evaluation of the clinical efficacy of AST-120 in dogs with CIE. **Animals:** Ten client-owned dogs with mild (n = 7) to moderate (n = 3) CIE. **Methods:** Explorative, prospective, randomized, placebo-controlled, double-blinded pilot study. Dogs with chronic diarrhea and no or insufficient response to an elimination diet were included. The dogs received either AST-120 (n = 5) or placebo (n = 5) for a duration of 21 days. The canine inflammatory bowel disease activity index (CIBDAI) was used to assess disease severity at baseline and clinical outcome after 3 weeks of treatment. Furthermore, changes in body weight and the parameters stool consistency and frequency were compared within and between groups. **Results:** The mean CIBDAI score decreased from 5.6 (SD 1.5) to 2.0 (SD 1.2) in the AST-120 group (P = .125) and from 4.8 (SD .8) to 3.6 (SD 2.3) in the placebo group (P = .688). Compared with baseline, posttreatment CIBDAI scores decreased more than 60% in 4/5 dogs treated with AST-120 and in 1/5 dogs treated with placebo (P = .206).

Changes in CIBDAI scores, body weights, stool consistency, and frequency within and between groups did not achieve statistical significance after 3 weeks of treatment. No adverse effects of AST-120 were noted. **Conclusions and Clinical Importance:** This study investigated potential efficacy of AST-120 as an alternative therapy in dogs with mild-to-moderate CIE.

**Vascular Endothelial Growth Factor Concentrations in Dogs with Spirocercosis**
V. Mukerora, R.M. Kirberger, P. Mabeta, and E. Dviv

**Background:** Vascular endothelial growth factor (VEGF) is a potent proangiogenic factor associated with tumor development. Spirocercus lupi is a nematode of canids that induces an esophageal nodule that progresses to a sarcoma in 25% of cases. Determination of neoplastic transformation is challenging and usually based on endoscopy-guided biopsies under general anesthesia, an expensive procedure that often yields nondiagnostic, necrotic samples. **Hypothesis:** Circulatory VEGF concentrations are increased in dogs with neoplastic spirocercosis and can distinguish between dogs with neoplastic and nonneoplastic disease. **Animals:** A total of 24 client-owned dogs, 9 nonneoplastic, 9 neoplastic, and 6 controls. **Methods:** Case-control study. Plasma and serum VEGF concentrations at the time of diagnosis were compared with those of healthy controls. **Results:** The median plasma VEGF concentrations of dogs with neoplastic spirocercosis were 629 pg/mL (range, 282–2,366) higher than both the nonneoplastic (<39.5 pg/mL; range, <39.5–716) and control dogs (<39.5 pg/mL; all values, <39.5; P = .0003). The median serum VEGF concentration of the neoplastic dogs was 69 pg/mL (range, <39.5–212) higher than the nonneoplastic (<39.5 pg/mL; range, <39.5–44.13) and control dogs (<39.5 pg/mL; all values, <39.5; P = .001). **Conclusions and Clinical Importance:** Both plasma and serum VEGF concentrations can be used to differentiate nonneoplastic and neoplastic spirocercosis. The role of VEGF in neoplastic transformation of S. lupi-induced
nODULES AND THE POTENTIAL UTILITY OF ANTI-VEGF DRUGS IN SPIROCERCOSIS-INDUCED SARCOMA WARRANT FURTHER INVESTIGATION.

DIAGNOSTIC UTILITY OF D-DIMER CONCENTRATIONS IN DOGS WITH PULMONARY EMBOLISM
S.E. Epstein, K. Hopper, M.S. Mellema, and L.R. Johnson
Background: Pulmonary embolism (PE) is a complication of systemic disease in dogs. Antemortem diagnosis is challenging because of the lack of a confirmatory test.
Objectives: To retrospectively determine the diagnostic utility of D-dimer concentrations in dogs with necropsy-confirmed PE. Animals: Ten dogs with PE confirmed at necropsy that had D-dimer concentrations measured and 10 control dogs with D-dimer concentrations available that lacked PE on necropsy. Methods: The computerized medical record database was searched for dogs with necropsy-confirmed PE that had D-dimer concentrations measured at that visit. An age-, sex-, and breed-matched control group was identified. Signalment, location of PE, and coagulation profiles were collected. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated using a D-dimer concentration of 250 ng/mL. Results: Coagulation profiles were not different between dogs with and without PE. Using 250 ng/mL as a cut-off D-dimer concentration, the sensitivity and specificity were 80 and 30%, respectively, for the diagnosis of PE. The NPV and PPV were 60 and 53.0%, respectively. D-dimer concentration <103 ng/mL had 100% sensitivity for ruling out PE and no value was 100% specific. Conclusions and Clinical Importance: D-dimer concentrations <250 ng/mL have a high sensitivity for the absence of PE, but PE still can occur in dogs with a normal D-dimer concentration. Increased D-dimer concentrations are not specific for PE.

THE VETERINARY JOURNAL (OCTOBER JOURNAL)

CANCER VACCINES: HARNESING THE POTENTIAL OF ANTI-TUMOR IMMUNITY
Mark A. Succow
Although the presence of cancer suggests failure of the immune system to protect against development of tumors, the possibility that immunity can be redirected and focused to generate an anti-tumor response offers great translational possibility. The key to this is identifying antigens likely to be present in any given tumor and functionally critical to tumor survival and growth. Such tumor-associated antigens (TAAs) are varied and optimally should be absent from normal tissue. Of particular interest are TAAs associated with the tumor stroma, as immunity directed against the stroma may restrict the ability of the tumor to grow and metastasize. Important to directing the immune system toward an effect anti-tumor response is the understanding of how TAAs are processed and how the tumor is able to evade immune elimination. The process of immunoeediting happens in response to the selective pressure that the immune system places upon tumor cell populations and allows for emergence of tumor cells capable of escaping immune destruction. Efforts to harness the immune system for clinical application has been aided by vaccines based on purified recombinant protein or nucleic acid TAAs. For example, a vaccine for canine melanoma has been developed and approved based on immunization with DNA components of tyrosinase, a glycoprotein essential to melanin synthesis. The performance of cancer vaccines has been aided in some cases when supplemented with immunostimulatory molecules such as interleukin 2 or a novel extracellular matrix vaccine adjuvant. Vaccines with the broadest menu of antigenic targets may be those most likely to succeed against cancer. For this reason, tissue vaccines produced from harvested tumor material may offer significant benefit. With several cancer vaccines on the veterinary and human markets, efforts to understand basic tumor immunology are soon to yield great dividends.

VETERINARY APPLICATIONS OF INDUCED PLURIPOTENT STEM CELLS: REGENERATIVE MEDICINE AND MODELS FOR DISEASE?
Alberto Cebrian-Serrano, Tom Stout, Andras Dinnyes
Induced pluripotent stem cells (iPSCs) can now be derived from a tissue biopsy and represent a promising new platform for disease modelling, drug and toxicity testing, biomarker development and cell-based therapies for regenerative medicine. In regenerative medicine, large animals may represent the best models for man, and thereby provide invaluable systems in which to test the safety and the potential of iPSCs. Hence, testing iPSCs in veterinary species may serve a double function, namely, developing therapeutic products for regenerative medicine in veterinary patients while providing valuable background information for human clinical trials. The production of iPSCs from livestock or wild species is attractive because it could improve efficiency and reduce costs in various fields, such as transgenic animal generation and drug development, preservation of biological diversity, and because it also offers an alternative to xenotransplantation for in vivo generation of organs. Although the technology of cellular reprogramming using the so-called ‘Yamanaka factors’ is in its peak expectation phase and many concerns still need to be addressed, the rapid technical progress suggests that iPSCs could contribute significantly to novel therapies in veterinary and biomedical practice in the near future. This review provides an overview of the potential applications of iPSCs in veterinary medicine.
Prognosis and monitoring of leishmaniasis in dogs: A working group report
Xavier Roura, Alessandra Fondati, George Lubas, Luigi Gradoni, Michele Maroli, Gaetano Oliva, Saverio Paltrinieri, Andrea Zatelli, Eric Zini
This review presents the consensus opinion of the Canine Leishmaniasis Working Group on the prognosis and monitoring of leishmaniasis in dogs. While the prognosis for both exposed and infected dogs is considered to be favourable, this changes if infection progresses to overt disease. For clinically affected animals undergoing treatment, the prognosis is dictated by the severity of the signs (and in particular the severity of renal dysfunction) when therapy is initiated; assessing the degree of proteinuria is useful in this context. Approximately 75% of dogs without evidence of renal involvement live for >4 years if adequately treated. Monitoring the response to treatment includes ongoing clinical and clinicopathological assessment, as well as quantifying serological responses and the parasite load in the patient.

Correlations between severity of clinical signs and histopathological changes in 60 dogs with spinal cord injury associated with acute thoracolumbar intervertebral disc disease
D. Henke, M. Vandevelde, M.G. Doherr, M. Stöckli, F. Forterre
The outcome of spinal surgery in dogs with absent voluntary motor function and nociception following intervertebral disc (IVD) herniation is highly variable, which likely attests to differences in the severity of spinal cord damage. This retrospective study evaluated the extent to which neurological signs correlated with histologically detected spinal cord damage in 60 dogs that were euthanased because of thoracolumbar IVD herniation. Clinical neurological grades correlated significantly with the extent of white matter damage (P < 0.001). However, loss of nociception also occurred in 6/31 (19%) dogs with relatively mild histological changes. The duration of clinical signs, Schiff-Sherrington posture, loss of reflexes and pain on spinal palpation were not significantly associated with the severity of spinal cord damage. Although clinical-pathological correlation was generally good, some clinical signs frequently thought to indicate severe cord injury did not always correlate with the degree of cord damage, suggesting functional rather than structural impairment in some cases.

Uterine fluid from bitches with mating-induced endometritis reduces the attachment of spermatozoa to the uterine epithelium
Persistence of free fluid in the uterine lumen of bitches with endometrial hyperplasia appears to be diagnostic for mating-induced endometritis and is associated with reduced chances of pregnancy. This study investigated the possibility that reduced fertility might be associated with an effect of uterine fluid on sperm. Uterine lavage fluid was collected pre- and post-insemination from normal bitches without ultrasonographically-detectable luminal fluid (n = 4), and previously non-pregnant bitches with endometrial hyperplasia and luminal fluid (n = 4). Concentrations of polymorphonuclear neutrophils (PMNs) were measured and the effect of the fluid on the attachment of spermatozoa to the uterine epithelium was studied using medium (M) 199 as a control. To elucidate whether any effect was accounted for by the presence of PMNs, attachment was also measured in M199 with PMNs added at the concentration found in lavage fluid. Pre-insemination lavage fluid from both groups contained low concentrations of PMNs which increased post-insemination; the increase was larger for bitches with uterine fluid. Compared with M199 controls, lavage fluid reduced the attachment of spermatozoa; fluid from bitches with endometrial hyperplasia and uterine fluid had a greater effect than normal bitches, and post-insemination fluid had a greater effect than pre-insemination fluid. Spermatozoal attachment was reduced by a similar magnitude for M199 with added PMNs, although post-insemination fluid from bitches with endometrial hyperplasia reduced attachment more than M199 with added PMNs. Poor fertility in bitches with uterine luminal fluid might be partially associated with impaired attachment of spermatozoa to uterine epithelium, mediated principally, but not solely, by PMN influx into the uterine lumen.

Assessment of cerebellar pulsation in dogs with and without Chiari-like malformation and syringomyelia using cardiac-gated cine magnetic resonance imaging
Canine Chiari-like malformation (CM) is characterised by herniation of part of the cerebellum through the foramen magnum. In humans with Chiari type I malformation (CM-I), abnormal pulsation of the cerebellum during the cardiac cycle has been documented and is pivotal to theories for the pathogenesis of syringomyelia (SM). In this retrospective study, cardiac-gated cine balanced fast field echo (bFEE) magnetic resonance imaging (MRI) was used to assess pulsation of the brain in dogs and to objectively measure the degree of cerebellar pulsation with the neck in a flexed position. Overall, 17 Cavalier King CharlesSpaniels (CKCS) with CM, including eight with SM and nine without SM, were compared with six small breed control dogs. Linear regions of interest were generated for the length of cerebellar herniation from each phase of the cardiac cycle and the degree of cerebellar pulsation was subsequently calculated. Age, bodyweight and angle of neck flexion were also compared. CKCS with CM and SM had significantly greater pulsation of the cerebellum than control.
Effect of age and severity of cognitive dysfunction on two simple tasks in pet dogs

The findings suggest that mitoxantrone, vinblastine and vincristine, were significantly enhanced by combining use with BCH or LPM.

conventional anti-cancer drugs used for MGT treatment, including carboplatin, cyclophosphamide, doxorubicin, mitoxantrone, vinblastine and vincristine, were significantly enhanced by combining use with BCH or LPM. The findings suggest that LAT1 could be a new therapeutic target for canine MGT.

Big-endothelin 1 (big ET-1) and homocysteine in the serum of dogs with chronic kidney disease

Gabriele Rossi, Alessia Giordano, Sara breda, Chiara Lisi, Xavier Roura, Andrea Zatelli, Saverio Paltrinieri

This study was aimed at determining the serum concentration of homocysteine (Hcy) and big endothelin-1 (big ET-1, the precursor of endothelin) in dogs with chronic kidney disease (CKD) with and without hypertension, proteinuria and inflammation, in order to explore their role as biomarkers of hypertension associated with CKD. Hcy and big ET-1 were measured using an enzyme-linked immunosorbent assay and an enzymatic cyclic reaction, respectively, in dogs with CKD staged, as proposed by the International Renal Interest Society (IRIS), using serum creatinine, urinary protein to creatinine (UPC) ratio and systolic blood pressure, and classified as affected or not by inflammation based on the serum concentration of C-reactive protein (CRP).

Serum Hcy was significantly higher in dogs of IRIS stages II, III and IV compared with controls and in proteinuric compared with non-proteinuric dogs. No differences relating to the degree of hypertension or to the CRP concentration were found. Serum big ET-1 significantly increased in dogs of IRIS stage IV compared with controls, in proteinuric compared with non-proteinuric dogs, in dogs with severe hypertension compared with those without hypertension, and in dogs with increased CRP compared to those with normal CRP concentrations. Hcy only correlated with serum creatinine but big ET-1 significantly correlated with serum creatinine, UPC ratio, systolic blood pressure, and increased CRP. In conclusion, both Hcy and big ET-1 increase in dogs with CKD. Although further research is needed, big ET-1, but not Hcy, may also be considered as a biomarker of hypertension.

Immunohistochemical expression of Bax and Bak in canine non-neoplastic tissues

Martina Croci, Martina Dettwiler, Lloyd Vaughan, Franco Gussetti

Apoptosis is critical for embryonic development, maintenance of tissue homeostasis and protection against malignant transformation. The Bcl-2 family of proteins plays a key role in intrinsic apoptosis by controlling the integrity of the outer mitochondrial membrane, and the multidomain pro-apoptotic Bcl-2 family members Bak and Bax are essential components of this pathway. The aim of this study was to provide data on the expression of these proteins in normal canine tissues. Two antibodies against Bax recognising different conformations of the protein and one antibody against Bak were validated by immunohistochemistry and immunoblotting using canine recombinant proteins and keratinocytes treated with ultraviolet light. The antibodies were used immunohistochemically to label a wide panel of histologically normal tissues assembled on tissue microwells.

In addition, a subset of the tissues was evaluated by Western blot analysis. Immunohistochemical and Western blot analyses revealed that both Bax and Bak are widely expressed in non-neoplastic tissues from adult dogs. Immunohistochemistry showed almost exclusively cytoplasmic labelling and prominent labelling of epithelial cells. In lymph nodes, immunohistochemical labelling was diffuse for both proteins and showed enhanced intensities in the mantle zones for Bax and the germinal centres for Bak. Strong reactivity for the active conformation of Bak was detected only in enterocytes and Leydig cells and in scattered lymphocytes. These data indicate widespread expression of Bax and Bak in normal canine tissues. Knowledge of the expression of Bax and Bak in normal tissues is a prerequisite in assessing the role of these proteins in canine neoplastic disease.

L-type amino acid transporter 1 (LAT1): A new therapeutic target for canine mammary gland tumour

Shinya Fukumoto, Kiwamu Hanazono, Takahiro Komatsu, Hiroshi Ueno, Tsuyoshi Kadosawa, Hitotomo Iwano, Tsuyoshi Uchide

L-type amino acid transporter 1 (LAT1), an isoform of amino acid transport system L, transports branched or aromatic amino acids essential for fundamental cellular activities, such as cellular growth, proliferation and maintenance. LAT1 has recently received attention because of its preferential and upregulated expression in a variety of human tumours which is in contrast to its limited distribution and low-level expression in normal tissues. In this study, the feasibility of using an LAT1 inhibitor as a new therapeutic agent was explored for mammary gland tumours (MGT). [3H]-leucine uptake by CHM, a cell line established from MGT, and effects on cell growth were analysed in the presence or absence of two LAT1 inhibitors, namely, BCH (2-amino-2-norbornane-carboxylic acids) or melphalan (LPM).[3H]-leucine uptake and cellular growth activities in CHM were inhibited in a dose-dependent manner by both LAT1 inhibitors. The inhibitory growth activities of various conventional anti-cancer drugs used for MGT treatment, including carboplatin, cyclophosphamide, doxorubicin, mitoxantrone, vinblastine and vincristine, were significantly enhanced by combining use with BCH or LPM. The findings suggest that LAT1 could be a new therapeutic target for canine MGT.

Effect of age and severity of cognitive dysfunction on two simple tasks in pet dogs
Dogs exhibit age-dependent losses in learning and memory as well as a progressive accumulation of neuropathology that parallels that observed in normal human aging and early Alzheimer’s disease. These deficits have been extensively studied using a number of standard cognitive tasks in the laboratory; however, appropriate tools for their assessment in veterinary clinics are still lacking. The aim of this study was to evaluate the effect of age and the severity of cognitive dysfunction syndrome (CDS) on two simple tests conducted in a clinical setting. A food searching (FS) task and a problem-solving (PS) task were administered to young (1–4 years, n = 9), middle-aged (5–8 years, n = 10), cognitively unimpaired aged (≥9 years, n = 31), and cognitively impaired aged (≥9 years, n = 37) dogs. Cognitive status was classified using an owner-based questionnaire, and in the impaired group, dogs were categorized as either mild or severe CDS. During the FS task, younger dogs (<9 years) were able to locate the food more quickly and with more success than the aged groups (≥9 years). Dogs with severe CDS exhibited poorer performance than those with mild CDS or their healthy counterparts. In the PS task, younger dogs performed better than the aged dogs in obtaining food, but there were no differences related to CDS severity. The FS task might help to better characterize cognitively affected dogs in the clinical setting than the PS task. These and similar tasks require further investigations in the field.

Evaluation of a conjunctival swab polymerase chain reaction for the detection of Leishmania infantum in dogs in a non-endemic area
Due to the increasing numbers of dogs imported from or visiting Mediterranean countries, canine leishmaniasis has become an important infectious disease in countries where natural transmission typically does not occur. Although conjunctival swabs have recently been described as a useful diagnostic tool in endemic areas, their usefulness in non-endemic areas is unknown. The aim of this study was to evaluate the sensitivity and specificity of a conjunctival swab polymerase chain reaction (PCR) in dogs in a non-endemic area. Dogs (n = 74) that were presented for suspected canine leishmaniasis or for screening purposes after a history of travelling were prospectively included. PCR results from conjunctival swabs were compared to those from bone marrow, lymph nodes and blood and also to antibody results determined by an indirect immunofluorescence antibody test or enzyme-linked immunosorbent assay. Dogs were considered infected if bone marrow PCR, the gold standard of testing, was negative. The sensitivity and specificity of the conjunctival swab PCR were 78.4% (confidence interval [CI] 95%, 62.8–88.6) and 93.8% (CI 95%, 79.8–98.3), respectively. There was substantial agreement between PCR results from conjunctival swabs and lymph nodes (κ = 0.642), fair to moderate agreement between conjunctival swabs and bone marrow (κ = 0.483), and almost no agreement between conjunctival swabs and blood (κ = 0.070). Dogs with high antibody titres were more likely to be positive on conjunctival swab PCR than dogs with negative or doubtful antibody titres (P < 0.001). Thus, conjunctival swab PCR is a good non-invasive test to diagnose Leishmania infection in dogs in non-endemic countries.

Analytical validation of radioimmunoassays for the quantification of select pancreatic enzymes in jejunal fluid and fecal extracts from dogs
Niels Grützner, Ingrid Hang, Romy M. Heilmann, Thomas Spillmann, Jan S. Suchodolski, Jörg M. Steiner
Pancreatic enzymes, such as trypsin and lipase, are essential for the digestion of dietary components in the small intestine. Measurement of both enzymes in jejunal fluid and fecal specimens from dogs has not been reported and will be a prelude for further investigations. Therefore, the aim of the study was to validate radioimmunoassays (RIAs) for the measurement of canine trypsin-like immunoreactivity (cTLI) and pancreatic lipase immunoreactivity (cPLI) in jejunal fluid and fecal specimens from dogs. Jejunal fluid and fecal specimens were collected from five healthy Beagles. A commercial 125I-RIA was used for measuring cTLI concentrations and an in-house 125I-RIA was modified for the quantification of cPLI in jejunal fluid and fecal specimens. Both RIAs were analytically validated for canine jejunal fluid and fecal specimens by determining dilutional parallelism, spiking recovery, and intra- and inter-assay variability. For both cTLI and cPLI in jejunal fluid, observed-to-expected ratios for dilutional parallelism and spiking recovery ranged from ≥77.0% to ≤115.3% and ≥79.0% to ≤120.0%, respectively, and from ≥87.2% to ≤118.5% and ≥74.6% to ≤116.1%, respectively, for fecal specimens. Intra- and inter-assay coefficients of variation (%CV) for both cTLI and cPLI in jejunal fluid were ≤7.6% and ≤10.0%, respectively, and were ≤10.8% and ≤9.0%, respectively, for fecal specimens. Both RIAs were demonstrated to be linear, accurate, precise, and reproducible for use with jejunal fluid and fecal specimens from dogs. These results are important for the investigation of pancreatic enzyme concentrations in the gastrointestinal lumen in response to changes in dietary components.

De novo expression of human leukocyte antigen-DR (HLA-DR) and loss of beta-catenin expression in tubular epithelial cells: A possible event in epithelial–mesenchymal transition in canine renal diseases

Tubulointerstitial fibrosis (TIF) plays a central role in the progression to end-stage renal disease. Tubular epithelial cells (TECs) undergo epithelial–mesenchymal transition (EMT) and may contribute to the progression of TIF. Using immunohistochemistry, the primary aim of this study was to assess the expression of β-catenin, human leukocyte antigen-DR (HLA-DR) and vimentin in renal biopsies from dogs with spontaneous kidney diseases of varying severities. Morphological diagnosis, severity of inflammation, TIF, HLA-DR expression and clinicopathological variables were compared in dogs with renal injury to identify any potential relationship between the different factors; β-catenin down-regulation was used as a marker of EMT. Fibrosis, HLA-DR expression, serum creatinine concentration (SCR), and urine protein-to-creatinine ratio (UPC) were all increased and β-catenin expression decreased in dogs with primary glomerular disease compared with dogs with acute tubular necrosis. HLA-DR expression by TECs was positively correlated to fibrosis, inflammation, UPC, and SCR. β-catenin expression was negatively correlated to fibrosis, inflammation and HLA-DR expression. The progression of renal failure correlated closely with tubulointerstitial damage. De novo HLA-DR expression associated with β-catenin down-regulation by TECs may represent a possible step in the progression of TIF and EMT.

Evaluation of snake envenomation-induced renal dysfunction in dogs using early urinary biomarkers of nephrotoxicity

Hrovat, J.P. Schoeman, B. de Laat, E. Meyer, P. Smets, A. Goddard, S. Nagel, S. Daminet

Renal dysfunction in dogs envenomed by poisonous snakes is currently detected using traditional serum and urinary biomarkers such as creatinine and proteinuria. However, these markers lack sensitivity at the early stages of renal dysfunction and their diagnostic accuracy is affected by pre-analytical factors commonly occurring in these dogs, such as haemolysis and haemoglobinuria. Early detection of renal dysfunction would allow for the identification of dogs requiring intensive treatment and monitoring and may help inform prognosis. The aim of this study was to evaluate the performance of several novel urinary biomarkers of glomerular dysfunction, namely, urinary albumin (uAlb), immunoglobulin G (uIgG) and C-reactive protein (uCRP) and of proximal tubular dysfunction (urinary retinol binding protein (uRBP)) compared to traditional end points in dogs with renal damage caused by snake envenomation. Biomarker results were compared between 19 dogs bitten by snakes producing either neurotoxins or cytotoxins and 10 clinically healthy controls. uAlb, uIgG, and uRBP were significantly increased in snake-envenomed dogs at presentation compared to controls, whereas only uIgG and uCRP were significantly elevated 24 h post-envenomation. The urinary protein:creatinine ratio was also increased in envenomed dogs compared to controls, but because of the presence of haematuria and haemoglobinuria, differentiation between pre-renal and renal proteinuria was not possible. The results showed that these novel urinary biomarkers may assist in better detecting renal dysfunction in dogs envenomed by poisonous snakes at the acute disease stage compared to traditional laboratory endpoints.

Effect of cefovecin on the fecal flora of healthy dogs

M. Lawrence, K. KuKanich, B. KuKanich, E. Heinrich, J.F. Coetzee, G. Grauer, S. Narayanan

Cefovecin is an extended-spectrum third generation cephalosporin used to treat canine infections. The study objective was to determine the effect of cefovecin on the absolute number and antimicrobial susceptibility of fecal enteric bacteria in healthy dogs. Fourteen Beagles were randomly assigned to a treated (n=7, 8 mg/kg cefovecin subcutaneously on day 1) or untreated (n=7) group. LC/MS was used to determine plasma cefovecin concentration on day 14. E. coli, enterococci, and Salmonella were isolated and enumerated from fecal samples collected on days 0, 3, 7, 14, and 28. Antimicrobial resistance was determined using disc diffusion, MIC, and detected using PCR for the blaCMY-2 gene on select isolates. Mean plasma concentration of cefovecin on day 14 was 9.59 µg/mL in treated dogs; untreated dogs had no measurable plasma cefovecin. The absolute number of E. coli was lower in treated dogs on day 3 (P \leq 0.0001), and the absolute number of cefovecin-resistant E. coli was higher in treated dogs on days 7 (P = 0.002), 14 (P = 0.004) and 28 (P \leq 0.0001), compared to untreated dogs. Enterococci increased and were higher in the treatment group on day 7 (P = 0.0226). Isolation of Salmonella was rare. After cefovecin treatment, beta-lactam resistance was more common in fecal E. coli from treated dogs than untreated dogs, while resistance of enterococci was not altered. On day 28, treated dogs were 3.25 times more likely to carry the blaCMY-2 gene than untreated dogs (95% CI 1.27 – 8.35). The implications of these findings in clinically ill patients require further research.

Imatinib-associated tumour response in a dog with a non-resectable gastrointestinal stromal tumour harbouring a c-kit exon 11 deletion mutation

Masato Kobayashi, Shiori Kuroki, Keita Ito, Akiko Yasuda, Harumi Sawada, Kenichiro Ono, Tsukimi Washizu, Makoto Bonkobara

A 10-year-old female Miniature Dachshund with a non-resectable gastrointestinal stromal tumour was treated with imatinib. The neoplastic cells had a deletion mutation (c.1667_1672del) within exon 11 of the c-kit gene,
which resulted in deletion of three amino acids and insertion of one amino acid (p.Trp556 Val558delinsPhe) in the juxtamembrane domain of KIT. Following treatment with imatinib, the dog achieved partial remission on Day 21 with a continuous decrease in tumour size until Day 67 of treatment. Although no additional decrease in size was observed after Day 67 of treatment, the tumour remained stable in size as of Day 140 of treatment. The c-kit mutation found in the tumour cells appears to be a mutation driving oncogenesis, as evidenced by the partial remission elicited by imatinib in this dog.

Fluorescence flow cytometry methodology to exclude platelet aggregate interference when measuring feline CD4 and CD8 lymphocyte counts

JuiMing Lin, Annette Lütster
Changes in individual feline lymphocyte subsets over the course of infection, immune-mediated disease, or treatment can be used clinically to monitor disease progression. However, interference by platelet aggregates is a common problem when measuring feline lymphocyte subtype counts using flow cytometry in whole blood specimens. In this study, buffer was used to lyse red blood cells so that lymphocytes could be isolated, and then a gate containing a highly purified population of lymphocytes was characterized and fixed using fluorescence flow cytometry analysis. After tagging platelets with anti-CD61AF647 antibody to reduce aggregate interference, lymphocyte subtypes were measured using simultaneous 3-color channels with fluorescent anti-CD markers. When CD61AF647 exclusion of platelet aggregates was used, CD4%, CD8%, CD8low% and CD4:CD8 counts increased significantly (all specimens, n = 66, P < 0.001; >20% CD61 in the fixed gate, n = 21, P < 0.01). The methodology showed robust stability and precision over 3 days (n = 10 specimens), yielding average day-to-day coefficients of variation (CVs) of 2.15%, 5.01%, 7.33%, 7.77% and 9.35% for white blood cell (WBC) counts, lymphocyte counts, CD4 lymphocyte counts, CD8 lymphocyte counts and CD4:CD8, respectively.

Incidence of intraoperative hypotension during isoflurane–fentanyl and propofol–fentanyl anaesthesia in dogs

Tomoya Iizuka, Masatoshi Kamata, Masashi Yanagawa, Ryohei Nishimura
Most anaesthetic and analgesic drugs affect the cardiovascular system and can cause intraoperative hypotension (IOH). This study aimed to compare the incidence of IOH in anaesthetised dogs when isoflurane–fentanyl was used, compared to propofol–fentanyl. Intraoperative hypotension was defined as an episode of mean blood pressure below 60 mmHg for more than 5 min during anaesthesia. The incidence of IOH was 65.3% for isoflurane–fentanyl and 27.6% for propofol–fentanyl. The adjusted odds ratio for IOH when propofol–fentanyl was compared to isoflurane–fentanyl was 0.2 (95% CI 0.11–0.38). These results suggest that propofol–fentanyl is associated with a lower risk of IOH than isoflurane–fentanyl anaesthesia.

Acetylcholinesterase activity in the cerebrospinal fluid of dogs with seizures

Orit Chai, Adi Sommer, Gabriel Zimmerman, Hermona Soreq, Alon Friedman, Tali Bdoah-Abram, Itamar Aroch, Merav H. Shamir
Recent studies in animal models have focused on the role of cholinergic elements, mainly acetylcholinesterase (AChE) and the ‘readthrough’ acetylcholinesterase isoform (AChE-R), in seizures. A prospective double-masked study was conducted to assess the activity of AChE and AChE-R in cerebrospinal fluid (CSF) of 26 dogs post-seizure, 28 dogs with intervertebral disc disease (IVDD) and 16 healthy dogs. AChE was also measured in the serum in the post-seizure and IVDD groups. The results showed no significant differences in CSF AChE among the three groups. AChE-R was not detected in any dog and AChE-R in the serum was similar between groups. This preliminary study provides new information on AChE and AChE-R in the CSF and sera of dogs following naturally-occurring seizures.

Australian Veterinary Journal

Cutaneous adverse food reactions in cats: retrospective evaluation of 17 cases in a dermatology referral population (2001–2011)

LJ Vogelnest, KY Cheng
Objective To better characterise cutaneous adverse food reactions (AFR) in cats, including the diagnostic challenges. Design Retrospective evaluation of cases presenting to a dermatology referral service. Methods Cats were identified by a computerised medical record search. AFR was confirmed by clear deterioration on normal food re-challenge after completing an elimination diet, followed by improvement returning to the test diet. Prevalence, and breed, sex or age predispositions were compared with the base referral population. Patient records were reviewed for historical features, clinical presentations, concurrent dermatoses and dietary details. Results A total of 17 cats were identified with cutaneous AFR, with no breed or sex predisposition determined. Age of onset ranged from 3 months to 9 years, with a mean of 3.5 years. Prevalence...
was 6% of dermatoses and 10% of cutaneous hypersensitivities in the referral cat population. Cats typically presented with severe, perennial, non-seasonally flaring pruritus affecting the face/head, neck and/or ventral abdomen. Concurrent hypersensitivities were confirmed in 6 cats and/or suspected in another 5 cats. Home-prepared elimination diets were completed by 16 cats; 8 cats had initial poor response to minimum 6-week commercial hydrolysed protein diets. Identified adverse foods included fish in 2 cats, and chicken, beef, commercial dry, and some canned foods, each in 1 cat. Conclusions The prevalence of cutaneous AFR in the general cat population is likely to be greater than 6%. A range of clinical presentations occur and practical challenges to diagnosis include reliance on strict adherence to dietary exclusion/provocation trials and misleading responses related to concurrent dermatoses and owner perceptions.

**Haematological and biochemical variations among eight sighthound breeds (pages 452–459)**

I Uhríková, A Lačháková, K Tandlerová, V Kuchařová, K Řeháková, E Jánová and J Doubek

Objective The aim of the study was to compare the haematological and biochemical profiles of eight sighthound breeds. Design Samples were taken from 192 individuals of the sighthound breeds (Whippet, Greyhound, Italian Greyhound, Sloughi, Saluki, Borzoi, Pharaoh Hound and Azawakh). Routine haematological and biochemical examinations were performed and the results were evaluated statistically. Results There were significant differences in haematology and clinical biochemistry among the sighthound breeds. The most similar laboratory profile to Greyhounds was found in Whippets. Italian Greyhounds had significantly higher alanine aminotransferase activity than other sighthounds, except Pharaoh Hounds. Conclusion Application of the Greyhound laboratory profile to other sighthounds is not recommended because of the frequent differences in haematological and clinical biochemical reference intervals.

**Unique presentation of normolipaemic cutaneous xanthoma in a cat (pages 460–463)**

PA Ravens, A normolipaemic

7-year-old female spayed Domestic Shorthair was initially presented with a history of pruritus for several years and diagnosed with concurrent atopic dermatitis, flea bite hypersensitivity and adverse food reaction. The hypersensitivities were controlled with cyclosporin, allergen-specific immunotherapy, topical flea control and a restricted diet. Five months after initial presentation, the cat developed a non-healing nodular ulcerated cutaneous lesion in the left axilla and also developed immune-mediated haemolytic anaemia (IMHA). The IMHA was stabilised, but the axillary lesion persisted and progressed to diffuse, firm, yellowed subcutaneous swelling over the ventral body approximately 20 months later. Histopathology was consistent with cutaneous xanthoma. The cat was normolipaemic and being fed a home-prepared diet of lean kangaroo meat and pumpkin to manage pruritus associated with adverse food reactions. No underlying malignancy was detected on routine screening tests. Conclusion A diffuse, planar form of cutaneous xanthoma occurring without associated lipaemia has not been previously reported in cats.

**Evaluation of routine hematology profile results and fructosamine, thyroxine, insulin, and proinsulin concentrations in lean, overweight, obese, and diabetic cats**

Margarethe Hoenig, Dr med vet, PhD; Anne M. Traas, DVM, DACT; David J. Schaeffer, PhD

Objective—To compare results of hematologic testing in nondiabetic and diabetic cats to identify possible indicators of alterations in long-term glucose control. Design—Cross-sectional study. Animals—117 client-owned cats (76 nondiabetic cats [25 with normal body condition, 27 overweight, and 24 obese] and 41 naïve [n = 21] and treated [20] diabetic cats). Procedures—Signalment and medical history, including data on feeding practices, were collected. A body condition score was assigned, and feline body mass index was calculated. Complete blood counts and serum biochemical analyses, including determination of fructosamine, thyroxine, insulin, and proinsulin concentrations, were performed. Urine samples were obtained and analyzed. Results—Glucose and fructosamine concentrations were significantly higher in the naïve and treated diabetic cats than in the nondiabetic cats. Insulin and proinsulin concentrations were highest in the obese cats but had great individual variation. Few other variables were significantly different among cat groups. Most cats, even when obese or diabetic, had unlimited access to food. Conclusions and Clinical Relevance—Results suggested that cats at risk of developing diabetes (ie, overweight and obese cats) could not be distinguished from cats with a normal body condition on the basis of results of isolated hematologic testing. A longitudinal study is indicated to follow nondiabetic cats over a period of several years to identify those that eventually develop diabetes. Findings also suggested that dietary education of cat owners might be inadequate.

**Clinicopathologic and atypical features of naturally occurring leptospirosis in dogs: 51 cases (2000–2010)**

Lindsay E. Tangeman, DVM; Meryl P. Littman, VMD, DACVIM
Objective—To determine clinicopathologic features, percentage of atypical abnormalities, antibody titers against Leptospira serogroups, and importance of convalescent titers in dogs with leptospirosis. Design—Retrospective case series. Animals—51 dogs with leptospirosis. Procedures—Criteria for inclusion were at least 1 positive microscopic agglutination test (MAT) result (titer ≥ 1:1,600 in vaccinated dogs, titer ≥ 1:800 in nonvaccinated dogs, or ≥ 4-fold increase in convalescent titer), a complete medical record (including leptospirosis vaccination date, reason for initial evaluation, and CBC, serum biochemical analysis, and urinalysis results), and clinical signs or laboratory findings consistent with leptospirosis. Results—Initial clinical signs, temporal distribution, and signalment were similar to previous reports. Convalescent MAT titers were necessary for diagnosis in 45% of cases. Atypical abnormalities included radiographic evidence of pulmonary disease in 10 of 23 dogs and hepatic involvement alone in 7 of 51 dogs. Other abnormalities included proteinuria in 34 of 51 dogs, thrombocytopenia in 26 of 51, coagulopathy in 7 of 24 dogs, hypoalbuminemia in 14 of 51 dogs, and glucosuria in 9 of 51 dogs. Significant associations were found between antibodies against serogroup Grippotyphosa and renal involvement and serogroup Icterohaemorrhagiae and hepatic involvement. Conclusions and Clinical Relevance—Increased awareness of atypical abnormalities may decrease misdiagnosis of leptospirosis in dogs. Results of concurrent infectious disease testing should be interpreted with caution; misdiagnosis of leptospirosis could pose a public health risk. Convalescent titers were necessary to identify infection when acute testing results were negative. Further research is needed to determine the true associations between antibodies against identified serogroups and clinical features.

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Factors influencing veterinarian referral to oncology specialists for treatment of dogs with lymphoma and osteosarcoma in Ontario, Canada
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Objective—To elucidate factors influencing practitioner decisions to refer dogs with cancer to veterinary oncology specialists. Design—Cross-sectional study. Sample—2,724 Ontario primary care companion animal veterinarians. Procedures—Practitioners were invited to participate in a survey involving clinical scenarios of canine cancer patients, offered online and in paper format from October 2010 through January 2011. Analyses identified factors associated with the decision to refer patients to veterinary oncology specialists. Results—1,071 (39.3%) veterinarians responded, of which 603 (56.3%) recommended referral for dogs with multicentric lymphoma and appendicular osteosarcoma. Most (893/1,051 [84.3%]) practiced within < 2 hours’ drive of a specialty referral center, and most (981/1,047 [93.7%]) were completely confident in the oncology service. Few (230/1,056 [21.8%]) to 349/1,056 [33.0%]) were experienced with use of chemotherapeutics, whereas more (627/1,056 [59.7%]) were experienced with amputation. Referral was associated with practitioner perception of patient health status (OR, 1.54; 95% confidence interval [CI], 1.15 to 2.07), the interaction between the client’s bond with the dog and the client’s financial status, practitioner experience with treating cancer (OR, 1.66 to 3.09; 95% CI, 1.08 to 4.72), and confidence in the referral center (OR, 2.20; 95% CI, 1.11 to 4.34). Conclusions and Clinical Relevance—Several factors influenced practitioner decisions to refer dogs with lymphoma or osteosarcoma for specialty care. Understanding factors that influence these decisions may enable practitioners to appraise their referral decisions and ensure they act in the best interests of patients, clients, and the veterinary profession.

Long-term outcome of sudden acquired retinal degeneration syndrome in dogs
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Objective—To investigate long-term outcomes and owner-perceived quality of life associated with sudden acquired retinal degeneration syndrome (SARDS) in dogs. Design—Survey study. Animals—100 dogs with SARDS examined at 5 academic veterinary institutions from 2005 to 2010. Procedures—The diagnosis was based on documented acute vision loss, normal results of ophthalmic examinations, and evaluation of extinguished bright-flash electroretinograms. Primary owners of affected dogs completed a questionnaire addressing outcome measures including vision, systemic signs, and perceived quality of life for their dogs. Results—Age at diagnosis was significantly correlated with positive outcome measures; dogs in which SARDS was diagnosed at a younger age were more likely to have alleged partial vision and higher owner-perceived quality of life. Polyphagia was the only associated systemic sign found to increase in severity over time. Medical treatment was attempted in 22% of dogs; visual improvement was not detected in any. Thirty-seven percent of respondents reported an improved relationship with their dog after diagnosis, and 95% indicated they would discourage euthanasia of dogs with SARDS. Conclusions and Clinical Relevance—Blindness and concurrent systemic signs associated with SARDS appeared to persist indefinitely, but only polyphagia
increased in severity over time. Most owners believed their pets had good quality of life and would discourage euthanasia of dogs with SARDS.


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Objective—To evaluate a modified proportional margins approach to resection of mast cell tumors (MCTs) in dogs. Design—Retrospective case series. Animals—40 dogs with subcutaneous and cutaneous MCTs undergoing curative intent surgery. Procedures—Medical records were searched to identify dogs with a cytologically or histologically confirmed diagnosis of MCT that had not previously been treated surgically and that had undergone full oncological staging. In those dogs, tumors were resected with lateral margins equivalent to the widest measured diameter of the tumor and a minimum depth of 1 well-defined fascial plane deep to the tumor. Surgical margins were evaluated histologically. Cutaneous tumors were graded by use of the Patnaik system and the 2-tier system described by Kiupel et al. The prognosis for subcutaneous tumors was assessed in accordance with published recommendations. Follow-up information on dog health status was obtained through clinical examination, the dog owners, and the referring veterinarians. Results—The 40 dogs had 47 tumors. Forty-one (87%) tumors were cutaneous, and 6 (13%) were subcutaneous. On the basis of the Patnaik system, 21 (51%) cutaneous tumors were considered grade I, 18 (44%) were considered grade II, and 2 (5%) were considered grade III. On the basis of the Kiupel system, 37 (90%) cutaneous tumors were considered low grade, and 4 (10%) were considered high grade. The prognosis for the 6 subcutaneous tumors was classified as likely resulting in a shorter (2) or longer (4) survival time. Forty tumors were deemed to have been excised with clear margins and 7 with incomplete margins. Local recurrence was not recorded for any dog but was suspected for 1 (2%) tumor, although not confirmed. Interval from tumor excision to follow-up ranged from 30 to 1,140 days (median, 420 days). Conclusions and Clinical Relevance—The modified proportional margins system resulted in satisfactory local disease control in dogs with MCTs.

Clinical features, treatment options, and outcome in dogs with thymoma: 116 cases (1999–2010)

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Objective—To describe clinical signs, diagnostic findings, treatment, and outcome and determine factors associated with survival time for dogs with thymoma. Design—Multi-institutional retrospective case series. Animals—116 dogs with thymoma. Procedures—Medical records were searched for information regarding signalment, physical examination findings, results of laboratory testing and diagnostic imaging, medical and surgical treatment, and survival data. Results—Of the 116 dogs with thymoma, 44 (38%) were Labrador Retrievers and Golden Retrievers. Twenty of 116 (17%) dogs had signs of myasthenia gravis (diagnosis was confirmed for 13 dogs). At the time of thymoma diagnosis, 40 (34%) dogs had hypercalcemia, 8 (7%) dogs had a concurrent immune-mediated disease, and 31 (27%) dogs had another tumor; 16 (14%) dogs developed a second nonthymic tumor at a later date. Tumor excision was performed for 84 dogs, after which 14 (17%) had tumor recurrence; prognosis was good for dogs undergoing a second surgery. Median survival time with and without surgical treatment was 635 and 76 days, respectively. Presence of another tumor at the time of thymoma diagnosis, lack of surgical excision, and higher pathological stage were significantly associated with shorter survival time. Hypercalcemia and presence of myasthenia gravis or megaeosophagus at the time of thymoma diagnosis, histopathologic subtype of thymoma, or tumor development at a later date was not associated with survival time. Conclusions and Clinical Relevance—Dogs with thymoma, even those with a large tumor burden or a paraneoplastic syndrome, had a good prognosis following surgery. Surgical treatment, tumor stage, and the presence of a second tumor at diagnosis influenced survival time.

Diagnosis of chronic small bowel disease in cats: 100 cases (2008–2012)

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Objective—To determine whether a diagnosis of chronic small bowel disease could be established in a subset of cats that had clinical signs of chronic vomiting, chronic small bowel diarrhea, weight loss, or a combination of these, combined with ultrasonographically determined thickening of the small bowel. Design—Retrospective case series. Animals—100 client-owned domestic cats. Procedures—Medical records of cats with clinical signs of chronic vomiting, chronic small bowel diarrhea, weight loss, or a combination of these, combined with ultrasonographically determined small bowel thickening, that underwent laparotomy and multiple small bowel biopsies between 2008 and 2012 were examined. Biopsy specimens were submitted for histologic evaluation, immunohistochemical evaluation, and, when findings were ambiguous, PCR assay for antigen receptor rearrangement. Results—Chronic small bowel disease was diagnosed in 99 of the 100 cats. The most common
diagnoses were chronic enteritis and intestinal lymphoma. Conclusions and Clinical Relevance—Results suggested that cats with clinical signs of chronic small bowel disease should undergo detailed diagnostic testing because they are likely to have clinically important, diagnosable, treatable disease. Clinical signs of small bowel disease, especially weight loss and chronic or recurrent vomiting, are extremely common in cats. These signs should not be considered a normal condition and should not be ignored, regardless of common explanations given by owners, and cats with these signs should undergo appropriate diagnostic testing.

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