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**The Use of IV Lipid Emulsion for Lipophilic Drug Toxicities**
Amy Kaplan, DVM, Megan Whelan, DVM, DACVECC

**ABSTRACT**
IV lipid emulsion (ILE) therapy is emerging as a potential antidote for lipophilic drug toxicities in both human and veterinary medicine. ILE has already gained acceptance in human medicine as a treatment of local anesthetic systemic toxicity, but its mechanism of action, safety margins, and standardized dosing information remains undetermined at this time. Experimental and anecdotal use of ILE in the human and veterinary literature, theorized mechanisms of action, current dosing recommendations, potential adverse effects, and indications for use in human and veterinary emergency medicine are reviewed herein.

**Pharmaceutical Evaluation of Compounded Trilostane Products**
Audrey K. Cook, BVM&S, Cornelia D. Nieuwoudt, PharmD, Susan L. Longhofer, MS, DVM

**ABSTRACT**
Compounded trilostane capsules (15 mg, 45 mg, or 100 mg) were purchased from eight pharmacies and assayed for content and dissolution characteristics. Capsules made in-house containing either inert material or 15 mg of the licensed product and proprietary capsules (30 mg and 60 mg) served as controls. Findings were compared with regulatory specifications for the licensed product. Altogether, 96 batches of compounded trilostane and 16 control batches underwent analysis. In total, 36 of 96 (38%) compounded batches were below the acceptance criteria for content. The average percentage label claim (% LC) for each batch ranged from 39% to 152.6% (mean, 97.0%). The range of average % LC for the controls was 96.1–99.6% (mean, 97.7%). The variance in content of the purchased compounded products was substantially greater than for the controls (234.65 versus 1.27; P<0.0001). All control batches exceeded the acceptance criteria for dissolution, but 19 of 96 batches (20%) of purchased compounded products did not. Mean percent dissolution for the purchased compounded products was lower than for controls (75.96% versus 85.12%; P=0.013). These findings indicate that trilostane content of compounded capsules may vary from the prescribed strength, and dissolution characteristics may not match those of the licensed product. The use of compounded trilostane products may therefore negatively impact the management of dogs with hyperadrenocorticism.

J. Brad Case, DVM*, Catriona M. MacPhail, PhD, DVM, DACVS, Stephen J. Withrow, DVM, DACVS

**ABSTRACT**
Intermuscular lipomas (IML) in dogs can be associated with ominous clinical signs, especially in the thoracic limb. However, the prognosis is excellent following surgical excision. There is a paucity of information in the veterinary literature regarding IML. Our objective was to describe the anatomical location, imaging techniques, and clinical findings in a series of dogs that were diagnosed and treated for IML. The prevalence of thoracic versus pelvic limb IML was not different. Most IML of the thoracic limb were located in the axilla. Operative time for IML of the thoracic and pelvic limb averaged 60 minutes. Complications were rare after marginal surgical excision and recurrence was not seen in any of the cases in this report. Intermuscular lipomas of the axilla are as common as IML of the caudal thigh. Surgical treatment of both axillary and caudal-thigh IML is associated with an excellent prognosis in dogs.

**Clinical Signs of Cardiovascular Effects Secondary to Suspected Pimobendan Toxicosis in Five Dogs**
L. Noelani Reinker, DVM*, Justine A. Lee, DVM, DAVECC, Lynn R. Hovda, RPh, MS, DVM, DACVIM

**ABSTRACT**
The purpose of this study was to review the medical records of dogs that were either suspected or known to have ingested large doses of pimobendan and to describe the clinical signs associated with pimobendan toxicosis. The database of Pet Poison Helpline, an animal poison control center located in Minneapolis, MN, was searched for cases involving pimobendan toxicoses from Nov 2004 to Apr 2010. In total, 98 cases were identified. Of those, seven dogs that ingested between 2.6 mg/kg and 21.3 mg/kg were selected for further evaluation. Clinical signs consisted of cardiovascular abnormalities, including severe tachycardia (4/7), hypotension (2/7), and hypertension (2/7). In two dogs, no clinical signs were seen. Despite a wide safety profile, large overdoses of pimobendan may present risks for individual pets. Prompt decontamination, including emesis induction and the administration of activated charcoal, is advised in the asymptomatic patient. Symptomatic and supportive care should include the use of IV fluid therapy to treat hypotension and address hydration requirements and blood pressure and electrocardiogram monitoring with high-dose toxicosis. Practitioners should be aware of the
Clinical signs associated with high-dose pimobendan toxicosis. Of the dogs reported herein, all were hospitalized, responded to supportive care, and survived to discharge within 24 hr of exposure.

Josianne Arbour, DVM, Marie-Claude Blais, DMV, DACVIM, Lisa Carioto, DVM, DVSc, DACVIM, Doris Sylvestre, DMV, MSc
ABSTRACT
Based on previous research, cats were thought to have been resistant to the development of clinical signs following infection with Leptospira spp. This case report presents three confirmed, naturally infected clinical cases of feline leptospirosis. The cases presented were all indoor/outdoor cats that were known to hunt. They were also all presented at different stages of renal insufficiency; however, they did not show any liver involvement. The authors suggest that there may be a longer incubation period in cats than dogs and recommend further research in the form of a large, clinical study.

Cholesteatoma After Lateral Bulla Osteotomy in Two Brachycephalic Dogs
Riccarda Martina Schuenemann, DVM, Gerhard Oechtering, Prof. Dr.med.vet, DECVAA
ABSTRACT
This report describes a French bulldog and a pug that presented to the authors’ hospital following total ear canal ablation (TECA) and lateral bulla osteotomy (LBO), with signs of recurring otitis media and difficulty opening their mouths. The bulldog also had unilateral facial paralysis and sensory deficits of the trigeminal nerve on the ipsilateral side. Computed tomography and MRI scans suggested cholesteatoma in the bulldog, but showed only slight enlargement of the bulla in the pug. Histopathologic examination of samples yielded cholesteatoma in both cases. The authors suspect that development of the cholesteatomas was linked to the TECA/LBO surgery in both cases. Cholesteatomas may occur more frequently than currently thought. Even if only slight changes of the bulla wall are detected on CT, early-stage cholesteatoma should be considered. The narrow anatomic conditions in brachycephalic dogs possibly predispose such breeds to develop cholesteatoma after middle ear surgery because complete removal of all inflammatory and epithelial tissue can be more difficult than in other breeds. To the authors’ knowledge, this is the first report of an aural cholesteatoma causing sensory deficits of the trigeminal nerve.

Novel Cutaneous Use of Implantable Loop Recorders in Two Dogs with Unexplained Episodes of Collapse
Robert Sanders, MS, DVM, DACVIM (Cardiology), N. Bari Olivier, PhD, DVM, DACVIM (Cardiology)
ABSTRACT
Determining the cause of episodes of collapse can be difficult. Even in patients with frequent collapsing episodes due to cardiac causes, diagnostic surface electrocardiogram and 24 hr ambulatory electrocardiographic (Holter) monitoring are sometimes inconclusive. Event monitors with multiple leads can be challenging to use in veterinary medicine over long periods of time due to lead dislodgment. Implantable leadless loop recorders (ILRs) are useful, but owners are sometimes unwilling to have an ILR implanted due to the associated risks and/or costs. In this case report, the authors describe the use of cutaneously placed ILRs in two dogs with unexplained episodes of collapse/exercise intolerance. Data recorded provided clinically useful information. Cutaneously placed ILRs can be used effectively in veterinary medicine to evaluate patients with unexplained episodes of collapse.

Diagnosis and Treatment of Tracheal Basal Cell Carcinoma in a Maine Coon and Long-Term Outcome
Michael L. Green, DVM, Julie Smith, DVM, DACVS, Linda Fineman, DVM, DACVIM (Oncology), David Proulx, DVM, DACVIM (Oncology), DACVR (Radiation Oncology)
ABSTRACT
A 6 yr old castrated male Maine coon presented with a 2 wk history of progressive dyspnea. Thoracic radiographs revealed a 2 cm diameter intratracheal mass at the level of the fourth rib. The tracheal mass was marginally excised via a combination of resection and anastomosis. Infiltrative basal cell carcinoma (BCC) with nodular osseous metaplasia was diagnosed. The thoracic trachea was then irradiated postoperatively for definitive treatment. The cat remained asymptomatic following surgical excision and radiation therapy for 32 mo when this report was written. The purpose of this report is to describe the treatment and long-term outcome of a Maine coon diagnosed with, and treated for, tracheal BCC.

Goiter with Vascular Anomalies in a Litter of Polish Lowland Sheepdogs
Leslie Anne Kuczynski, VMD* Paul Schwartz, DVM, Gordon Peddle, VMD
ABSTRACT
At approximately 4–5 mo of age, three Polish Lowland sheepdog puppies from a single litter of eight puppies presented to their respective primary veterinarians with bilateral subcutaneous masses in their ventral cervical
regions. Evaluation, including thyroid function testing, surgical exploration with resection, computed tomography, and angiography, identified the masses as enlarged thyroid glands with severely dilated and abnormal vasculature in the regions of the glands. The dogs were also found to have serum concentrations of thyroid hormones that were below the reference ranges. None of the three dogs showed clinical signs of hypothyroidism, except for the presence of goiter. One dog also had a patent ductus arteriosus that was surgically repaired. All dogs were clinically normal at 2 yr of age. This is the first report of major vascular anomalies associated with goiter in any species. The mechanism is unknown.

**Vet Clinics**

**Clinical Pathology Interpretation in Geriatric Veterinary Patients**
Fred L. Metzger, DVM, Alan H. Rebar, DVM, PhD

**INTRODUCTION**
Early disease recognition can help improve the quality of life for all dogs and cats, but especially for older dogs and cats and their owners. Complete diagnostic efforts, including laboratory profiling, are critical because geriatric pets frequently have abnormalities in multiple body systems and often receive long-term medications for chronic diseases or conditions related to aging. Veterinarians should evaluate serial hematologic and biochemical data on an individual patient when performing yearly wellness testing and when following the progression or regression of a disease once recognized. Serial data evaluations on an individual animal can prove to be a highly objective and effective means of characterizing...

**Geriatric Veterinary Pharmacology**
Butch KuKanich, DVM, PhD

**INTRODUCTION**
Geriatric dogs and cats are an important demographic in the pet population. However, not all geriatric animals should be thought of as being the same. The geriatric population can be subclassified as (1) healthy geriatric patients, (2) geriatric patients with subclinical organ dysfunction, and (3) geriatric patients with an overt disease condition. Healthy geriatric animals are similar to adult animals, with only minor differences in organ function (see later). Geriatric patients with subclinical organ dysfunction are overtly healthy, but decreased function of 1 or more organs such as the heart, liver, or kidneys is present. Geriatric patients with an overt disease may or may not appear healthy but have a diagnosed disease such as heart disease (ie, chronic valvular disease), endocrine disease (ie, hypothyroidism, hyperthyroidism), renal disease (chronic renal failure), or neoplasia, among other conditions. Data recently published on the most common causes of death can help guide the clinician in identifying the most common types of fatal diseases occurring in geriatric animals. The most common cause of death in adult dogs and cats is neoplasia.1–3 However, differences within dog breeds occur with degenerative and metabolic diseases, accounting for the primary causes of death in small breed dogs and neoplasia predominating in large breed dogs.3 Smaller dogs also live longer than large...

**Anesthesia and Analgesia for Geriatric Veterinary Patients**
Courtney L. Baetge, DVM, Nora S. Matthews, DVM

**INTRODUCTION**
Although exact numbers are not available, the number of geriatric patients presented for anesthesia appears to be increasing. One study estimated that nearly one-fifth of all pet dogs are now over the age of 10 years,1 and more than $1.5 billion is spent annually on these geriatric pets.2 Another study reported that in 2002, 30% of the US pet population were expected to be geriatric.3 These studies did not include cats, which have outnumbered dogs as pets in the United States; exact figures may not be available, but most practitioners would agree that geriatric cats are becoming more common in every practice! While age may not be a disease, the physiologic deterioration that normally occurs with age can cause significant complications during the anesthetic period.1 Brodbelt and colleagues4 estimated the risk of anesthetic death increased with age as much as 7 times for patients over the age of 12 years. Given the increasing number of geriatric dogs and cats and awareness of these risks, planning for the anesthetic period can help the practitioner avoid complications often seen in the older patient; these include hypotension, bradycardia...

**The Diagnosis and Management of Age-Related Veterinary Cardiovascular Disease**
Ashley B. Saunders, DVM

**INTRODUCTION**
At last count, the American Veterinary Medical Association reported 81.7 million cats and 72.1 million dogs in the United States with more than 10% over 11 years of age.1 Disorders of the cardiovascular system are one of the most commonly encountered disease entities in the aging pet population.2,3 Guidelines developed by the American Association of Feline Practitioners categorize cats as mature at 7 years old and senior by 11 years.4
Systemic hypertension and cardiomyopathies are of particular importance in the aging cat. Dogs age at different rates depending on breed, and small breeds typically have longer life spans than giant...

**Chronic Kidney Disease in Dogs and Cats**
Joseph W. Bartges, DVM, PhD
Chronic kidney disease (CKD) occurs commonly in older dogs and cats and is the most common renal disease occurring in elderly patients. It is defined as structural and/or functional impairment of one or both kidneys that has been present for more than approximately 3 months. In most patients, there is loss of function and structure with CKD; however, degree of functional impairment does not always mirror loss of structure. CKD implies irreversible loss of renal function and/or structure that remains stable for some period of time but is ultimately progressive. In some patients, CKD may be complicated by concurrent prerenal and/or postrenal problems that may worsen the condition, but if managed, they may improve the situation. CKD is considered a disease of older animals, although it occurs at all ages. The estimated incidence of CKD in the general population of dogs and cats is 0.5% to...

**Alimentary Neoplasia in Geriatric Dogs and Cats**
Michael D. Willard, DVM, MS*
Alimentary neoplasia is a common and important problem in geriatric dogs and cats. While there are numerous possible cell types, locations, and associated clinical signs, there are some that are particularly common that should be high on the clinician’s “radar screen” when dealing with older pets. This article will focus on the more common neoplastic problems of the esophagus and gastrointestinal tract (GIT) of geriatric dogs and cats.

**LYMPHOMA**
Lymphoma is the most common neoplasm of the feline GIT and is either the most common or second most common in the canine GIT. Up to 70% of cats with lymphoma have GIT involvement.1–3 Alimentary lymphoma in cats can be B cell (more commonly but not exclusively in lymphoblastic lymphoma [LBL]) or T cell (more commonly but not exclusively in small cell, lymphocytic lymphoma [SCL]). Different studies have found different preponderances of T- versus B-cell intestinal lymphoma...

**Thyroid Disorders in the Geriatric Veterinary Patient**
J. Catharine Scott-Moncrieff, MA, MS, Vet MB, MRCVS
INTRODUCTION
Thyroid disorders are an important cause of morbidity in geriatric dogs and cats. The diagnosis of thyroid dysfunction is more difficult in older animals because of the impact of age, concurrent illness, and administered medications on serum concentrations of thyroid hormone. This article will review the physiology of the thyroid gland specifically focusing on geriatric patients, discuss the most common causes of thyroid disease in geriatric patients, and review the special concerns of diagnosis and treatment in this subset of patients.

**THYROID PHYSIOLOGY**
Thyroxine (T4) and triiodothyronine (T3) are iodine-containing amino acids synthesized in the thyroid gland. Thyroid hormones are highly bound to serum proteins with T4...

**Painful Decisions for Senior Pets**
Steven M. Fox, MS, DVM, MBA, PhD
In 2010, Fleming and colleagues1 reported on the mortality patterns of North American dogs. Their findings revealed that older dogs tend to die from neurologic and neoplastic causes. In addition, although neoplastic processes were the leading cause of death among adult dogs in the study, degenerative processes ranked 6th overall. Further, increasing breed size was associated with increasing risk of death because of musculoskeletal (or gastrointestinal) system disease. These data suggest a focus on pain management of degenerative joint disease and cancer in the senior/geriatric pet.

**MALADAPTIVE PAIN**
Pain is both a good and potentially very bad phenomenon. From an advantageous perspective, pain is an early warning sign that we should avoid potential tissue...

**Cognitive Dysfunction Syndrome A Disease of Canine and Feline Brain Aging**
Gary M. Landsberg, DVM, Jeff Nichol, DVM
INTRODUCTION
As pets age, behavior changes may be the first indication of declining health and welfare. This is particularly true for some of the most common problems associated with aging, such as pain, sensory decline, and cognitive dysfunction syndrome (CDS). Early identification of these signs provides an opportunity for effective intervention. GML is an employee of CanCog Technologies Inc. JAA is an employee of InterVivo Solutions Inc and a consultant for CanCog Technologies Inc...
Veterinary Dentistry in Senior Canines and Felines
Steven E. Holmstrom, DVM
As with many other systems in the “senior” pet, the oral cavity undergoes aging changes that need to be addressed for the comfort of the patient. In their Senior Care Guidelines, the American Animal Hospital Association states that there should be focused attention to client education for the increased veterinary attention to dental/oral care and to home dental prophylaxis. 1 In reality, this dental care should start at an early age to prevent or manage problems when the pet is older. 2 This article will discuss findings that may be discovered by complete oral exam. Typical conditions that can occur in senior dogs and cats include undiagnosed orthodontic disease, periodontal disease, tooth resorption, and oral tumors.

DENTAL WEAR
Attresion is wear of a tooth against another tooth. It may take many years for attresion caused by orthodontic malocclusion to become clinical. For example, a patient with a prognathic mandible may have chronic wear of the maxillary lateral incisors against

Alternative Medicines for the Geriatric Veterinary Patient
J. Randy Kidd, DVM, PhD
INTRODUCTION
The author discusses how holistic practitioners might use some of today’s more popular “alternative” medicines as they apply to the geriatric pet. Many practitioners are currently using one or more of the alternative medicines (other terms have been used to describe these medicines, including complimentary, integrative, holistic, and complementary and alternative medicine [CAM]), but they are not without controversy...

Australian Veterinary Journal
Neoadjuvant chemoradiotherapy and surgery as treatment for oral maxillary squamous cell carcinoma in a dog (pages 264–268)
LA Mestrinho, E Bernardo, MMRE Niza, A Lloret and P Buracco
A gingival maxillary squamous cell carcinoma was diagnosed in a 12-year-old male Yorkshire Terrier. After a complete diagnostic work-up, including a computed tomography scan, the tumour was staged as T3bN1aM0 and considered non-resectable at presentation. The combination of neoadjuvant megavoltage radiotherapy and neoadjuvant and adjuvant chemotherapy with carboplatin and doxorubicin decreased the size of the tumour, allowing for surgery. The dog was free from local disease for 421 days after which it was euthanased at the owners' request.

The Veterinary Journal
Identification of tumour initiating cells in feline head and neck squamous cell carcinoma and evidence for gefitinib induced epithelial to mesenchymal transition
L.Y. Pang, G.T. Bergkvist, A. Cervantes-Arias, D.A. Yool, R. Muirhead, D.J. Argyle
Feline oral squamous cell carcinoma is considered a highly invasive cancer that carries a high level of morbidity. Despite aggressive surgery, patients often succumb to disease, the tumour having inherent insensitivity to radiation and chemotherapy. In this study we sought to identify cells within the feline SCC1 line that have stem cell properties, including inherent resistance mechanisms. When feline cells were subjected to harsh growth conditions, they formed sphere colonies consistent with a stem cell phenotype. Utilising CD133, we were able to identify a small fraction of cells within the population that had enhanced sphere-forming ability, reduced sensitivity to radiation and conventional chemotherapy and demonstrated resistance to the EGFR-targeting drug, gefitinib. In addition, long-term culture of feline SSC1 cells in gefitinib caused a change in cell morphology and gene expression reminiscent of an epithelial to mesenchymal transition. Taken together, these results suggest that feline SCC may be driven by small subset of cancer stem cells.

Haemostatic abnormalities in cats with naturally occurring liver diseases
Brigitte Dircks, Ingo Nolte, Reinhard Mischke
Alterations in the haemostatic system were characterized in cats with different naturally occurring liver diseases. The study looked at 44 healthy cats and 45 cats with different liver diseases confirmed histologically or
cytologically (neoplasia, \(n = 9\); inflammation, \(n = 12\); hepatic lipidosis, \(n = 13\); other degenerative liver diseases, \(n = 11\)). The following parameters were evaluated: platelet count; prothrombin time; activated partial thromboplastin time; thrombin time; factor (F) II, FV, FVII, FX, and FXIII activities; fibrinogen concentration; activities of antithrombin, protein C, plasminogen, and \(\alpha_2\)-plasmin inhibitor, and D-dimer concentration. In cats with liver diseases, 44/45 (98%) had one or more abnormalities of the coagulation parameters measured. In cats with inflammatory liver diseases, increased D-dimer concentrations and decreased FXIII activity were the most consistent abnormalities and were found in 83% and 75% of cats, respectively. The most common abnormality in cats with neoplastic liver disease was FXIII deficiency (78%). The most consistent abnormalities in cats with hepatic lipidosis were increased FV activity and D-dimer concentration with 54% of cats having values above the reference range for both parameters. Cats with miscellaneous degenerative liver disease most frequently showed FXIII deficiency (64%). The results of this study show that alterations of single haemostatic components are a frequent finding in cats with liver disease. Activation of haemostasis with subsequent consumptive coagulopathy (rather than decreased synthesis) seems to be responsible for these alterations. Increased blood levels of different haemostatic components in cats with inflammatory lesions may be related to an acute phase reaction.

**Breed, age and gender distribution of dogs with chronic hepatitis in the United Kingdom**


Standardised histological criteria are now available for the diagnosis of canine chronic hepatitis (CH). CH is common in dogs, but no studies have reported breed, age and gender distributions in the United Kingdom (UK). The objective of this study was to determine which breeds had an increased risk for developing CH in the UK and to report the age and gender distribution for those breeds. The databases of six veterinary histopathology laboratories were searched for cases with a histological diagnosis of CH according to standardised criteria. The breed, age and gender of dogs was recorded and compared to a control population to calculate the odds ratio and 95% confidence intervals for developing CH.

A total of 551 cases of CH were identified, consisting of 61 breeds. Nineteen breeds were represented by five or more cases. Breeds with an increased risk for developing CH included the American cocker spaniel, Cairn terrier, Dalmatian, Dobermann pinscher, English cocker spaniel, English springer spaniel, Great Dane, Labrador retriever and Samoyed. The median age at diagnosis for all breeds with CH was 8 years (range 7 months to 16 years). Dalmatians, Dobermann pinschers and English springer spaniels with CH were significantly younger than Cairn terriers, English cocker spaniels and Labrador retrievers with CH. Females were over-represented when all cases were examined together. In conclusion, several breeds in the UK have an increased risk of CH, some of which have not been previously reported.

**Evaluation of the presence of *Leishmania* spp. by real-time PCR in the lacrimal glands of dogs with leishmaniosis**

Carolina Naranjo, Dolors Fondevila, Laura Alet, Olga Francino, José Ríos, Xavier Roura, Teresa Peña

*Leishmania infantum* infection is highly prevalent in endemic areas. Dogs with leishmaniosis may develop keratoconjunctivitis sicca (KCS). The goals of this study were (1) to quantify *Leishmania* amastigotes in the Meibomian glands (MG), main lacrimal gland (MLG) and nictitating membrane gland (NMG) from dogs with leishmaniosis; (2) to compare these results to immunohistochemistry (IHC), and (3) to explore the association between the *Leishmania* parasite load and the presence of ocular clinical signs. Twenty-five dogs diagnosed with leishmaniosis were included. MG, MLG and NMG from both eyes were collected. Histopathology, IHC and real-time PCR were performed.

All specimens yielded positive real-time PCR results. For all three glands, samples from dogs with ocular clinical signs had mean \(\Delta Ct\) (cycle threshold) values significantly lower (higher parasite loads) than those from dogs without signs. Cut-off values of \(\Delta Ct < 0\), \(\Delta Ct < 4\) and \(\Delta Ct < 4.9\) for MG, MLG and NMG, resulted in a likelihood ratio of positives of 5.9, 6.38 and 6.38, respectively. Samples with \(\Delta Ct\) values below the reported cut-off were significantly more likely to display clinical signs related to KCS than those with results above the cut-off, for all three glands. Similarly, \(\Delta Ct\) values below the cut-off were significantly associated with positive IHC. In this study real-time PCR has been standardised for use in MG, MLG and NMG. A cut-off value established
for each of these tissues may aid the clinician in the discrimination between ocular signs related to *Leishmania* from those associated with other causes of KCS.

**Electroencephalographic recordings in dogs suffering from idiopathic and symptomatic epilepsy:**

*Diagnostic value of interictal short time EEG protocols supplemented by two activation techniques*

Christina Brauer, Sabine B.R. Kästner, Karl Rohn, Henning C. Schenk, Julia Tünsmeyer, Andrea Tipold

The diagnostic value of interictal short time electroencephalographic (EEG) recordings in epileptic dogs under general anaesthesia with propofol and the muscle relaxant rocuronium bromide was investigated. Two activation techniques, namely photic stimulation and hyperventilation, were evaluated for their potential to enhance the diagnostic validity of these recordings. Sixty-one dogs suffering from idiopathic epilepsy and 28 dogs suffering from symptomatic epilepsy were included. Electroencephalograms were recorded using five subdermal EEG electrodes (F3, F4, Cz, O1 and O2). All 89 EEGs were analysed visually and 61 were also evaluated quantitatively with fast Fourier transformation.

Interictal paroxysmal epileptiform activity was found in 25% of idiopathic and in 29% of symptomatic epileptic dogs. Quantitative analysis of the EEGs (qEEGs) detected significant differences of frequency analysis in single reading points without any continuous changes of frequency bands. A comparison between healthy and affected brain hemispheres in seven dogs with focal lesions of one hemisphere did not show any significant differences in qEEG analysis. qEEG was not more sensitive than visual evaluation. Despite the use of activation techniques, the results showed that short time EEG recordings in epileptic dogs can detect interictal epileptic activity in less than one third of all seizuring dogs and is not a useful screening method.

**Effects of obesity on lung function and airway reactivity in healthy dogs**

J. Manens, M. Bolognin, F. Bernaerts, M. Diez, N. Kirschvink, C. Clercx

The present study investigated the effects of bodyweight (BW) gain on respiratory function and airway responsiveness in healthy Beagles using barometric whole body plethysmography (BWBP). Six adult dogs were examined before and after a fattening diet. The high-energy diet induced a mean increase in BW of 41 ± 6%.

BWBP basal parameters were recorded prior to airway reactivity testing (using increasing concentrations of histamine nebulisations). An airway responsiveness index (H-Penh300) was calculated as the histamine concentration necessary to reach 300% of basal enhanced pause (Penh, bronchoconstriction index). The same dogs underwent a doxapram hydrochloride (Dxp) stimulation testing 2 weeks later.

Basal measurements showed that obese dogs had tidal volume per kg (TV/BW) that was significantly decreased whilst respiratory rate (RR) increased significantly. H-Penh300 decreased significantly in obese Beagles, indicating increased bronchoreactivity. Dxp administration induced a significant increase in TV/BW, minute volume per kg (MV/BW), peak inspiratory and expiratory flows per kg (PIF/BW and PEF/BW) in both normal and obese dogs although the TV/BW increase was significantly less marked in the obese group.

In conclusion, obesity induced changes in basal respiratory parameters, increased bronchoreactivity and a blunted response to Dxp-induced respiratory stimulation. This combination of basal respiratory parameters, bronchoreactivity testing and pharmacological stimulation testing using non-invasive BWBP can help characterize pulmonary function and airway responsiveness in obese dogs.

**Correlation of Foxp3 positive regulatory T cells with prognostic factors in canine mammary carcinomas**


Regulatory T cells (Treg) cells play a crucial role in tumor progression by suppressing anti-tumor immunity, but are not well-documented in veterinary oncology. To identify the characteristics of Treg cells in tumor microenvironments, the numbers of Treg cells were analyzed and compared with histological prognostic factors and molecular biomarkers in canine mammary carcinoma (MC) tissues \((n = 37)\).

Abundant Treg cells were associated with high histological grade and lymphatic invasion. The numbers of Treg cells infiltrating intratumoral areas markedly increased in tumors with poor prognostic factors, such as high histological grade, lymphatic invasion, and necrosis. These findings suggest that Treg cells play a role in canine MC progression. Furthermore, Treg cell numbers in intratumoral compartments may provide a potential prognostic factor when assessing canine MCs, which may in turn lead to the development of new immunologic therapeutics.
A comparison of in vitro relaxant responses to ipratropium bromide, β-adrenoceptor agonists and theophylline in feline bronchial smooth muscle
Jérôme Leemans, Nathalie Kirschvink, Pascal Gustin

This study compares the potency and efficacy of different relaxant drugs including anticholinergic, β-adrenergic and methylxanthine agents on acetylcholine-contracted feline bronchi, and investigates the influence of the initial muscarinic-induced tone on bronchodilator response. Feline bronchi were removed from euthanased client-owned cats and were contracted with acetylcholine to cause either 40% or 80% of the acetylcholine maximal contraction. The efficacy and potency of bronchodilating drugs were obtained from cumulative dose–response curves with efficacy ($E_{\text{max}}$) as the maximal relaxant response and potency ($-\log EC_{50}$) as the logarithm of the concentration of drug inducing 50% of maximal relaxation.

Under low contractile tone (40%), all bronchodilators relaxed feline bronchi in a concentration-dependent manner with the following rank order of potency: formoterol > ipratropium bromide > fenoterol > isoprenaline > salbutamol > salmeterol > theophylline. $E_{\text{max}}$ values ranged from 80% to 100% depending on the tested drug. Constriction of feline bronchi with high-dose acetylcholine (80%) caused a rightward and downward shift of the $\beta_2$-mimetic dose–response curves. Significant decreases in $-\log EC_{50}$ and $E_{\text{max}}$ values were reported for salbutamol, formoterol and salmeterol. This study provides evidence that existing classes of bronchodilators produce effective relaxation of acetylcholine-contracted feline bronchi and that airway responsiveness to $\beta_2$-stimulants is dependent on the magnitude of the initial muscarinic-induced tone. The clinical relevance of these in vitro findings has yet to be explored in clinical trials.

Journal of Feline Medicine and Surgery

Dermatophytosis and papular eosinophilic/mastocytic dermatitis (urticaria pigmentosa-like dermatitis) in three Devon Rex cats
Silvia Colombo1, Fabia Scarampella2, Laura Ordeix2, Paola Roccabianca3

Presenting signs: Three Devon Rex cats were presented with multiple erythematous papules, occasionally associated with crusting and hyperpigmentation, with a linear distribution on the head, neck, chest and abdomen. One cat also had multifocal alopecia with hyperpigmentation on the dorsum.

Diagnosis and treatment: Clinical and histopathological features were suggestive of papular eosinophilic/mastocytic dermatitis (urticaria pigmentosa-like dermatitis). In all cases, dermatophytosis was diagnosed: in cases 1 and 2 there was histopathological evidence of dermatophytosis, while fungal culture was positive for Microsporum canis in cases 2 and 3. In all cats, lesions disappeared following antifungal treatment.

Clinical significance: Papular eosinophilic/mastocytic dermatitis in Devon Rex cats may represent either an atypical presentation of dermatophytosis or a clinical and histological reaction pattern to various diseases, including dermatophytosis and allergic diseases. Clinical differentiation is crucial as there are important implications regarding treatment and, in particular, the use of glucocorticoids, which are contraindicated in cases of dermatophytosis.

Compendium

Vestibular Disease: Anatomy, Physiology, and Clinical Signs
The vestibular system is responsible for keeping an animal oriented with respect to gravity. It is a sensory system that maintains the position of the eyes, body, and limbs in reference to the position of the head. Proper interpretation of neurologic deficits and precise neuroanatomic localization are essential to diagnose and prognosticate the underlying disorder. Neurologic examination can confirm whether the vestibular dysfunction is of peripheral or central nervous system origin. Idiopathic vestibular syndrome is the most common cause of peripheral vestibular disease in dogs and, despite its dramatic clinical presentation, can improve without intervention. Central vestibular diseases generally have a poorer prognosis.
Vestibular Disease: Diseases Causing Vestibular Signs
Having determined whether a patient has central or peripheral vestibular disease, clinicians must then determine what diseases are likely to result in such a presentation. This article describes the more common diseases causing vestibular disease in dogs and cats. Having formulated a list of potential causes of vestibular disease, clinicians should proceed through a systematic investigation to diagnose the underlying condition. A companion article describes the anatomy, physiology, and clinical signs associated with vestibular disease.

Brachycephalic Airway Syndrome: Pathophysiology and Diagnosis
Brachycephalic airway syndrome (BAS) is a group of abnormalities that result in upper airway obstruction. Primary malformations include stenotic nares, elongated soft palate, and hypoplastic trachea, which cause an increase in negative pressure within the upper airways that can eventually lead to secondary abnormalities such as everted laryngeal sacculles, everted tonsils, and laryngeal and tracheal collapse. Abnormal nasopharyngeal turbinates are also encountered, but have not been classified as primary or secondary. BAS is readily diagnosed, and quality of life is improved with appropriate medical and/or surgical management. This is the first of two articles on BAS; the second article will be published in the August 2012 issue.

Focus on Nutrition: Nutritional Management of Protein-Losing Nephropathy in Dogs
Optimal treatment of protein-losing nephropathy (PLN) should address both medical and nutritional issues. In nonazotemic dogs with PLN, the main nutrients of concern are protein, calories, omega-3 fatty acids, and sodium. In azotemic dogs with PLN, requirements for additional nutrients should be addressed. The amount of protein and the specific diet must be individualized for every patient with PLN because commercial dog foods differ greatly in protein and other nutrients. It is critical to avoid excessive dietary protein restriction, which may contribute to loss of lean body mass. A thorough diet history must be obtained to account for the animal’s entire daily intake of protein and other nutrients.

Journal of Small animal practice

Acute pain in small animals: how far have we come and where are we going? (pages 369–370) Derek Flaherty. NO ABSTRACT


Pharmacological options for intra-operative and early postoperative analgesia: an update (pages 377–386) M. A. Gurney
The motto of the 2011 Global Year Against Acute Pain was ‘Anticipate, Assess, Alleviate’. Recent advances in acute pain management include novel applications of widely used drugs, new techniques, as well as further development in our knowledge of pain scoring in veterinary patients. The concept of preventive analgesia is introduced here and serves to strengthen the widely accepted practice of pre-emptive, multimodal analgesia.

Intra-articular morphine, bupivacaine or no treatment for postoperative analgesia following unilateral elbow joint arthroscopy. M. A. Gurney¹, M. Rysnik², E. J. Comerford², P. J. Cripps², I. Iff³
Objectives: To compare intra-articular morphine or bupivacaine against no treatment following unilateral elbow joint arthroscopy using force plate analysis and pain scoring.
Methods: Thirty-one dogs were randomly allocated to receive 0·1 mg/kg intra-articular morphine, 0·5 mg/kg bupivacaine or no treatment following elbow arthroscopy. Force plate analysis, pain scoring and kinematic evaluation were performed before anaesthesia, 4 and 24 hours after surgery. Peak vertical force index, symmetry index, rate of loading, rate of unloading, stance time and range of motion were obtained from gait analysis. Pain scoring was performed every 4 hours and interventional analgesia (0·3 mg/kg methadone) was administered if necessary.
Results: Of 29 dogs analysed, peak vertical force index (P<0·001), symmetry index (P=0·01) and rate of unloading (P=0·01) decreased significantly over time in each group; however, this was not affected by treatment. No significant differences were observed in stance time or rate of loading over time. Kinematic (range of motion) evaluation was not complete for all dogs. Pain scores increased significantly at both time points postoperatively in the no treatment group (P=0·007) and in morphine-treated dogs at 4 hours compared to
baseline (P=0.03). For intra-articular bupivacaine significant increases in pain scores were not detected (P=0.28).
Clinical Significance: No benefit to intra-articular bupivacaine or morphine was detected using peak vertical force index from force plate analysis. Bupivacaine prevented increases in pain scores at both time points as did morphine at the 24-hour evaluation, compared to no treatment.

**Effect of intratesticular lidocaine on isoflurane requirements in dogs undergoing routine castration (pages 393–397)** M. W. McMillan, C. J. Seymour and J. C. Brearley

Objectives: To evaluate the isoflurane sparing effect of intratesticular lidocaine administration in dogs undergoing castration.

Methods: Thirty dogs received a standardised anaesthetic regimen including systemic analgesia with intramuscular buprenorphine at a dose of 0.02 mg/kg and intravenous carprofen at a dose of 4 mg/kg. Dogs were randomly assigned to a lidocaine group receiving 1 mg/kg lidocaine into each testis or a control group receiving no lidocaine. Baseline physiological parameters were measured after 10 minutes at an end-tidal isoflurane concentration of 1:3%. End-tidal isoflurane concentration was altered throughout surgery to maintain these parameters within 10% of baseline and recorded at five time points. T0 was baseline, T1 was the start of surgery, T2 to T3 were clamping of the testicular pedicles and T4 was skin closure. End-tidal isoflurane concentrations were compared using analysis of variance and Bonferroni tests.

Results: Fifteen healthy dogs were included in each study group. End-tidal isoflurane concentration was significantly lower in the lidocaine group compared to the control group at T2 (P<0.01), T3 (P<0.01) and T4 (P<0.01).
Clinical Significance: Intratesticular lidocaine reduces isoflurane requirements in dogs undergoing castration.


Objectives: Haematologic profiles, electrolyte concentrations, blood gas values and acid–base balance have been studied and reported in healthy greyhounds; however, there is only one study published on blood gas values in Galgos Españoles. Because of their purported common origins with greyhounds (same group and class), it was hypothesised that Galgos Españoles also have differences in haematologic values, electrolyte concentrations, blood gas values and acid–base balance compared to other non

Methods: Venous blood samples from 30 Galgos Españoles and 20 dogs from different breeds were collected, and complete blood counts, electrolyte concentrations, blood gas values and acid–base balance were measured.

Results: From the 24 parameters analysed, 5 had statistically significant differences (P<0.05). Galgos Españoles had higher haematocrit (P<0.001), haemoglobin concentration (P=0.003), erythrocyte count (P=0.016) and pH (P=0.03), and lower platelet count (P=0.005), than those in other-breed dogs.
Clinical Significance: These results confirm that significant haematologic differences exist in Galgos Españoles when compared with other dogs, although these differences are not as striking as in greyhounds. Practitioners need to be aware of these breed-specific differences in order to make accurate diagnoses in Galgos Españoles.


Objectives: To investigate whether hospitalised dogs treated surgically may become culture positive for methicillin-resistant *Staphylococcus pseudointermidius* or methicillin-resistant *Staphylococcus aureus*.

Methods: Surgically treated dogs (n=45) were sampled for methicillin-resistant *Staphylococcus pseudointermidius* or methicillin-resistant *Staphylococcus aureus* on admission, before and after surgery and at the time of removal of surgical stitches. The hospital environment (n=57), including healthy dogs in the veterinary hospital environment (n=34), were sampled for methicillin-resistant *Staphylococcus pseudointermidius* or methicillin-resistant *Staphylococcus aureus*. Genetic variations among methicillin-resistant *Staphylococcus pseudointermidius* or methicillin-resistant *Staphylococcus aureus* isolates were identified through detection of restriction fragment polymorphisms.
Results: No dogs developed a wound infection due to methicillin-resistant *Staphylococcus pseudintermedius* or methicillin-resistant *Staphylococcus aureus*. However, there was a significant increase in the number of dogs carrying methicillin-resistant *Staphylococcus pseudintermedius* after hospitalisation compared to admission ($P<0.001$). No methicillin-resistant *Staphylococcus aureus* was isolated from dogs, but was present in the environment. Methicillin-resistant *Staphylococcus pseudintermedius* isolates were recovered from environmental surfaces and hospitalised animals, but not from healthy dogs. Methicillin-resistant *Staphylococcus pseudintermedius* isolates representing nine different restriction endonuclease digestion patterns were found, with two of these occurring in both the environment and on dogs.

Clinical Significance: Dogs may contract methicillin-resistant *Staphylococcus pseudintermedius* in association with surgery and hospitalisation. Resistant bacteria may be transmitted between dogs, staff and the environment. Dogs colonised with methicillin-resistant *Staphylococcus pseudintermedius* may be a source for hospital- and community-acquired infections.

**Effect of intraurethral administration of atracurium besylate in male cats with urethral plugs (pages 411–415).** F. Galluzzi, F. De Rensis, A. Menozzi and G. Spattini

Objective: To evaluate the effect of intraurethral administration of atracurium besylate for urinary obstruction resulting from urethral plugs in male cats.

Methods: Forty-five male cats were divided into the treatment group (n=25), in which 4 mL atracurium besylate solution (0.5 mg/mL) was injected into the urethral lumen, and the control group (n=20), treated with saline. All cats were then submitted to retrograde flushing until the removal of the occlusion was obtained.

Results: The percentage of cats in which the plug was removed at the first attempt was significantly ($P<0.05$) higher in the treatment group (64%) than in the control group (15%). Moreover, the mean ($\pm$SD) time required for the removal of the urethral obstruction was significantly shorter in the treatment group than in the control group (21.1 ±16.2 seconds versus 235.2 ±132.4 seconds; $P<0.001$).

Clinical Significance: The results of this study indicate that in adult male cats with urethral plugs, urethral administration of atracurium besylate increases the proportion of animals in which the obstruction is removed at the first attempt and reduces the time required to remove the urethral plugs.


Ultrasonography of a cat with diarrhoea and vomiting revealed a multi-layered, discrete linear structure within the large intestine with retention of the intestinal layers which could potentially be confused with an intestinal intussusception. The structure was ultimately expelled from the large intestine during defecation, and confirmed as a fibrinonecrotic cast. The origin of the fibrinonecrotic cast was assumed to be an intestinal pseudo-membrane formed in enteritis caused by immune suppression due to the panleukopenia virus. To our knowledge, this is the first ultrasonographic description of a fibrinonecrotic cast and spontaneous passage of the colonic cast in the veterinary field.

**Subclinical leishmaniasis associated with infertility and chronic prostatitis in a dog (pages 419–422).** F. Mir, E. Fontaine, E. Reyes-Gomez, M. Carlus and A. Fontbonne

A stud dog was presented for acquired infertility. Haematospermia and teratozoospermia were found on two ejaculates 2 weeks apart. A presumptive diagnosis of prostatitis was made follo-wing ultrasound examination. An ultrasound-guided needle core biopsy was performed under general anaesthesia, revealing a mild chronic macrophagic and plasma cell prostatitis with intracytoplasmic amastigotes consistent with *Leishmania* spp. infection. Presence of *Leishmania infantum*, *Leishmania donovani* or *Leishmania chagasi* was confirmed by polymerase chain reaction in seminal plasma. Serology and serum protein electrophoresis confirmed the diagnosis of a subclinical active systemic leishmaniasis. A meglumine antimoniate and allopurinol treatment was given which clearly improved within 3 months both general condition and the quality of sperm. To the authors’ knowledge, this is the first reported case of a prostatitis secondary to a *Leishmania* spp. infection. Subclinical systemic leishmaniasis should be considered in the differential diagnosis of infertility in dogs suffering from semen alterations.

A nine-year-old female Rottweiler presented with a 6-week history of progressive impairment of hindlimb adduction. Clinical examination showed abduction of both hind legs when walking on a smooth surface, pain at the medial surface of the left thigh, and an intrarectal palpable mass at the pelvic floor. Electromyography demonstrated fibrillation potentials in the adductor muscles on both sides. Pelvic radiographs showed severe osteolysis of the ischium. Gross post-mortem examination following euthanasia disclosed a large retroperitoneal mass, invading the obturator foramina and compressing both obturator nerves. Histopathological examination revealed a high-grade anaplastic sarcoma. Immunohistochemically, the tumour cells labelled positively for vimentin and alpha-smooth muscle actin, hence the tumour was considered a “myofibroblastic fibrosarcoma”. This unique case report describes a novel cause of obturator neuropathy in veterinary medicine. To date, clinical descriptions of obturator nerve lesions have been limited to pelvic fractures in small animals and following difficult labour in large animals.

American Journal of Veterinary Research

Platelet-neutrophil aggregate formation in blood samples from dogs with systemic inflammatory disorders

Brigitte Hedwig Dircks, Reinhard Mischke, Hans-Joachim Schuberth

Objective—To evaluate platelet-neutrophil aggregate (PNA) formation and neutrophil shape as indicators of neutrophil activation in dogs with systemic inflammatory diseases and after blood sample incubation with various platelet and neutrophil agonists.

Animals—20 dogs with systemic inflammatory response syndrome (SIRS) and 10 healthy Beagles.

Procedures—Neutrophils were isolated from blood samples directly after blood sample collection and after incubation of blood samples with phorbol myristate acetate, collagen, adenosine diphosphate, epinephrine, or various concentrations of lipopolysaccharide or arachidonic acid. CD61+ neutrophils as an indicator of PNA formation were evaluated, and neutrophil size and granularity were assessed via flow cytometry.

Results—Dogs with SIRS had more PNA formation, larger neutrophil size, and less granularity relative to control dogs, but no differences were evident when these dogs were grouped by whether they had sepsis (n = 6) or disseminated intravascular coagulation (12). A significant increase in PNA formation occurred after neutrophil incubation with all agonists, and incubation with phorbol myristate acetate elicited the strongest response. Neutrophils increased in size and decreased in granularity after incubation with all agonists except epinephrine. Incubation with lipopolysaccharide or arachidonic acid resulted in a dose-dependent effect on PNA formation and neutrophil shape.

Conclusions and Clinical Relevance—SIRS appeared to increase the degree of PNA formation and neutrophil shape change. Similar changes after neutrophil incubation with platelet agonists suggested that platelet activation has a role in PNA formation. Additional studies are necessary to determine the clinical importance and diagnostic value of PNA formation in dogs with SIRS and sepsis.

Journal of the American Veterinary Medical Association

Effect of brachycephalic, mesaticephalic, and dolichocephalic head conformations on olfactory bulb angle and orientation in dogs as determined by use of in vivo magnetic resonance imaging.

Aseel K. Hussein, BVMS, MSc; Martin Sullivan, BVMS, PhD; Jacques Penderis, BVSc, PhD.

Objective: To determine the effect of head conformation (brachycephalic, mesaticephalic, and dolichocephalic) on olfactory bulb angle and orientation in dogs by use of in vivo MRI.

Animals—40 client-owned dogs undergoing MRI for diagnosis of conditions that did not affect skull conformation or olfactory bulb anatomy.

Procedures—For each dog, 2 head conformation indices were calculated. Olfactory bulb angle and an index of olfactory bulb orientation relative to the rest of the CNS were determined by use of measurements obtained from sagittal T2-weighted MRI images.

Results—A significant negative correlation was found between olfactory bulb angle and values of both head conformation indices. Ventral orientation of olfactory bulbs was significantly correlated with high head conformation index values (ie, brachycephalic head conformation).
Conclusions and Clinical Relevance—Low olfactory bulb angles and ventral olfactory bulb orientations were associated with brachycephalia. Positioning of the olfactory bulbs, cribriform plate, and ethmoid turbinates was related. Indices of olfactory bulb angle and orientation may be useful for identification of dogs with extremely brachycephalic head conformations. Such information may be used by breeders to reduce the incidence or severity of brachycephalic-associated diseases.

Diagnosis of lameness in dogs by use of artificial neural networks and ground reaction forces obtained during gait analysis. Makiko Kaijima, MS; Timothy L. Foutz, PhD, PE; Ronald W. McClendon, PhD; Steven C. Budsberg, DVM, MS.

Objective—To evaluate the accuracy of artificial neural networks (ANNs) for use in predicting subjective diagnostic scores of lameness with variables determined from ground reaction force (GRF) data.

Animals—21 adult mixed-breed dogs.

Procedures—The left cranial cruciate ligament of each dog was transected to induce osteoarthritis of the stifle joint as part of another study. Lameness scores were assigned and GRF data were collected 2 times before and 5 times after ligament transection. Inputs and the output for each ANN were GRF variables and a lameness score, respectively. The ANNs were developed by use of data from 14 dogs and evaluated by use of data for the remaining 7 dogs (ie, dogs not used in model development).

Results—ANN models developed with 2 preferred input variables had an overall accuracy ranging from 96% to 99% for 2 data configurations (data configuration 1 contained patterns or observations for 7 dogs, whereas data configuration 2 contained patterns or observations for 7 other dogs). When additional variables were added to the models, the highest overall accuracy ranged from 97% to 100%.

Conclusions and Clinical Relevance—ANNs provided a method for processing GRF data of dogs to accurately predict subjective diagnostic scores of lameness. Processing of GRF data via ANNs could result in a more precise evaluation of surgical and pharmacological intervention by detecting subtle lameness that could have been missed by visual analysis of GRF curves.

Cannabinoid receptor type 1 and 2 expression in the skin of healthy dogs and dogs with atopic dermatitis. Luca Campora, DVM, PhD; Vincenzo Miragliotta, DVM, PhD; Emanuele Ricci, DVM, PhD; Luigia Cristino, Biol D, PhD; Vincenzo Di Marzo, Chem D, PhD; Francesco Albanese, DVM; Maria Federica della Valle, MSc; Francesca Abramo, DVM.

Objective—To determine the distribution of cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2) in skin (including hair follicles and sweat and sebaceous glands) of clinically normal dogs and dogs with atopic dermatitis (AD) and to compare results with those for positive control samples for CB1 (hippocampus) and CB2 (lymph nodes).

Sample—Skin samples from 5 healthy dogs and 5 dogs with AD and popliteal lymph node and hippocampus samples from 5 cadavers of dogs.

Procedures—CB1 and CB2 were immunohistochemically localized in formalin-fixed, paraffin-embedded sections of tissue samples.

Results—In skin samples of healthy dogs, CB1 and CB2 immunoreactivity was detected in various types of cells in the epidermis and in cells in the dermis, including perivascular cells with mast cell morphology, fibroblasts, and endothelial cells. In skin samples of dogs with AD, CB1 and CB2 immunoreactivity was stronger than it was in skin samples of healthy dogs. In positive control tissue samples, CB1 immunoreactivity was detected in all areas of the hippocampus, and CB2 immunoreactivity was detected in B-cell zones of lymphoid follicles.

Conclusions and Clinical Relevance—The endocannabinoid system and cannabimimetic compounds protect against effects of allergic inflammatory disorders in various species of mammals. Results of the present study contributed to knowledge of the endocannabinoid system and indicated this system may be a target for treatment of immune-mediated and inflammatory disorders such as allergic skin diseases in dogs.

Influence of dietary supplementation with l-carnitine on metabolic rate, fatty acid oxidation, body condition, and weight loss in overweight cats. Sharon A. Center, DVM; Karen L. Warner; John F. Randolph, DVM; Gregory D. Sunvold, PhD; Jason R. Vickers, MS.

Objective—To investigate the influence of dietary supplementation with l-carnitine on metabolic rate, fatty acid oxidation, weight loss, and lean body mass (LBM) in overweight cats undergoing rapid weight reduction.

Animals—32 healthy adult neutered colony-housed cats.

Procedures—Cats fattened through unrestricted ingestion of an energy-dense diet for 6 months were randomly assigned to 4 groups and fed a weight reduction diet supplemented with 0 (control), 50, 100, or 150 μg of carnitine/g of diet (unrestricted for 1 month, then restricted). Measurements included resting energy expenditure, respiratory quotient, daily energy expenditure, LBM, and fatty acid oxidation. Following weight loss, cats were allowed unrestricted feeding of the energy-dense diet to investigate weight gain after test diet cessation.
Results—Median weekly weight loss in all groups was ≥ 1.3%, with no difference among groups in overall or cumulative percentage weight loss. During restricted feeding, the resting energy expenditure-to-LBM ratio was significantly higher in cats that received l-carnitine than in those that received the control diet. Respiratory quotient was significantly lower in each cat that received l-carnitine on day 42, compared with the value before the diet began, and in all cats that received l-carnitine, compared with the control group throughout restricted feeding. A significant increase in palmitate flux rate in cats fed the diet with 150 μg of carnitine/g relative to the flux rate in the control group on day 42 corresponded to significantly increased stoichiometric fat oxidation in the l-carnitine diet group (> 62% vs 14% for the control group). Weight gain (as high as 28%) was evident within 35 days after unrestricted feeding was reintroduced.

Conclusions and Clinical Relevance—Dietary l-carnitine supplementation appeared to have a metabolic effect in overweight cats undergoing rapid weight loss that facilitated fatty acid oxidation.

Effects of inulin or yeast cell-wall extract on nutrient digestibility, fecal fermentative end-product concentrations, and blood metabolite concentrations in adult dogs fed raw meat–based diets. Alison N. Beloshapka, MS; Laura M. Duclos, PhD; Brittany M. Vester Boler, PhD; Kelly S. Swanson, PhD.

Objective—To determine the effects of raw meat–based diets with and without inulin or yeast cell-wall (YCW) extract on macronutrient digestibility, blood cell counts, serum metabolite concentrations, and fecal fermentative end-product concentrations in healthy adult dogs.

Animals—6 healthy adult spayed female dogs (mean ± SD age, 5.5 ± 0.5 years; mean body weight, 8.5 ± 0.5 kg).

Procedures—Dogs were fed each of the following 6 diets for 21 days, the order of which was randomly assigned in a Latin square design: beef control, beef and 1.4% inulin, beef and 1.4% YCW extract, chicken control, chicken and 1.4% inulin, and chicken and 1.4% YCW extract. Each diet trial consisted of a phase for diet adaptation (days 0 to 14) and a phase for measurement of urine and fecal output and content (days 15 to 20). On day 21, food was withheld for blood sample collection. Afterward, the next diet trial began immediately.

Results—All dogs maintained desirable fecal quality characteristics and produced low fecal volume. All diets were highly digestible (protein digestibility > 88%; fat digestibility > 97%). Differences in fermentative end-product concentrations among all diets were minor, but a significant increase in fecal short-chain fatty acid concentrations was evident when dogs were fed beef-based diets with inulin and YCW extract. Fecal spermine concentrations were higher with diets containing inulin and YCW extract than with control diets. Blood cell counts and serum metabolite values were within reference limits after each trial. All diets resulted in maintenance of nitrogen balance.

Conclusions and Clinical Relevance—Results suggested the raw meat–based diets evaluated were highly digestible in dogs. The increase in fecal short-chain fatty acid concentrations achieved when inulin and YCW extract were included may be beneficial to canine health.

Prevalence and types of tooth resorption in dogs with oral tumors. Ana Nemec, DVM, PhD; Boaz Arzi, DVM; Brian Murphy, DVM, PhD; Philip H. Kass, DVM, PhD; Frank J. M. Verstraete, DrMedVet.

Objective—To determine the prevalence and types of tooth resorption in dogs with oral tumors and to compare findings with those for control dogs.

Animals—101 dogs with oral tumors and 128 control dogs that did not have oral tumors and for which dental radiographs were available.

Procedures—Exclusion criteria for dogs included systemic disease, long-term administration of anti-inflammatory drugs, traumatic occlusion, severe semigeneralized or generalized periodontitis, and endodontic disease. For each dog with an oral tumor, histologic sections of biopsy specimens of tumors were examined. Dental radiographic images of dogs were examined, and the presence and type of tooth resorption were determined for each tooth. Statistical analyses were performed to compare data regarding prevalence of tooth resorption.

Results—Teeth at tumor sites in dogs with nonodontogenic tumors were significantly more frequently affected with external inflammatory resorption, compared with teeth at tumor sites in dogs with odontogenic tumors. Teeth at sites distant from tumors in dogs with oral tumors were 3.2 times as likely to have external surface resorption (OR, 3.2; 95% confidence interval, 1.3 to 7.9) and 83.4 times as likely to have external inflammatory resorption (OR, 83.4; 95% confidence interval, 9.7 to 719.6) as teeth in control dogs.

Conclusions and Clinical Relevance—Resorption of teeth at tumor sites and at sites distant from tumors was common in dogs with oral tumors. Results of the present study will contribute to an understanding of the complex effects of oral tumors on local and distant hard tissues.

Effects of ocular administration of ophthalmic 2% dorzolamide hydrochloride solution on aqueous humor flow rate and intraocular pressure in clinically normal cats. Amy J. Rankin, DVM, MS; William R. Crumley, DVM, MS; Rachel A. Allbaugh, DVM, MS. Kansas State University.
Objective—To determine the effects of ocular administration of ophthalmic 2% dorzolamide hydrochloride solution on aqueous humor flow rate (AHFR) and intraocular pressure (IOP) in clinically normal cats.

Animals—20 clinically normal domestic shorthair cats.

Procedures—Following an acclimation period, IOP was measured in each eye of all cats 5 times daily for 3 days to determine baseline values. Fifteen cats received 1 drop of 2% dorzolamide solution and 5 cats received 1 drop of control solution in each eye every 8 hours for 5 days (treatment phase). The IOP of each eye was measured 5 times during each day of the treatment phase. Prior to and after the treatment phase, AHFR in both eyes of each cat was measured via fluorophotometry.

Results—Prior to treatment, AHFR or IOP did not differ between the treatment and control groups. In dorzolamide-treated cats, mean AHFR after the treatment phase (3.47 ± 1.5 μL/min) was significantly lower than the value prior to treatment (5.90 ± 2.2 μL/min) and mean IOP during the treatment phase (11.1 ± 1.0 mm Hg) was significantly lower than the baseline mean IOP (14.9 ± 1.0 mm Hg). In the control group, IOP values did not differ before or during the treatment phase and AHFRs did not differ before and after the treatment phase.

Conclusions and Clinical Relevance—Ocular administration of 2% dorzolamide solution significantly decreased AHFR and IOP in clinically normal cats. Application of 2% dorzolamide solution may be an effective treatment in cats with glaucoma.

Frequency of spontaneous canine herpesvirus-1 reactivation and ocular viral shedding in latently infected dogs and canine herpesvirus-1 reactivation and ocular viral shedding induced by topical administration of cyclosporine and systemic administration of corticosteroids. Eric C. Ledbetter, DVM; Erotides C. da Silva, DVM, MS; Sung G. Kim, PhD; Edward J. Dubovi, PhD; Wayne S. Schwark, DVM, PhD.

Objective—To determine the frequency of spontaneous canine herpesvirus-1 (CHV-1) reactivation and ocular viral shedding in latently infected dogs and the effect of topical ocular administration of cyclosporine.

Animals—8 mature Beagles with experimentally induced latent CHV-1 infection.

Procedures—Following induction of primary ocular CHV-1 infection, the presence of reactivatable CHV-1 latency was confirmed by systemically administering prednisolone to the dogs. Dogs were then monitored for 36 weeks via clinical examination and conjunctival sample CHV-1 PCR assay performed at 4-day intervals and CHV-1 virus neutralization antibody assay performed at 2-week intervals. During weeks 16 to 32, dogs were administered 0.2% cyclosporine ointment in both eyes twice daily and blood cyclosporine concentrations were monitored. During weeks 33 to 36, the presence of reactivatable CHV-1 latency was reconfirmed via systemic administration of prednisolone.

Results—Reactivation of latent CHV-1 was not detected via clinical examination or viral shedding during the initial 32 weeks, including before and during topical ocular administration of cyclosporine, and there were no significant differences in CHV-1 virus neutralization titer increases between the study periods. Blood cyclosporine concentrations were less than assay detection limits in all dogs on the sampling days. Systemic administration of corticosteroids repeatedly resulted in ocular disease and viral shedding.

Conclusions and Clinical Relevance—Spontaneous CHV-1 reactivation did not occur frequently in latently infected mature dogs, and this was not altered by topical ocular administration of cyclosporine. This characteristic may be a factor contributing to the lower frequency of recurrent herpetic ocular disease in dogs relative to other host species and their associated alphaherpesviruses.

Ciprofloxacin pharmacokinetics and oral absorption of generic ciprofloxacin tablets in dogs. Mark G. Papich, DVM, MS.

Objective—To determine the pharmacokinetics of ciprofloxacin in dogs, including oral absorption following administration of generic ciprofloxacin tablets.

Animals—6 healthy Beagles.

Procedures—In a crossover study design, ciprofloxacin was administered as a generic tablet (250 mg, PO; mean dose, 23 mg/kg) and solution (10 mg/kg, IV) to 6 dogs. In a separate experiment, 4 of the dogs received ciprofloxacin solution (10 mg/mL) PO via stomach tube (total dose, 250 mg). Blood samples were collected before (time 0) and for 24 hours after each dose. Plasma concentrations were analyzed with high-pressure liquid chromatography. Pharmacokinetic analysis was performed by means of compartmental modeling.

Results—When ciprofloxacin was administered as tablets PO, peak plasma concentration was 4.4 μg/mL (coefficient of variation [CV], 55.9%), terminal half-life (t1/2) was 2.6 hours (CV, 10.8%), area under the time-concentration curve was 22.5 μg·h/mL (CV, 62.3%), and systemic absorption was 58.4% (CV, 45.4%). For the dose administered IV, t1/2 was 3.7 hours (CV, 52.3%), clearance was 0.588 L/kg/h (CV, 33.9%), and volume of distribution was 2.39 L/kg (CV, 23.7%). After PO administration as a solution versus IV administration, plasma concentrations were more uniform and consistent among dogs, with absorption of 71% (CV, 7.3%), t1/2 of 3.1 hours (CV, 18.6%), and peak plasma concentration of 4.67 μg/mL (CV, 17.6%).
Conclusions and Clinical Relevance—Inconsistent oral absorption of ciprofloxacin in some dogs may be formulation dependent and affected by tablet dissolution in the small intestine. Because of the wide range in oral absorption of tablets, the dose needed to reach the pharmacokinetic-pharmacodynamic target concentration in this study ranged from 12 to 52 mg/kg (CV, 102%), with a mean dose of 25 mg/kg, once daily, for bacteria with a minimum inhibitory concentration ≤ 0.25 μg/mL.

Pharmacokinetics of penciclovir in healthy cats following oral administration of famciclovir or intravenous infusion of penciclovir. Sara M. Thomasy, DVM, PhD; Ted Whittem, BVSc, PhD; Jerry L. Bales, Pharm D; Marcus Ferrone, PhD, Pharm D; Scott D. Stanley, PhD; David J. Maggs, BVSc.

Objective—To investigate the pharmacokinetics of penciclovir in healthy cats following oral administration of famciclovir or IV infusion of penciclovir.

Animals—6 cats.

Procedures—Cats received famciclovir (40 [n = 3] or 90 [3] mg/kg, PO, once) in a balanced crossover-design study; the alternate dose was administered after a ≥ 2-week washout period. After another washout period (≥ 4 weeks), cats received an IV infusion of penciclovir (10 mg/kg delivered over 1 hour). Plasma penciclovir concentrations were analyzed via liquid chromatography-mass spectrometry at fixed time points after drug administration.

Results—Mean ± SD maximum plasma concentration (Cmax) of penciclovir following oral administration of 40 and 90 mg of famciclovir/kg was 1.34 ± 0.33 μg/mL and 1.28 ± 0.42 μg/mL and occurred at 2.8 ± 1.8 hours and 3.0 ± 1.1 hours, respectively; penciclovir elimination half-life was 4.2 ± 0.6 hours and 4.8 ± 1.4 hours, respectively; and penciclovir bioavailability was 12.5 ± 3.0% and 7.0 ± 1.8%, respectively. Following IV infusion of penciclovir (10 mg/kg), mean ± SD penciclovir clearance, volume of distribution, and elimination half-life were 4.3 ± 0.8 mL/min/kg, 0.6 ± 0.1 L/kg, and 1.9 ± 0.4 hours, respectively.

Conclusions and Clinical Relevance—Penciclovir pharmacokinetics following oral administration of famciclovir were nonlinear within the dosage range studied, likely because of saturation of famciclovir metabolism. Oral administration of famciclovir at 40 or 90 mg/kg produced similar Cmax and time to Cmax values. Therefore, the lower dose may have similar antiviral efficacy to that proven for the higher dose.

Evaluation of long-term glucose homeostasis in lean and obese cats by use of continuous glucose monitoring. Margarethe Hoenig, Dr med vet, PhD; Nicole Pach, MS; Karl Thomaseeth, Dr Ing, PhD; Frerich DeVries, Dr med vet; Duncan C. Ferguson, VMD, PhD.

Objective—To evaluate intraday and interday variations in glucose concentrations in cats and to test the utility of a continuous glucose monitoring system (CGMS).

Animals—6 lean and 8 long-term (> 5 years) obese cats.

Procedures—Blood glucose concentrations were measured during the course of 156 hours by use of a laboratory hexokinase-based reference method and a handheld glucometer. Interstitial glucose concentrations were evaluated with a CGMS.

Results—Paired measures of glucose concentrations obtained with the CGMS typically were marginally higher than concentrations for the reference method and less biased than concentrations obtained with the glucometer. This was partially confirmed by the concordance correlation coefficients of the concentration for the CGMS or glucometer versus the concentration for the reference method, although the correlation coefficients were not significantly different. Mean ± SD area under the curve for the glucose concentration (AUCG) did not differ significantly between lean (14.0 ± 0.5 g/dL•h) and obese (15.2 ± 0.5 g/dL•h) cats during the 156-hour period, but one of the obese cats had a much higher AUCG. Within-day glucose variability was small in both lean and obese cats.

Conclusions and Clinical Relevance—Glucose homeostasis was maintained, even in long-term obese cats, and intraday glucose fluctuations were small. One obese cat might have been classified as prediabetic on the basis of the AUCG, which was approximately 25% higher than that of the other obese and lean cats. The CGMS can be useful in the evaluation of long-term effects of drugs or diet on glucose homeostasis in cats.

Journal of the American Veterinary Medicine Association

Antimicrobial drug use in dogs prior to admission to a veterinary teaching hospital. Sarah A. Baker, MPH-VPH; Joany Van-Balen, DVM; Bo Lu, PhD; Andrew Hillier, BVSc, DACVD; Armando E. Hoet, DVM, PhD, DACVPM.

Objective—To determine frequency of antimicrobial drug (AMD) use in dogs within 12 months prior to admission to a veterinary teaching hospital.

Design—Owner survey and medical records review.

Animals—435 dogs admitted to a veterinary teaching hospital.
Procedures—Demographic characteristics and information regarding AMD use in dogs were obtained from medical records and results of surveys completed by owners of dogs.

Results—242 (55.6%) dogs received at least 1 AMD within 12 months prior to hospital admission; 125 (51.7%) of these dogs had a disease of the integument at the time of admission. β-Lactam AMDs were used more frequently than AMDs of any other class (176/242 [72.7%] dogs). Three hundred sixty-eight dogs had a medical problem at the time of hospital admission; 225 (61.1%) of these dogs had received at least 1 AMD within 12 months prior to hospital admission. Dogs referred by a veterinarian to the hospital were 2.39 times as likely to have received at least 1 AMD within 30 days prior to hospital admission as were dogs admitted without a referral.

Conclusions and Clinical Relevance—Results indicated AMDs were frequently administered to dogs prior to admission to the teaching hospital. Use of AMDs in animals could be a risk factor for coselection and spread of multidrug-resistant pathogens, and colonization or infection of dogs with such pathogens could have a negative impact on the health of other animals and humans.

Comparison of the efficacy of amoxicillin-clavulanic acid, cefovecin, and doxycycline in the treatment of upper respiratory tract disease in cats housed in an animal shelter. Annette L. Litster, BVSc, PhD, MMedSci; Ching Ching Wu, DVM, PhD; Peter D. Constable, BVSc, PhD, DACVIM.

Objective—To compare efficacy of amoxicillin-clavulanic acid, cefovecin, and doxycycline in shelter-housed cats with clinical signs of upper respiratory tract disease (URTD).

Design—Randomized prospective clinical trial.

Animals—48 cats with URTD.

Procedures—Conjunctival and nasal swab specimens were obtained for culture and susceptibility testing, and cats were randomly assigned to 3 treatment groups (16 cats/group) on day 1: amoxicillin-clavulanic acid (12.5 mg/kg [5.68 mg/lb], PO, q 12 h, for 14 days), cefovecin (8.0 mg/kg [3.64 mg/lb], SC, once), or doxycycline (10.0 mg/kg [4.55 mg/lb], PO, q 24 h, for 14 days). Oculonasal discharge, sneezing, coughing, dyspnea, demeanor, and food intake were scored twice daily for 14 days (scale, 0 [subjectively normal] to 3 [markedly abnormal]).

Results—The most common bacterial isolates were Mycoplasma spp (n = 22) and Bordetella bronchiseptica (9). Cats treated with amoxicillin-clavulanic acid or doxycycline had significantly increased body weight by day 14. Cats that received doxycycline had significantly lower overall oculonasal discharge scores than those treated with amoxicillin-clavulanic acid or cefovecin. Cats treated with amoxicillin-clavulanic acid or doxycycline had significantly lower overall sneezing scores than those that received cefovecin. Cats that received amoxicillin-clavulanic acid had significantly decreased demeanor and food intake scores on day 2, whereas this was detected later in other groups (demeanor score on days 5 and 7 and food intake score on days 10 and 11 in the cefovecin and doxycycline groups, respectively).

Conclusions and Clinical Relevance—Oral administration of amoxicillin-clavulanic acid or doxycycline appeared to be more effective than a single SC injection of cefovecin in treating cats with clinical signs of URTD.

Erythrocyte-bound immunoglobulin isotypes in dogs with immune-mediated hemolytic anemia: 54 cases (2001–2010). Kenneth R. Harkin, DVM, DACVIM; Jill A. Hicks, DVM; Melinda J. Wilkerson, DVM, PhD, DACVP.

Objective—To identify erythrocyte-bound immunoglobulin (Ig) isotypes in dogs with primary immune-mediated hemolytic anemia (IMHA).

Design—Retrospective case series.

Animals—54 dogs with IMHA

Procedures—Medical records of dogs with IMHA diagnosed between January 2001 and April 2010 were examined. Immunoglobulin isotype (tested via direct immunofluorescence by flow cytometry to identify erythrocyte-bound Ig), Hct, serum bilirubin concentration, presence of autoagglutination, degree of spherocytosis, duration of hospitalization, and 90-day outcome were recorded.

Results—The Hct on admission was significantly lower in dogs with IgG and IgM isotypes bound to erythrocytes, compared with dogs with a single Ig isotype, and the degree of spherocytosis was greater in dogs with IgG and IgM bound to erythrocytes, compared with dogs that only had IgM. Dogs with only IgM were not more likely to have autoagglutination, compared with dogs that only had IgG on the erythrocyte surface. Although Ig isotype was not associated with survival time, initial serum total bilirubin concentration was higher in nonsurvivors

Conclusions and Clinical Relevance—Results suggested that dogs with IMHA with ≥ 2 Ig isotypes bound to erythrocytes, particularly IgG and IgM, are likely to have a more severe degree of anemia, spherocytosis, and autoagglutination.
Evaluation of preoperative serum concentrations of ionized calcium and parathyroid hormone as predictors of hypocalcemia following parathyroidectomy in dogs with primary hyperparathyroidism: 17 cases (2001–2009). Melissa Arbaugh, DVM; Daniel Smeak, DVM, DACVS; Eric Monnet, DVM, PhD, DACVS.

Objective—To determine whether preoperative serum ionized calcium (iCa) or parathyroid hormone (PTH) concentrations help predict postoperative hypocalcemia following parathyroidectomy in dogs with primary hyperparathyroidism.

Design—Retrospective case series.

Animals—17 dogs with primary hyperparathyroidism treated with parathyroidectomy.

Procedures—Medical records were evaluated from years 2001 to 2009. Data evaluated included age, breed, sex, clinical signs, diagnostic tests performed, preoperative and postoperative iCa concentrations, preoperative PTH concentrations, and whether calcium supplementation was provided following surgery. Two groups were identified on the basis of whether dogs became hypocalcemic (iCa < 1.2 mmol/L) following parathyroidectomy.

Results—12 dogs developed hypocalcemia after surgery. Preoperative (within 24 hours before surgery) iCa concentrations for the hypocalcemic group (mean ± SD, 1.82 ± 0.22 mmol/L) and the nonhypocalcemic group (1.83 ± 0.29 mmol/L) were not significantly different. Calcium concentrations decreased in a linear fashion during the 24 hours following parathyroidectomy, and the slopes of the decrease over that time were not significantly different between the 2 groups. Preoperative PTH concentrations were not significantly different between the hypocalcemic and nonhypocalcemic groups.

Conclusions and Clinical Relevance—Preoperative iCa and PTH concentrations were not predictive of postoperative hypocalcemia in dogs undergoing parathyroidectomy for primary hyperparathyroidism. Future studies to evaluate whether calcium supplementation should be provided on an individual basis with perhaps more emphasis on clinical signs than iCa concentrations after surgery may be warranted.

The Veterinary Journal

Nanomedicine and veterinary science: The reality and the practicality
C. Underwood, A.W. van Eps

Abstract
Nanomedicine is a rapidly expanding field with a promising future that is already permeating veterinary science. This review summarises the current applications for nanoparticles in human medicine and explores their potential applicability for veterinary use. The principles underlying the use of nanoparticles in drug delivery, imaging and as vaccine adjuvants are explored along with the unique issues surrounding nanoparticle toxicity and regulatory approval. A brief overview of the properties of different nanoparticle systems including, liposomes, micelles, emulsions and inorganic nanoparticles, is provided, along with a description of their current and potential future applications in veterinary medicine.

Prognostic studies of canine and feline mammary tumours: The need for standardized procedures
A.J.F. Matosa, C.S. Baptista, M.F. Gärtner, G.R. Rutteman

Abstract
For several years, veterinary oncologists have been struggling with the prognosis of mammary tumours in dogs and cats. Translation of tumour characteristics into prognostic information is an invaluable tool for the use of the most appropriate therapies, as well as for planning innovative therapeutic trials. Moreover, canine and feline spontaneous mammary gland tumours are good models for the study of human breast cancer. Collecting and interpreting information regarding the prognosis of canine and feline mammary tumours is difficult due to the fact that different methods have been applied to study various components and characteristics. This review identifies some of the challenges of prognostic studies of spontaneous canine and feline mammary tumours and suggests standardized procedures to overcome these challenges and facilitate reproducibility and assessment of results.

Identification of tumour initiating cells in feline head and neck squamous cell carcinoma and evidence for gefitinib induced epithelial to mesenchymal transition
L.Y. Pang, G.T. Bergkvist, A. Cervantes-Arias, D.A. Yool, R. Muirhead, D.J. Argyle

Abstract
Feline oral squamous cell carcinoma is considered a highly invasive cancer that carries a high level of morbidity. Despite aggressive surgery, patients often succumb to disease, the tumour having inherent insensitivity to radiation and chemotherapy. In this study we sought to identify cells within the feline SCC1 line that have stem cell properties, including inherent resistance mechanisms. When feline cells were subjected to harsh growth conditions, they formed sphere colonies consistent with a stem cell phenotype. Utilising CD133,
we were able to identify a small fraction of cells within the population that had enhanced sphere-forming ability, reduced sensitivity to radiation and conventional chemotherapy and demonstrated resistance to the EGFR-targeting drug, gefitinib. In addition, long-term culture of feline SCC1 cells in gefitinib caused a change in cell morphology and gene expression reminiscent of an epithelial to mesenchymal transition. Taken together, these results suggest that feline SCC may be driven by small subset of cancer stem cells.

Haemostatic abnormalities in cats with naturally occurring liver diseases
Brigitte Dircks, Ingo Nolte, Reinhard Mischke

Abstract
Alterations in the haemostatic system were characterized in cats with different naturally occurring liver diseases. The study looked at 44 healthy cats and 45 cats with different liver diseases confirmed histologically or cytologically (neoplasia, n = 9; inflammation, n = 12; hepatic lipidosis, n = 13; other degenerative liver diseases, n = 11). The following parameters were evaluated: platelet count; prothrombin time; activated partial thromboplastin time; thrombin time; factor (F) II, FV, FVII, FX, and FXIII activities; fibrinogen concentration; activities of antithrombin, protein C, plasminogen, and α2-plasmin inhibitor, and D-dimer concentration. In cats with liver diseases, 44/45 (98%) had one or more abnormalities of the coagulation parameters measured. In cats with inflammatory liver diseases, increased D-dimer concentrations and decreased FXIII activity were the most consistent abnormalities and were found in 83% and 75% of cats, respectively. The most common abnormality in cats with neoplastic liver disease was FXIII deficiency (78%). The most consistent abnormalities in cats with hepatic lipidosis were increased FV activity and D-dimer concentration with 54% of cats having values above the reference range for both parameters. Cats with miscellaneous degenerative liver disease most frequently showed FXIII deficiency (64%). The results of this study show that alterations of single haemostatic components are a frequent finding in cats with liver disease. Activation of haemostasis with subsequent consumptive coagulopathy (rather than decreased synthesis) seems to be responsible for these alterations. Increased blood levels of different haemostatic components in cats with inflammatory lesions may be related to an acute phase reaction.

Comparison of injectable robenacoxib versus meloxicam for peri-operative use in cats: Results of a randomised clinical trial
Masatoshi Kamata*, Masatoshi Kamata, Jonathan N. King**, Wolfgang Seewaldb, Nobuhiro Sakakihara*, Kazuto amashita*, Ryohei Nishimura*

Abstract
The objective of this study was to evaluate the efficacy and tolerability of robenacoxib, a selective cyclooxygenase-2 inhibitor, for the treatment of post-operative pain and inflammation in cats. The study was a prospective, multi-centre, randomised, blinded, non-inferiority design clinical study to compare robenacoxib to meloxicam. Ninety-six cats undergoing surgery at eight centres in Japan were allocated randomly to receive a single SC injection of robenacoxib (2 mg/kg, n = 67) or meloxicam (0.3 mg/kg, n = 29) shortly before induction of anaesthesia. Most cats underwent soft tissue surgery (n = 87), mainly ovariectomy (n = 68). Post-operative pain and inflammation were assessed at 3, 8 and 22 h after recovery from anaesthesia using numerical rating scales. For the primary efficacy endpoint (total clinician score), robenacoxib had significantly better efficacy than meloxicam, the relative efficacy ratio being 1.47 (95% confidence interval 1.19–1.78, P = 0.0003). For the secondary efficacy endpoints, robenacoxib was superior to meloxicam when assessed on the basis of posture, behaviour, pain on palpation and overall pain control, while meloxicam was superior with respect to wound heat. No cat in either group required rescue analgesia therapy. In tolerability assessments, pain during injection and pain and inflammation at the injection site 22 h after recovery from anaesthesia were rated significantly less with robenacoxib compared to meloxicam. Both treatments were well tolerated on the basis of clinical observations and blood tests, with no significant differences between groups. In conclusion, single pre-operative administration of robenacoxib was well tolerated and had superior efficacy to meloxicam in reducing post-operative pain in cats.

Breed, age and gender distribution of dogs with chronic hepatitis in the United Kingdom

Abstract
Standardised histological criteria are now available for the diagnosis of canine chronic hepatitis (CH). CH is common in dogs, but no studies have reported breed, age and gender distributions in the United Kingdom (UK). The objective of this study was to determine which breeds had an increased risk for developing CH in the UK and to report the age and gender distribution for those breeds. The databases of six veterinary histopathology laboratories were searched for cases with a histological diagnosis of CH according to standardised criteria. The breed, age and gender of dogs was recorded and compared to a control population to calculate the odds ratio and
Immunological differences in the global release of the major cat allergen Fel d 1 are influenced by sex and behavior

Cécile Bienboire-Frosinia, Alessandro Cozzi, Céline Lafont-Lecuelle, Daniel Vervloet, Catherine onin, Patrick Pageat

Abstract

The biological function of Fel d 1, the major cat allergen released in the environment, is still unclear despite studies suggesting a putative role in chemical communication. Structural and immunological polymorphisms of Fel d 1 have been described. This study examined how Fel d 1 immunological polymorphism may have a physiological origin by estimating a potential relationship with the sex of cats and cat–human interactions.

Samples from bath washes of 21 cats were screened to study antibody binding to Fel d 1 using an ELISA. Personality and Tolerance Handling scores were used to assess the behaviour of the cats. In the washes, Fel d 1 concentrations were significantly lower in females than in males (P < 0.05). Slopes from the ELISA dose–dependent curves varied among the cats: males secreted Fel d 1 variants with higher antibody recognition than females (P < 0.01). Females that were aggressive and difficult to handle displayed a diminished slope value, and therefore a weaker Fel d 1 immunoreactivity in global washes, compared to females that were sociable (P = 0.09) and easy to handle (P = 0.07). This study shows a variable immunological polymorphism of Fel d 1 within a cat population, particularly between males and females, and this polymorphism appears to be related to cat–human interactions.

Evaluation of the presence of Leishmania spp. by real-time PCR in the lacrimal glands of dogs with leishmaniosis

Carolina Naranjo, Dolors Fondevilla, Laura Altep, Olga Francino, José Rios, Xavier Roura, Teresa Peña

Abstract

Leishmania infantum infection is highly prevalent in endemic areas. Dogs with leishmaniosis may develop keratoconjunctivitis sicca (KCS). The goals of this study were (1) to quantify Leishmania amastigotes in the Meibomian glands (MG), main lacrimal gland (MLG) and nictitating membrane gland (NMG) from dogs with leishmaniosis; (2) to compare these results to immunohistochemistry (IHC), and (3) to explore the association between the Leishmania parasite load and the presence of ocular clinical signs. Twenty-five dogs diagnosed with leishmaniosis were included. MG, MLG and NMG from both eyes were collected. Histopathology, IHC and real-time PCR were performed.

All specimens yielded positive real-time PCR results. For all three glands, samples from dogs with ocular clinical signs had mean ΔCt (cycle threshold) values significantly lower (higher parasite loads) than those from dogs without signs. Cut-off values of ΔCt < 0, ΔCt < 4 and ΔCt < 4.9 for MG, MLG and NMG, resulted in a likelihood ratio of positives of 5.9, 6.38 and 6.38, respectively. Samples with ΔCt values below the reported cut-off were significantly more likely to display clinical signs related to KCS than those with results above the cut-off, for all three glands. Similarly, ΔCt values below the cut-off were significantly associated with positive IHC. In this study real-time PCR has been standardised for use in MG, MLG and NMG. A cut-off value established from each of these tissues may aid the clinician in the discrimination between ocular signs related to Leishmania from those associated with other causes of KCS.

Electroencephalographic recordings in dogs suffering from idiopathic and symptomatic epilepsy: Diagnostic value of interictal short time EEG protocols supplemented by two activation techniques

Christina Brauer, Sabine B.R. Kästner, Karl Rohn, Henning C. Schenk, Julia Tünsmeyer, Andrea Tipold

Abstract

The diagnostic value of interictal short time electroencephalographic (EEG) recordings in epileptic dogs under general anaesthesia with propofol and the muscle relaxant rocuronium bromide was investigated. Two activation techniques, namely photic stimulation and hyperventilation, were evaluated for their potential to enhance the diagnostic validity of these recordings. Sixty-one dogs suffering from idiopathic epilepsy and 28 dogs suffering from symptomatic epilepsy were included. Electroencephalograms were recorded using five subdermal EEG
lymphatic invasion, and necrosis. These findings suggest that Treg cells play a role in canine MC progression.

Intratumoral areas markedly increased in tumors with poor prognostic factors, such as high histological grade, associated with high histological grade and lymphatic invasion. The numbers of Treg cells infiltrating microenvironments, the numbers of Treg cells were analyzed and compared with histological prognostic factors in canine mammary carcinoma (MC) tissues (J.H. Kim 1). The distribution of Treg cells was not well-documented in veterinary oncology. To identify the characteristics of Treg cells in tumor microenvironments, the numbers of Treg cells were analyzed and compared with histological prognostic factors and molecular biomarkers in canine mammary carcinoma (MC) tissues (n = 37). Abundant Treg cells were associated with high histological grade and lymphatic invasion. The numbers of Treg cells in infiltrating intratumoral areas markedly increased in tumors with poor prognostic factors, such as high histological grade, lymphatic invasion, and necrosis. These findings suggest that Treg cells play a role in canine MC progression.

The effect of radiological hip dysplasia and breed on survival in a prospective cohort study of four large dog breeds followed over a 10 year period

Randi I. Krontveit 1, H. Hurb 2, M. Bolognina 3, Ane Nødtvedt 4, Ian Dohoob 5, Lars Moe 6, Bente K. vika 7

Abstract

The aim of the study was to measure the effect of radiological hip and elbow dysplasia status and breed on overall survival in a cohort of four large dog breeds in Norway. Privately owned dogs of the Newfoundland (NF), Labrador Retriever (LR), Leonberger (LEO), and Irish Wolfhound (IW) breeds were followed prospectively from birth to 10 years of age. The age of death/euthanasia was registered. A total of 501 dogs from 103 litters were enrolled. Kaplan–Meier survival curves were used to describe breed differences in survival times. The effects of radiological hip and elbow dysplasia status as well as breed were assessed using a Cox proportional hazards model. The variables ‘sex’ and ‘living region’ were explored as potential confounders. Among LRs, 60.2% of the dogs were still alive at 10 years of age, and the corresponding figures for NFs, LEOs, and IWs were 28.8%, 16.11%, and 6.4%, respectively. Radiological hip dysplasia status and breed were found to influence overall survival. Two different time-varying effects were observed in that with the IW the hazard of death increased linearly through time, while the effect of severe radiological hip dysplasia decreased logarithmically with time. Location influenced the death hazard and dogs living in suburban areas or cities had longer mean time to death and a lower hazard compared to dogs living in the countryside. Radiological elbow dysplasia status was not found to have an effect on overall survival.

Effects of obesity on lung function and airway reactivity in healthy dogs

J. Manens 8, M. Bolognina 3, F. Bernaerts 9, M. Diez 10, N. Kirschvink 11, C. Clercx 12

Abstract

The present study investigated the effects of bodyweight (BW) gain on respiratory function and airway responsiveness in healthy Beagles using barometric whole body plethysmography (BWBP). Six adult dogs were examined before and after a fattening diet. The high-energy diet induced a mean increase in BW of 41 ± 6%. BWBP basal parameters were recorded prior to airway reactivity testing (using increasing concentrations of histamine nebulisations). An airway responsiveness index (H-Penh300) was calculated as the histamine concentration necessary to reach 300% of basal enhanced pause (Penh, bronchoconstriction index). The same dogs underwent a doxapram hydrochloride (Dxp) stimulation testing 2 weeks later. Basal measurements showed that obese dogs had tidal volume per kg (TV/BW) that was significantly decreased whilst respiratory rate (RR) increased significantly. H-Penh300 decreased significantly in obese Beagles, indicating increased bronchoreactivity. Dxp administration induced a significant increase in TV/BW, minute volume per kg (MV/BW), peak inspiratory and expiratory flows per kg (PIF/BW and PEF/BW) in both normal and obese dogs although the TV/BW increase was significantly less marked in the obese group. In conclusion, obesity induced changes in basal respiratory parameters, increased bronchoreactivity and a blunted response to Dxp-induced respiratory stimulation. This combination of basal respiratory parameters, bronchoreactivity testing and pharmacological stimulation testing using non-invasive BWBP can help characterize pulmonary function and airway responsiveness in obese dogs.

Correlation of Foxp3 positive regulatory T cells with prognostic factors in canine mammary carcinomas


Abstract

Regulatory T cells (Treg) cells play a crucial role in tumor progression by suppressing anti-tumor immunity, but are not well-documented in veterinary oncology. To identify the characteristics of Treg cells in tumor microenvironments, the numbers of Treg cells were analyzed and compared with histological prognostic factors and molecular biomarkers in canine mammary carcinoma (MC) tissues (n = 37). Abundant Treg cells were associated with high histological grade and lymphatic invasion. The numbers of Treg cells infiltrating intratumoral areas markedly increased in tumors with poor prognostic factors, such as high histological grade, lymphatic invasion, and necrosis. These findings suggest that Treg cells play a role in canine MC progression.
Furthermore, Treg cell numbers in intratumoral compartments may provide a potential prognostic factor when assessing canine MCs, which may in turn lead to the development of new immunologic therapeutics.

**A comparison of in vitro relaxant responses to ipratropium bromide, β-adrenoceptor agonists and theophylline in feline bronchial smooth muscle**

Jérôme Leemansa, Nathalie Kirschvinkb, Pascal Gustin

Abstract

This study compares the potency and efficacy of different relaxant drugs including anticholinergic, β-adrenergic and methylxanthine agents on acetylcholine-contracted feline bronchi, and investigates the influence of the initial muscarinic-induced tone on bronchodilator response. Feline bronchi were removed from euthanased client-owned cats and were contracted with acetylcholine to cause either 40% or 80% of the acetylcholine maximal contraction. The efficacy and potency of bronchodilating drugs were obtained from cumulative dose–response curves with efficacy (E_{max}) as the maximal relaxant response and potency (−log EC_{50}) as the logarithm of the concentration of drug inducing 50% of maximal relaxation.

Under low contractile tone (40%), all bronchodilators relaxed feline bronchi in a concentration-dependent manner with the following rank order of potency: formoterol > ipratropium bromide > fenoterol > isoprenaline > salbutamol = salmeterol > theophylline. E_{max} values ranged from 80% to 100% depending on the tested drug. Constriction of feline bronchi with high-dose acetylcholine (80%) caused a rightward and downward shift of the β2-mimetic dose–response curves. Significant decreases in −log EC_{50} and E_{max} values were reported for salbutamol, formoterol and salmeterol. This study provides evidence that existing classes of bronchodilators produce effective relaxation of acetylcholine-contracted feline bronchi and that airway responsiveness to β2-stimulants is dependent on the magnitude of the initial muscarinic-induced tone. The clinical relevance of these in vitro findings has yet to be explored in clinical trials.

**Pharmacokinetics of intravenous and intramuscular parecoxib in healthy Beagles**

M. Giorgi, G. Saccomann, S. Del Carlo, C. Manera, E. Lavy

Abstract

Parecoxib is an inactive pro-drug that is rapidly converted to valdecoxib, a selective cyclooxygenase (COX)-2 inhibitor registered for the management of post-operative pain in humans. Recent studies have suggested that parecoxib has excellent clinical efficacy and safety in veterinary species. The aim of the current study was to assess the pharmacokinetics of parecoxib and valdecoxib after intravenous (IV) and intramuscular (IM) administration. Seven healthy male Beagle dogs received 2.5 mg/kg parecoxib by either the IV or IM route in a cross-over design, with the alternative route of administration used 1 week later. The plasma concentrations of both analytes were detected according to a previously validated method using high performance liquid chromatography with fluorescence detection (HPLC-FL).

No adverse effects were observed in any animal during the study. For both routes of administration, parecoxib was rapidly and almost completely converted to valdecoxib. The parecoxib/valdecoxib area under the curve (AUC) ratio for both routes of administration was 1.4. The half-life of valdecoxib was about 2 h, which was shorter than reported for humans, although the plasma concentrations following both routes of administration were likely to be effective for analgesia. The absolute bioavailability of parecoxib was 66%. The pharmacokinetic features of parecoxib make it suitable for treatment of acute pain in the canine species.

**Canine intestinal mast cell tumor with c-kit exon 8 mutation responsive to imatinib therapy**

Masato Kobayashia, Osamu Sugisakia, Noriko Ishia, Osamu Yamadaa, Keita Itoa, Shiiori Kuroki, Yu asakia, Kenichiro Onoa, Tsukimi Washizu, Makoto Bonkobara

Abstract

A canine intestinal mast cell tumor with splenic metastasis was treated with imatinib. The intestinal and metastatic tumor masses markedly decreased following treatment although the clinical response was short lasting. A c-kit internal tandem duplication mutation, c.1250_1261dup, which causes an insertion of four amino acids in KIT, was identified in cDNA isolated from the tumor cells. The phosphorylation status of the mutant KIT and the effect of imatinib on its phosphorylation were examined using 293 cells transfected with c-kit carrying the c.1250_1261dup mutation. This mutation caused ligand-independent phosphorylation of KIT, which was suppressed by imatinib. Inhibition of constitutively activated mutant KIT with imatinib could underlie the tumor response in this dog.
Successful resolution of oesophageal spirocercosis in 20 dogs following daily treatment with oral doramectin
Remo Lobetti
Abstract
The purpose of this study was to evaluate the effect of a daily oral dose of doramectin in dogs with spirocercosis. Twenty naturally infected dogs were treated with 0.5 mg/kg doramectin administered orally once daily for 42 days. In 13 of the dogs there was resolution of the nodules after 42 days. Nodules were eliminated in five of the remaining seven dogs following treatment for an additional 42 days. In the remaining two dogs, treatment continued for a further 42 days (total 126 days), resulting in complete resolution. No adverse events associated with treatment were observed. This study concluded that doramectin at 0.5 mg/kg once a day is effective in the elimination of Spirocerca lupi nodules in dogs.

Effects of the GnRH antagonist acyline on the testis of the domestic cat (Felis catus)
G. Garcia Romeroa, P.E. Fernándezb, E. Gimenoab, C. Barbeitob, C. Gobelloab
Abstract
The aim of this study was to describe the effects of a single dose of the gonadotrophin releasing hormone (GnRH) antagonist acyline on testicular characteristics of the domestic cat. Twelve mature cats were orchidectomised unilaterally (right testis) on Day -7 (n = 7) or Day 15 (n = 5). On Day 0, 330 μg/kg acyline was administered SC to all the animals. Left orchidectomy was carried out on Day 15 (n = 2), Day 30 (n = 4) and Day 60 (n = 6). Sperm were recovered from the epididymis and the testes were evaluated grossly, histologically and immunohistochemically. Significant differences (P < 0.05) were found between days for epididymal sperm motility, vigor, abnormal morphology, germinal epithelium height, spermatocytes, spermatids, spermatozoa, lumen and cellular debris. Conversely, no significant differences were found for gross testicular and tubular characteristics, spermatogonia, Sertoli and Leydig cells and intertubular compartments. It was concluded that a single dose of acyline reversibly impaired spermiogenesis, spermatocytogenesis and sperm motility for 2 weeks.

Genome-wide analysis of mitral valve disease in Cavalier King Charles Spaniels
Anne T. Frencha,b, Rob Ogdenb, Cathlene Elandb, Gibran Hemant, Ricardo Pong-Wongb, Brendan orcoranab, Kim M. Summersa,b
Abstract
The Cavalier King Charles Spaniel (CKCS) is prone to severe early onset mitral valve disease. In this study, 36 purebred CKCS dogs were evaluated for mitral valve murmur and divided into early and late onset groups. A genome-wide genetic approach was used to assess whether the condition is determined by a small number of genetic factors. There were no regions of highly discrepant homo/heterozygosity in the two groups. Similarly, there was no evidence for loci associated with mitral valve murmur in a genome-wide association study. This analysis suggests that familial occurrence of mitral valve murmur in the CKCS breed is not due to a single major gene effect, indicating that breeding strategies to eliminate the disease cannot be based on genotype information at this time.

Reference values and clinical application of magnetic peripheral nerve stimulation in cats
Iris Van Soensa, Michel M.R.F. Struysb,c, Sofie F.M. Bhattia, Luc M.L. Van Ham
Abstract
Magnetic stimulation of radial (RN) and sciatic (SN) nerves was performed bilaterally in 40 healthy cats. Reference values for onset latency and peak-to-peak amplitude of magnetic motor evoked potentials (MMEPs) were obtained and compared with values of electric motor evoked potentials (EMEPs) in 10/40 cats. Onset latencies and peak-to-peak amplitudes of the MMEPs of three cats with polyneuropathy (PNP) were compared to the reference values. Magnetic motor evoked responses were easily recorded in all normal cats. Significant differences were found in onset latencies between MMEPs and EMEPs, but peak-to-peak amplitudes were equal. The MMEPs of three cats with PNP can be seen as outliers in comparison to the reference values. MMEPs from the RN and SN were easily obtained and reproducible in normal cats. The technique could represent a useful adjunct in the assessment of peripheral nerve disorders.

Genotyping of exercise-induced collapse in Labrador retrievers using an allele-specific PCR
Masamine Takanosua, Hirokazu Morib, Hiroetsu Suzukic, Katsushi Suzuki
Abstract
Exercise-induced collapse (EIC) is an autosomal recessive disorder in Labrador retrievers. In this study, an allele-specific PCR was developed to detect the point mutation G767T in exon 6 of canine DNM1, previously shown to be responsible for canine EIC. Of 133 Labrador retrievers tested in Japan, 6 (4.5%) were homozygous (EIC) and 50 (37.6%) were heterozygous (carriers) for the G767T mutation.