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August 2012 abstracts

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Sinonasal aspergillosis in dogs: a review
M. J. Sharman, C. S. Mansfield

Sinonasal aspergillosis is an uncommon, yet debilitating and often frustrating condition to treat in dogs despite years of research evaluating pathogenesis, diagnosis and treatment. The disease is most commonly caused by non-invasive fungal infection, thought to be secondary to altered innate and/or adaptive immune responses. Attempts to confirm this have however failed. A variety of conflicting opinions regarding the diagnosis and treatment of sinonasal aspergillosis exist. Often the use of a particular treatment protocol is based upon personal or regional preference. Evaluation of the veterinary literature demonstrates that the evidence base in support of individual treatment recommendations is weak. A number of recent publications have helped to expand the current knowledge base and therefore our understanding of important practicalities for both diagnostic options and treatment protocols. The following review examines the current evidence for the pathogenesis of sinonasal aspergillosis in dogs, as well as the various diagnostic options. The available evidence for frequently utilised -therapeutic options and their likely outcomes is also explored.

Erythema multiforme and epitheliotropic T-cell lymphoma in the oral cavity of dogs: 1989 to 2009
A. Nemec, R. Zavodovskaya, V. K. Affolter and F. J. M. Verstraete

Objectives: To describe the clinical signs, major laboratory findings, diagnostic procedures and outcome in dogs with erythema multiforme or epitheliotropic T-cell lymphoma of the oral cavity.

Methods: Retrospective analysis identified 14 client-owned dogs with erythema multiforme or epitheliotropic T-cell lymphoma of the oral cavity. Histological changes were combined with immunohistochemistry and clonality testing data in selected cases, and a clinical follow-up was acquired.

Results: Ulcerative stomatitis with no significant or only minor abnormalities on haematology and serum biochemistry panels was common. Histological features were diagnostic in seven cases. The use of immunohistochemistry distinguished the two diseases in an additional three cases. In four cases, the diagnosis remained questionable, and clonality testing for T-cell receptor gamma gene rearrangement helped confirm erythema multiforme in one case. Clinical follow-up revealed erythema multiforme in two and epitheliotropic T-cell lymphoma in one of the remaining questionable cases.

Clinical Significance: Erythema multiforme and epitheliotropic T-cell lymphoma may affect, but are rarely limited to the oral cavity of dogs, and they usually present as stomatitis. Histological features alone are not always diagnostic. Immunohistochemistry and clonality testing may assist in the differentiation between the two, but in ambiguous cases, repeated biopsy and clinical follow-up are essential.

Biochemical assessment of canine body cavity effusions using three bench-top analysers
N. Hetzel, K. Papasouliotis, S. Dodkin and K. Murphy

Objectives: To assess the performance of three bench-top chemistry instruments for the analysis of canine effusions. Acceptable results were compared with those obtained by a reference chemistry analyser.

Methods: Total protein, albumin, creatinine and bilirubin concentrations were measured in 74 effusions using the VetScanVS2, VetTest8008 and SpotchemEZ analysers. Cholesterol and triglyceride concentrations were also measured by the VetTest and Spotchem. Results were analysed using Westgard’s error analysis, Spearman's correlation, Bland-Altman plots and Deming regression. Results were considered acceptable when observed total error (TE_{obs}) was less than allowable total error (TE_{A}).

Results: VetScan error analysis revealed acceptable results for total protein (TE_{obs}=1·11, TE_{A}=4·7) and creatinine (TE_{obs}=42·2, TE_{A}=78·1). Correlation was fair for protein (r_x=0·66) and creatinine (r_x=0·76), but poor and not significant for bilirubin (r_x=0·01, P=0·08), precluding error analysis. VetTest error analysis was acceptable for creatinine only (TE_{obs}=5·55, TE_{A}=25·5). Correlation was good (r_x=0·81). The difference plot revealed a bias (95% confidence interval) of −1·5 (−37 to 40) and four outliers. The Spotchem did not generate a precise arithmetic value in most (56·9 to 73·6%) samples, precluding further analysis.

Clinical Significance: Acceptable results were obtained for total protein (VetScan) and creatinine [VetScan, Vettest (with good correlation)]. The Spotchem is of limited value in canine effusion Analysis.

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The cutaneous trunci reflex for localising and grading thoracolumbar spinal cord injuries in dogs
R. Gutierrez-Quintana, J. Edgar, A. Wessmann, G. B. Cherubini and J. Penderis

Objectives: To evaluate the accuracy of the cutaneous trunci reflex to localise thoracolumbar spinal cord injuries and to assess the correlation between focal loss (cut-off) of the reflex and clinical severity of thoracolumbar spinal cord injury.

Methods: Prospective study of 41 dogs with thoracolumbar spinal cord injuries investigated by magnetic resonance imaging. Linear regression analysis was performed to determine the relationship between the vertebral level of the cutaneous trunci reflex cut-off and the maximal and cranial lesion extent. The association between cutaneous trunci reflex cut-off and spinal cord injury severity was tested using a Mann–Whitney U test.

Results: Cutaneous trunci reflex cut-off was evident in 33 (80%) of dogs. The cut-off level was 0 to 4 vertebrae caudal to the maximal spinal cord lesion in all dogs. In 16 (48.5%) dogs the cut-off was either 2 or 3 vertebrae caudal to the lesion. The presence of a cut-off significantly correlated with increasing severity (P=0.0001). Loss of the reflex occurred at less severe grades than loss of ambulation and in dogs with ambulatory paresis it was significantly (P=0.0084) associated with increasing severity.

Clinical Significance: The cutaneous trunci reflex allows localisation of thoracolumbar spinal cord lesions within four vertebrae and facilitates clinical segregation of dogs with ambulatory paresis into mild and severe categories.

Carcinocythaemia (carcinoma cell leukaemia) in a dog: an acute leukaemia-like picture due to metastatic carcinoma
M. Amati, F. Miele, G. Avallone, B. Banco and W. Bertazzolo

An eight-year-old entire female boxer was presented with a two-week history of anorexia and lethargy and two-day history of unilateral left epistaxis. Clinical findings and laboratory test results suggested disseminated intravascular coagulation. On blood smear evaluation, occasional large epithelioid-like unclassified cells were detected. Occasionally these cells were organised in small clusters. Bone marrow examination revealed a marked infiltration by a malignant population of the same epithelioid-like cells. The dog was euthanased because of the guarded prognosis. Following histology and immunohistochemistry, a widespread undifferentiated carcinoma of unknown primary origin was diagnosed. To the authors’ knowledge, this is the first case of carcinoma cell leukaemia reported in a dog. Carcinoma cell leukaemia is a rare oncological condition previously described in humans, characterised by non-haematopoietic neoplastic cells in peripheral blood.

Lingual osteoma in a dog
M. Fernandez, L. Grau-Roma, X. Roura and N. Majó

An 11-year-old male Belgian shepherd dog was evaluated for a one-week history of progressive lethargy, decreased appetite and excessive panting. On physical examination, a pedunculated mass protruding from the right side of the tongue base was observed. The mass was solid, irregular and multi-lobulated, and it measured approximately 4×2 cm. The mass was surgically excised. The histological examination was consistent with a lingual osteoma and the margins were free of neoplastic cells. The dog was euthanased eight months after the diagnosis because of an unrelated problem and no evidence of recurrence at the surgical site was appreciated at that time. To the author's knowledge, this is the first report of a lingual osteoma in a dog, and, therefore, it should be included in the differential diagnosis of masses on the tongue, especially pedunculated masses located at the base of the tongue.

Bacterial infective arthritis following a penetrating stick injury of the stifle joint in a dog
S. P. Clarke and J. F. Ferguson

An eight-year-old, Rottweiler was presented with a chronic non-weight bearing right pelvic limb-lameness and a discharging sinus at the right stifle joint. Fifteen weeks previously a diagnosis of bacterial infective arthritis had been made, presumed attributable to haematogenous spread. Failure to respond to appropriate surgical and medical management resulted in severe joint dysfunction. The poor prognosis for restoration of limb function resulted in limb amputation. Subsequent exploration of the sinus tract and the stifle joint revealed a stick within the craniolateral aspect of the joint. This penetrating stick injury had been responsible for the persistent bacterial infective arthritis.
Serum cobalamin, urine methylmalonic acid, and plasma total homocysteine concentrations in Border Collies and dogs of other breeds.


Objective—To determine reference ranges for serum cobalamin (Cbl), urine methylmalonic acid (uMMA), and plasma total homocysteine (tHcys) concentrations and to compare values for healthy control dogs with values for Border Collies (BCs), a breed in which hereditary cobalamin deficiency has been identified.

Animals—113 BCs, 35 healthy control dogs fed a typical diet, and 12 healthy dogs fed a bone and raw food diet exclusively.

Procedures—Urine and blood samples were obtained from each dog and Cbl, uMMA, and tHcys concentrations were determined.

Results—Reference ranges for Cbl (261 to 1,001 ng/L), uMMA (0 to 4.2 mmol/mol of creatinine), and tHcys (4.3 to 18.4 μmol/L) concentrations were determined. Four BCs had a Cbl concentration lower than the assay detection limit (150 ng/L); median uMMA and tHcys concentrations in these dogs were 4,064 mmol/mol of creatinine and 51.5 μmol/L, respectively. Clinical abnormalities included stunted growth, lethargy, anemia, and proteinuria. Abnormalities improved after administration of cobalamin. Of the 109 healthy BCs with Cbl and tHcys concentrations within reference ranges, 41 (37.6%) had a high uMMA concentration (range, 5 to 360 mmol/mol). Results for dogs fed raw food were similar to those for control dogs.

Conclusions and Clinical Relevance—Hereditary cobalamin deficiency is a rare disease with various clinical signs. The finding of methylmalonic aciduria in healthy eucobalaminemic BCs and BCs with clinical signs of Cbl deficiency was surprising and indicated these dogs may have defects in intracellular processing of Cbl or intestinal Cbl malabsorption, respectively. Studies investigating Cbl absorption and metabolic pathways are warranted.

Oncolysis of canine tumor cells by myxoma virus lacking the serp2 gene

Ashlee S. Urbasic, Stacy Hynes, Amy Somrak, Stacey Contakos, Masmudur M. Rahman, Jia Liu, Amy L. MacNeill.

Objective—To determine the oncolytic efficacy of an attenuated form of myxoma virus lacking the serp2 gene in canine tumor cells.

Sample—Primary cells were isolated from tumors that were surgically removed from dogs and from connective tissue obtained from the cadaver of a dog. Cells of various established cell lines from tumors and nontumorous tissues were obtained.

Procedures—Experiments were performed with cells in monolayer culture. Cell cultures were inoculated with wild-type myxoma viruses or myxoma viruses lacking the serp2 gene, and measures of cytopathic effects, viral growth kinetics, and cell death and apoptosis were determined.

Results—Myxoma viruses replicated in cells of many of the primary and established canine tumor cell lines. Canine tumor cells in which expression of activated protein kinase B was upregulated were more permissive to myxoma virus infection than were cells in which expression of activated protein kinase B was not upregulated. Myxoma viruses lacking the serp2 gene caused more cytopathic effects in canine tumor cells because of apoptosis than did wild-type myxoma viruses.

Conclusions and Clinical Relevance—Results of the present study indicated myxoma viruses lacking the serp2 gene may be useful for treatment of cancer in dogs.

Impact for Human Medicine—Results of the present study may be useful for development of novel oncolytic treatments for tumors in humans.

Effects of gemcitabine and gemcitabine in combination with carboplatin on five canine transitional cell carcinoma cell lines

Joao Felipe de Brito Galvao, MS; William C. Kisseberth, Sridhar Murahari, Saikaew Sutayatram, Dennis J. Chew, Nongnuch Inpanbutr

Objective—To evaluate in vitro effects of gemcitabine alone and in combination with carboplatin on canine transitional cell carcinoma (TCC) cell lines.

Sample—In vitro cultures of 5 canine TCC cell lines.
Procedures—Cells were treated with gemcitabine, carboplatin, or a combination of both at various concentrations. Cell proliferation was assessed via a fluorescence-based microplate cell proliferation assay. Cell cycle was evaluated via propidium iodide staining, and apoptosis was assessed by measurement of caspase 3 and 7 enzymatic activity. Synergy between gemcitabine and carboplatin was quantified via combination index analyses.

Results—Treatment of 5 canine TCC cell lines with gemcitabine or carboplatin decreased cell proliferation, increased apoptosis, and induced cell cycle arrest. Cell cycle arrest and apoptosis were markedly increased when cell lines were treated with both gemcitabine and carboplatin simultaneously or sequentially. Order of administration during sequential treatment did not consistently affect cell proliferation results in TCC cell lines. When TCC cell lines were treated with gemcitabine and carboplatin in combination at therapeutically relevant concentrations (gemcitabine concentration, < 10μM; carboplatin concentration, < 250μM), a significant decrease in cell proliferation was observed, compared with cell proliferation following treatment with gemcitabine or carboplatin alone. In combination, the effects of gemcitabine and carboplatin were synergistic in 3 of 5 cell lines and additive in the other 2.

Conclusions and Clinical Relevance—Gemcitabine had antitumor effects on canine TCC cells in vitro, and the combination of gemcitabine and carboplatin had synergistic activity at biologically achievable concentrations.

Effect of omega-3 polyunsaturated fatty acids and body condition on serum concentrations of adipokines in healthy dogs

Objective—To determine associations between serum concentrations of omega-3 polyunsaturated fatty acids or body condition and serum concentrations of adiponectin, leptin, insulin, glucose, or triglyceride in healthy dogs.

Animals—62 healthy adult client-owned dogs.

Procedures—Body condition score and percentage of body fat were determined. Blood samples were collected after food was withheld for 12 hours. Serum was harvested for total lipid determination, fatty acid analysis, and measurement of serum concentrations of adiponectin, leptin, insulin, glucose, and triglyceride. Associations between the outcome variables (adiponectin, leptin, insulin, glucose, and triglyceride concentrations) and each of several variables (age, sex, percentage of body fat, and concentrations of total lipid, α-linolenic acid, eicosapentaenoic acid, docosapentaenoic acid, and docosahexaenoic acid) were determined.

Results—Serum concentrations of docosapentaenoic acid were significantly positively associated with concentrations of adiponectin and leptin and negatively associated with concentrations of triglyceride. Serum concentrations of α-linolenic acid were significantly positively associated with concentrations of triglyceride. No significant associations were detected between serum concentrations of eicosapentaenoic acid or docosahexaenoic acid and any of the outcome variables. Percentage of body fat was significantly positively associated with concentrations of leptin, insulin, and triglyceride but was not significantly associated with adiponectin concentration. Age was positively associated with concentrations of leptin, insulin, and triglyceride and negatively associated with concentrations of adiponectin. Sex did not significantly affect serum concentrations for any of the outcome variables.

Conclusions and Clinical Relevance—Docosapentaenoic acid may increase serum concentrations of adiponectin and leptin and decrease serum triglyceride concentration in healthy dogs.

Refractive state following retinal reattachment and silicone oil tamponade in dogs


Objective—To evaluate the refractive error induced by intraocular administration of silicone oil (SiO) in dogs.

Animals—47 client-owned dogs evaluated for blindness secondary to retinal detachment.

Procedures—3-port pars plana vitrectomy with perfluoro-octane and SiO exchange (1,000- or 5,000-centistoke SiO) was performed in 1 or both eyes for all dogs (n = 63 eyes), depending on which eye or eyes were affected. Dogs were normotensive, had complete oil filling of the eyes, and were examined in a standing position for retinoscopic examination of both eyes (including healthy eyes).

Results—The mean refractive error for SiO-filled phakic and pseudophakic eyes was 2.67 and 3.24 D, respectively. The mean refractive error for SiO-filled aphakic eyes was 6.50 D. Dogs in which 5,000-centistoke SiO was used had consistently greater positive refractive errors (mean, 3.45 D); compared with dogs in which 1,000-centistoke SiO was used (mean, 2.10 D); however, the difference was nonsignificant. There was no
significant linear relationship between refractive error and the number of days between surgery and retinoscopy. Conclusions and Clinical Relevance—Hyperopia was observed in all dogs that underwent SiO tamponade, regardless of lens status (phakic, pseudophakic, or aphakic). Aphakic eyes underwent a myopic shift when filled with SiO. Pseudophakic eyes appeared to be more hyperopic than phakic eyes when filled with SiO; however, additional investigation is needed to confirm the study findings.

Isolation, characterization, and in vitro proliferation of canine mesenchymal stem cells derived from bone marrow, adipose tissue, muscle, and periosteum

Agatha H. Kisiel, Laurie A. McDuffee, Elmabrok Masaoud, Trina R. Bailey, Blanca P. Esparza Gonzalez, Rodolfo Nino-Fong.

Objective—To isolate and characterize mesenchymal stem cells (MSCs) from canine muscle and periosteum and compare proliferative capacities of bone marrow-, adipose tissue-, muscle-, and periosteum-derived MSCs (BMSCs, AMSCs, MMSCs, and PMSCs, respectively).

Sample—7 canine cadavers.

Procedures—MSCs were characterized on the basis of morphology, immunofluorescence of MSC-associated cell surface markers, and expression of pluripotency-associated transcription factors. Morphological and histochemical methods were used to evaluate differentiation of MSCs cultured in adipogenic, osteogenic, and chondrogenic media. Messenger ribonucleic acid expression of alkaline phosphatase, RUNX2, OSTERIX, and OSTEOPONTIN were evaluated as markers for osteogenic differentiation. Passage-1 MSCs were counted at 24, 48, 72, and 96 hours to determine tissue-specific MSC proliferative capacity. Mesenchymal stem cell yield per gram of tissue was calculated for confluent passage-1 MSCs.

Results—Successful isolation of BMSCs, AMSCs, MMSCs, and PMSCs was determined on the basis of morphology; expression of CD44 and CD90; no expression of CD34 and CD45; mRNA expression of SOX2, OCT4, and NANOG; and adipogenic and osteogenic differentiation. Proliferative capacity was not significantly different among BMSCs, AMSCs, MMSCs, and PMSCs over a 4-day culture period. Periosteum provided a significantly higher MSC yield per gram of tissue once confluent in passage 1 (mean ± SD of 19,400,000 ± 12,800,000 of PMSCs/g of periosteum obtained in a mean ± SD of 13 ± 1.64 days).

Conclusions and Clinical Relevance—Results indicated that canine muscle and periosteum may be sources of MSCs. Periosteum was a superior tissue source for MSC yield and may be useful in allogenic applications.

Journal of the American Veterinary Medical Association

Effects of two training curricula on basic laparoscopic skills and surgical performance among veterinarians

Boel A. Fransson, Claude A. Ragle, Margaret E. Bryan.

Objective—To compare laparoscopic skills among veterinarians before and after undertaking 1 of 2 programs of simulation training.

Design—Evaluation study.

Sample Population—17 veterinarians at 1 institution.

Procedures—Basic skills were tested by use of the McGill inanimate system for training and evaluation of laparoscopic skills (MISTELS). Surgical performance was assessed through an objective structured assessment of technical skills (OSATS). Both tests were performed prior to and after a 12-session training program, consisting of MISTELS exercises (curriculum A) or a variety of exercises (curriculum B).

Results—Curriculum B led to improvement of scores obtained with both the MISTELS and the OSATS. Curriculum A did not result in higher scores obtained with the MISTELS, compared with curriculum B. Curriculum A did not lead to an improvement of scores obtained with the OSATS. Participant-perceived value of the training program was correlated positively with the improvement of scores for MISTELS suturing tasks and scores obtained with the OSATS. Time spent in clinical laparoscopic surgery and curriculum B training were both positively correlated with the post-training OSATS scores but not with post-training MISTELS scores. Conversely, simulation training time correlated with an increase in MISTELS scores but not OSATS scores.

Conclusions and Clinical Relevance—MISTELS training resulted in significant improvement of basic laparoscopic skills but not in the assessment used for surgical performance. This may have been due to the small number of study participants, the assessment tool, or the method of training. A varied curriculum may be advantageous when training veterinarians for clinical laparoscopic practice.
Use of pleural access ports for treatment of recurrent pneumothorax in two dogs
Alane Kosanovich Cahalane, James A. Flanders.

Case Description—An 8-year-old castrated male mixed-breed dog (dog 1) and a 13-year-old spayed female mixed-breed dog (dog 2) were evaluated because of spontaneous pneumothorax.

Clinical Findings—Both dogs had decreased bronchovesicular sounds with coughing, tachypnea, cyanosis, lethargy, or a combination of these clinical signs. Radiographic examination revealed pneumothorax in both dogs and consolidation of a lung lobe in dog 2. Pneumothorax was alleviated following thoracocentesis in both dogs but recurred.

Treatment and Outcome—Dog 1 was initially treated by placement of a thoracostomy tube but underwent thoracotomy when pneumothorax recurred after tube removal; left caudal lung lobectomy was performed because a ruptured bulla was suspected, and a pulmonary bulla was histologically confirmed. Dog 2 underwent thoracotomy with left caudal lung lobectomy and partial removal of the left cranial lung lobe; diffuse pulmonary emphysema was diagnosed. This dog underwent a second surgery for right caudal lung lobectomy because of torsion. When pneumothorax recurred and additional surgery was not considered feasible, pleural access ports were placed in both dogs for repeated removal of air from the thoracic cavity. Ports were used clinically for 17 days in dog 1 and 14 days in dog 2. Dog 1 successfully underwent another surgery when pneumothorax recurred 18 days after port placement but was euthanized 17 months later when dyspnea and tachypnea recurred. Pneumothorax had not recurred further in dog 2 twenty-three months after port placement.

Clinical Relevance—Findings suggested that pleural access ports may have a role in the management of spontaneous pneumothorax in dogs.

Use of three-dimensional conformal radiation therapy for treatment of a heart base chemodectoma in a dog
Nicholas J. Rancilio, Takashi Higuchi, Jerome Gagnon, Elizabeth A. McNiel

Case Description—A 9-year-old spayed female mixed-breed dog was evaluated because of a progressively worsening, nonproductive cough and gagging of 1 year’s duration.

Clinical Findings—Physical examination results were unremarkable. A cranial mediastinal mass was identified at the heart base with 3-view thoracic radiography. A CT scan of the thorax revealed an invasive mass surrounding major vessels at the heart base that was not considered surgically resectable. Thoracoscopic biopsy specimens of the cranial mediastinal mass were obtained, and histologic evaluation revealed that the tumor was a chemodectoma.

Treatment and Outcome—On the basis of results of the CT scan, a 3-D conformal radiation therapy plan was generated with computer treatment-planning software. The patient was treated with external beam radiation therapy; a 6-MV linear accelerator was used to deliver a prescribed dose of 57.5 Gy in twenty-three 2.5-Gy fractions. The cough improved following radiation therapy. Prior to treatment, the tumor volume was calculated to be 126.69 cm³. Twenty-five months following radiation therapy, a follow-up CT scan was performed and there was a >50% reduction in tumor volume at that time. Disease progression causing pericardial, pleural, and peritoneal effusion and syncopal episodes occurred 32 months following radiation therapy, which were treated with pericardectomy and additional radiation therapy. The dog was still alive and doing well 42 months following initial radiation treatment.

Clinical Relevance—Conformal radiation therapy provided an additional treatment option for a nonresectable heart base chemodectoma in the dog of this report; conformal radiation therapy was reasonably tolerable and safe.

Australian Veterinary Journal

Coeliotomy-assisted intrauterine insemination in dogs: a study of 238 inseminations
DM Burgess, KE Mitchell and PGA Thomas

Objective: (1) To report whelping rates and litter sizes following coeliotomy-assisted intrauterine inseminations (CAII) performed commercially and (2) to identify factors that may influence these outcomes.

Design: Retrospective single cohort observational study.
Procedure: All oestrous cycles in bitches that presented to the study hospital for CAII between 1 January 2005 and 31 December 2010 were included. One insemination was performed per oestrus. Whelping and litter size following CAII were recorded. Potential determinants of these outcomes were assessed.

Results: Of 238 inseminations performed, 174 (73.1%) resulted in whelping. The known litter size ranged from 1 to 16 pups (mean ± SD 6.12 ± 3.12 pups). From univariable analyses, progressive motility percentage was the only variable significantly associated with odds of whelping (P = 0.020); bitch parity and weight were associated with litter size when adjusted for each other (P = 0.035 and 0.003, respectively). Inseminations performed with >200 × 10⁶ progressively motile sperm were more likely to result in whelping relative to inseminations with >100–200 × 10⁶ progressively motile sperm (odds ratio 3.61, 95% confidence interval 0.84–15.5, P = 0.084), and, in a separate model, relative to >75–125 × 10⁶ progressively motile sperm (odds ratio 6.09, 95% confidence interval 1.41–26.36, P = 0.016).

Conclusion: Whelping rates and litter sizes were similar to other case studies and the experimental reports of CAII. Progressive motility percentage affects the odds of whelping, and litter size is affected by both the weight and parity of the bitch. Importantly, these findings provide some evidence that whelping rates with CAII are not maximised unless more than 200 × 10⁶ progressively motile sperm are inseminated.

**Flow cytometric detection of alpha-1-acid glycoprotein on feline circulating leucocytes**
S Paltrinieri, I Marchini and ME Gelain

Objective: To assess whether alpha-1-acid glycoprotein (AGP) can be detected on the membrane of feline circulating leucocytes.

Design: The presence of AGP on circulating leucocytes was investigated in both clinically healthy cats and cats with different diseases. A group of feline coronavirus (FCoV)-positive cats, comprising cats with feline infectious peritonitis (FIP) and cats not affected by FIP but seropositive for FCoV, were included in this study because the serum concentration of AGP increases during FCoV infection.

Procedure: Flow cytometry (using an anti-feline AGP antibody), serum protein electrophoresis, routine haematology and measurement of the serum AGP concentration were performed using blood samples from 32 healthy cats (19 FCoV-seropositive), 13 cats with FIP and 12 with other diseases (6 FCoV-seropositive). The proportion of cats with AGP-positive leucocytes in the different groups (e.g. controls vs sick; FIP vs other diseases, etc.) or in cats with different intensities of inflammatory response was compared using a Chi-square test.

Results: AGP-positive leucocytes were found in 23% of cats. Compared with controls, the proportion of patients with positive granulocytes and monocytes was higher among sick cats (especially cats with diseases other than FIP) and cats with high serum AGP concentration, but not in cats with leucocytosis or that were FCoV-seropositive.

Conclusion: AGP-positive leucocytes can be found in feline blood, especially during inflammation. Conversely, no association between AGP-positive leucocytes and FIP was found. Further studies are needed to elucidate the mechanism responsible for this finding and its diagnostic role in cats with inflammation.

**Resolution of life-threatening dysphagia caused by caudal occipital malformation syndrome following foramen magnum decompressive surgery**
KJ Graham, AP Black and PH Brain

A Cavalier King Charles Spaniel was presented with acute onset, life-threatening dysphagia suspected to be secondary to medulla oblongata compression caused by caudal occipital malformation syndrome. The patient required urgent tracheostomy tube placement to remain stable and was subsequently cured of the presenting neurological deficits by foramen magnum decompressive surgery. Neurogenic dysphagia is a relatively common presenting sign in human Chiari malformation syndromes, but has not been described as a major clinical sign in veterinary patients. Caudal occipital malformation syndrome should be included in the differential diagnosis list for susceptible breeds presenting with dysphagia. Early recognition favours expeditious surgical intervention and a positive outcome in human patients, and this may also be the case in veterinary patients.
Idiopathic Chylothorax: Pathophysiology, Diagnosis, and Thoracic Duct Imaging
Ameet Singh, DVM, DVSc, DACVS, Brigitte Brisson, DMV, DVSc, DACVS, Stephanie Nykamp, DVM, DACVR

Idiopathic chylothorax is a debilitating disease that can lead to respiratory and metabolic compromise and fibrosing pleuritis. Previous investigation has provided theories for the etiology of this poorly understood disease. This article provides an overview of the pathophysiology and diagnosis of chylothorax. Thoracic duct imaging, including minimally invasive techniques, is also discussed, as it is frequently performed in the perioperative period. A companion article reviews nonsurgical and surgical techniques for treating and managing idiopathic chylothorax in dogs and cats.

Chylothorax is a debilitating disease that occurs when disruption of the thoracic duct (TD) results in chyle leakage into the pleural space. Trauma to the TD during cardiothoracic surgery is the most common cause of chylothorax in humans. While traumatic causes of chylothorax have been reported in veterinary patients, most cases in dogs and cats are considered idiopathic because a predisposing cause cannot be identified.

Idiopathic Chylothorax: Nonsurgical and Surgical Management
Ameet Singh, DVM, DVSc, DACVS, Brigitte Brisson, DMV, DVSc, DACVS, Stephanie Nykamp, DVM, DACVR

Idiopathic chylothorax is a debilitating disease that can lead to respiratory and metabolic compromise and fibrosing pleuritis. Several treatment options are available once a diagnosis has been made. Although large-scale studies on the outcome of treatment for idiopathic chylothorax are lacking, long-term resolution of clinical signs is possible. Pathophysiology, diagnosis, and thoracic duct imaging are discussed in a companion article. This article provides an overview of nonsurgical and surgical management techniques for idiopathic chylothorax in dogs and cats. Evidence-based recommendations for optimal treatment of idiopathic chylothorax in dogs and cats are lacking from the veterinary literature. This is because idiopathic chylothorax is a rare disease, making randomized, prospective clinical trials of treatment strategies difficult to undertake.

Brachycephalic Airway Syndrome: Management
Dena L. Lodato, DVM, Cheryl S. Hedlund, DVM, MS, DACVS

Brachycephalic airway syndrome (BAS) is a group of primary and secondary abnormalities that result in upper airway obstruction. Several of these abnormalities can be addressed medically and/or surgically to improve quality of life. This article reviews potential complications, anesthetic considerations, recovery strategies, and outcomes associated with medical and surgical management of BAS.

Journal of Feline Medicine and Surgery

Clinical evaluation of urine Histoplasma capsulatum antigen measurement in cats with suspected disseminated histoplasmosis
Audrey K Cook, Lauren Y Cunningham, Annette K Cowell, and L Joseph Wheat

Diagnosis of Histoplasma capsulatum infection in cats traditionally relies upon identification of organisms in circulating monocytes or in tissue specimens from affected organs. In this retrospective study, results of a urine antigen assay were compared with standard diagnostic methods in cats with clinical signs suggestive of histoplasmosis. Antigenuria was detected in 17/18 cats with a histopathologic or cytopathologic diagnosis of histoplasmosis. This preliminary evaluation of the Histoplasma urine antigen test suggests it may be a useful aid in diagnosing this disease in cats.

Evaluation of propofol containing 2% benzyl alcohol preservative in cats
Polly M Taylor, Christopher P Chengelis, Walter R Miller, George A Parker, Teresa R Gleason, and Elizabeth Cozzi

Propofol emulsion containing benzyl alcohol preservative (BA) was evaluated in cats. Eight (PB) received 1% propofol containing 2% benzyl alcohol and eight (PC) preservative-free propofol. In phase 1, cats were anaesthetised (8 mg/kg) three times at 48 h intervals. In phase 2, cats underwent three anaesthetic procedures at 48 h intervals where anaesthesia was maintained until 24 mg/kg had been administered. Clinical examination
and haematological and biochemical analyses were performed regularly. Cardiorespiratory function was monitored throughout anaesthesia. Neurological examination was performed daily for 7 days after phase 2. All cats were euthanased 7 days after phase 2 and examined post mortem to determine any organ toxicity and to comply with regulatory requirements. Anaesthesia was as expected for propofol in cats and no clinically relevant differences between PB and PC were detected. The addition of BA has no additional effect when propofol is used at normal-to-high clinical doses in healthy cats.

Comparison of two formulations of buprenorphine in cats administered by the oral transmucosal route
Elisa Bortolami, Louisa Slingsby, and Emma J Love
This randomised, blinded, cross-over study investigated the ease of oral transmucosal administration of two formulations of buprenorphine using glucose as a control in 12 cats. The cats received three treatments: buprenorphine multi-dose, buprenorphine and the equivalent volume of glucose 5%. Ease of treatment administration, observation of swallowing, changes in pupil size, sedation, salivation, vomiting, behaviour and food intake were assessed. The data were analysed using MLwiN and multi-level modelling. Ease of administration of buprenorphine multi-dose was statistically different from glucose (P < 0.001), and the administration of all treatments became easier over the study periods. Swallowing was not statistically different between groups (P > 0.05). Mydriasis was evident after the administration of both formulations of buprenorphine. Sedation, salivation, vomiting, behavioural changes or in-appetence were not observed after any treatment. Cats tolerated oral transmucosal administration of glucose better than buprenorphine multi-dose, while buprenorphine administration was tolerated as well as glucose.

Single dose pharmacokinetics of terbinafine in cats
Ang Wang, Huanzhong Ding, Yiming Liu, Yan Gao, and Zhenling Zeng
The pharmacokinetics of terbinafine was studied in six healthy fasted cats following a single intravenous and oral administration at a dose of 10 mg/kg and 30 mg/kg, respectively, according to a two-period crossover design. Plasma terbinafine concentrations were determined using a reverse phase liquid chromatographic method. The pharmacokinetic parameters were calculated by non-compartmental analysis with WinNonlin 5.2.1 software. After intravenous administration, the terminal half-life and area under the curve from time 0 to infinity were 10.40 ± 4.56 h, 15.20 ± 3.61 h·µg/ml, respectively. After oral dosing, the mean maximum concentration was 3.22 ± 0.60 µg/ml, reached at 1.33 ± 0.41 h. The terminal half-life, area under the curve from time 0 to infinity and apparent volume of distribution were 8.01 ± 3.46 h, 13.77 ± 4.99 h·µg/ml, 25.63 ± 6.29 l/kg, respectively. The absolute bioavailability of terbinafine hydrochloride tablets after oral administration was 31.00 ± 10.85%. Although bioavailability was low, excellent penetration at the site of infection and low minimum inhibitory concentrations values provided terbinafine with good efficacy against dermatophyte infections.

Ultrasound-guided block of the feline sciatic nerve
Paulina Haro, Francisco Laredo, Francisco Gil, Eliseo Belda, María D Ayala, Marta Soler, and Amalia Agut
This study was conducted to validate an ultrasound-guided technique to block the sciatic nerve in cats. An anatomical study was first carried out in four feline cadavers to evaluate the feasibility of the glutea (cranial and caudal), femoris and poplitea ultrasonographical approaches for the sciatic nerve block. The results showed that the femoris approach was optimal because the region was free of vascular and bony structures, and the needle was easily visualised in-plane. Then, the efficacy of the femoris ultrasonographical approach to block the sciatic nerve was tested in six healthy adult experimental cats. A dose of 2 mg/kg lidocaine 2% diluted in saline to a final volume of 1 ml was administered in all cats. The blockade was successful in all cases and the cats recovered uneventfully. This study shows the usefulness of the femoris approach in performing an ultrasound-guided blockade of the sciatic nerve in cats.

Analgesia after feline ovariohysterectomy under midazolam-medetomidine-ketamine anaesthesia with buprenorphine or butorphanol, and carprofen or meloxicam: a prospective, randomised clinical trial
Sally Polson, Polly M Taylor, and David Yates
One hundred female cats undergoing routine ovariohysterectomy under midazolam-medetomidine-ketamine anaesthesia were included in a blinded, randomised, prospective clinical study to compare postoperative analgesia produced by four analgesic drug combinations given preoperatively (n = 25 per group). A secondary
aim was to assess the effects in kittens and pregnant animals. Buprenorphine 180 µg/m² or butorphanol 6 mg/m² were given with either carprofen 4 mg/kg (groups BUPC and BUTC, respectively) or meloxicam 0.3 mg/kg (groups BUPM or BUTM, respectively). Medetomidine was not antagonised. A simple, descriptive scale (SDS; 0–4), a dynamic and interactive visual analogue scale (DIVAS; 0–100 mm) and mechanical nociceptive thresholds (MT; 2.5-mm diameter probe) were used to evaluate postoperative pain. All pain scores were low (DIVAS <10 mm, SDS <2 and MT >10 N) and there were no significant differences between the groups. It was concluded that all protocols provided adequate analgesia and when used with midazolam-medetomidine-ketamine are effective for routine feline ovariohysterectomy.

**Treatment-related toxicities in tumor-bearing cats treated with temozolomide alone or in combination with doxorubicin: a pilot assessment**
Jerome Gagnon, Nikolaos G Dervisis, and Barbara E Kitchell
A retrospective study assessing treatment-related toxicities in tumor-bearing cats treated with temozolomide (TMZ) alone or in combination with doxorubicin was conducted. TMZ was administered orally once a day for 5 days every 3 weeks at a dose of 20 mg/cat. Tumor response was evaluated with standard World Health Organization criteria and toxicity was monitored using veterinary co-operative oncology group—common terminology criteria for adverse events (VCOG—CTCAE) criteria. Ten tumor-bearing cats with various types of malignancies were treated with TMZ-based chemotherapy. Eight cats were evaluable for response. Two cats achieved a complete response, one achieved stable disease and five achieved a partial response. Four grade III and one grade IV hematological toxicities, and one grade IV gastrointestinal toxicity were observed. Four cats were euthanased as a result of apparent toxicity. One cat was euthanased as a result of severe and prolonged myelosuppression with fever. Three were euthanased for grade III pleural and pericardial effusions. Effusion was seen in cats treated with higher cumulative dose of TMZ (P = 0.0046). Planned additional case accrual was discontinued because of unacceptable levels of toxicity despite evidence of efficacy in some of the cats. Additional investigation is needed to elucidate this unexpected apparent cumulative toxicity.

**Evaluation of detemir in diabetic cats managed with a protocol for intensive blood glucose control**
Kirsten Roomp and Jacquie Rand
The aim of this study was to report outcomes using detemir and a protocol aimed at intensive blood glucose control with home monitoring in diabetic cats, and to compare the results with a previous study using the same protocol with glargine. Eighteen cats diagnosed with diabetes and previously treated with other insulins were included in the study. Data was provided by owners who joined the online German Diabetes-Katzen Forum. The overall remission rate was 67%. For cats that began the protocol before or after 6 months of diagnosis, remission rates were 81% and 42%, respectively (P = 0.14). No significant differences were identified between the outcomes for the glargine and detemir studies, with the exception of three possibly interrelated factors: a slightly older median age of the detemir cohort at diabetes diagnosis, a higher rate of chronic renal disease in the detemir cohort and lower maximal dose for insulin detemir.

**Markers of Borna disease virus infection in cats with staggering disease**
Borna disease virus (BDV) is a RNA-virus causing neurological disorders in a wide range of mammals. In cats, BDV infection may cause staggering disease. Presently, staggering disease is a tentative clinical diagnosis, only confirmed at necropsy. In this study, cats with staggering disease were investigated to study markers of BDV infection aiming for improvement of current diagnostics. Nineteen cats fulfilled the inclusion criteria based on neurological signs and pathological findings. In 17/19 cats, BDV infection markers (BDV-specific antibodies and/or BDV-RNA) were found, and antibodies in serum (13/16, 81%) were the most common marker. BDV-RNA was found in 11/19 cats (58%). In a reference population without neurological signs, 4/25 cats were seropositive (16%). The clinical history and neurological signs in combination with presence of BDV infection markers, where serology and rRT-PCR on blood can be helpful tools, improve the diagnostic accuracy in the living cat.
The Veterinary Journal

The use of ciclosporin A in veterinary dermatology
Marcel Kovalik, Keith L. Thoday, Adri H.M. van den Broek

Ciclosporin A (CsA) has potent immunosuppressive and immunomodulatory activity that has been exploited in human medicine to prevent the rejection of transplanted organs and to manage atopic dermatitis and psoriasis. Over the past decade, CsA has been employed more frequently in veterinary dermatology and its value in the management of several canine and feline dermatoses is now well established. CsA inhibits calcineurin phosphatase, suppressing T cell activation and the synthesis of T cell cytokines consequently impairing the activity of B cells, antigen-presenting cells, mast cells, basophils and eosinophils. The pharmacokinetics of CsA are similar in humans, dogs and cats and the drug has a wide safety margin in dogs, cats and rabbits. Adverse effects, principally transient vomiting and soft faeces/diarrhoea, may be seen shortly after instituting treatment but often resolve despite continuing treatment. Gingival hyperplasia and cutaneous effects such as hirsutism may occur after prolonged treatment.

An overview of the physiology of pain for the veterinarian
Roy A. Meintjes

The degree of depolarisation in a nociceptor created by a painful stimulus is influenced by numerous substances, including nerve growth factor, prostanoids, substance P and a range of inflammatory mediators. In the dorsal horn of the spinal cord, the frequency of an action potential may be increased or decreased by neurotransmitters, including substance P, calcitonin gene-related peptide, galanin, γ-amino butyric acid and glycine, as well as pro-inflammatory substances. The perception of pain can also be altered in the brain, where the sensation of pain is cognitively integrated. A range of analgesic drugs with different mechanisms of action are available for selection by veterinarians for pain relief.

Accuracy of a point-of-care ELISA test kit for predicting the presence of protective canine parvovirus and canine distemper virus antibody concentrations in dogs
A.L. Litster, B. Pressler, A. Volpe, E. Dubovi

Canine parvovirus (CPV) and canine distemper virus (CDV) are highly infectious and often fatal diseases with worldwide distributions, and are important population management considerations in animal shelters. A point-of-care ELISA test kit is available to detect serum antibodies to CPV and CDV, and presumptively to predict protective status. The aim of this study was to determine the diagnostic accuracy of the test compared to CPV hemagglutination inhibition titers and CDV serum neutralization titers determined by a reference laboratory, using sera collected from dogs housed at animal shelters. The ELISA test was used under both field and laboratory conditions and duplicate specimens were processed using an extra wash step. The test kit yielded accurate results (CPV: sensitivity 92.3%, specificity 93.5%; CDV: sensitivity 75.7%, specificity 91.8%) under field conditions. CDV sensitivity was improved by performing the test under laboratory conditions and using an optical density (OD) meter (laboratory performed 94.0%; OD 88.1%). Point-of-care ELISA testing for serum CPV and CDV antibody titers was demonstrated to be a useful tool for determining antibody status when making decisions regarding the need for CPV and/or CDV vaccination and also in animal shelters for population management.

Post-anesthetic cortical blindness in cats: Twenty cases

The medical records of 20 cats with post-anesthetic cortical blindness were reviewed. Information collected included signalment and health status, reason for anesthesia, anesthetic protocols and adverse events, post-anesthetic visual and neurological abnormalities, clinical outcome, and risk factors. The vascular anatomy of the cat brain was reviewed by cadaver dissections. Thirteen cats were anaesthetised for dentistry, four for endoscopy, two for neutering procedures and one for urethral obstruction. A mouth gag was used in 16/20 cats. Three cats had had cardiac arrest, whereas in the remaining 17 cases, no specific cause of blindness was identified. Seventeen cats (85%) had neurological deficits in addition to blindness. Fourteen of 20 cats (70%) had documented recovery of vision, whereas four (20%) remained blind. Two cats (10%) were lost to follow up while still blind. Ten of 17 cats (59%) with neurological deficits had full recovery from neurological disease,
two (12%) had mild persistent deficits and one (6%) was euthanased as it failed to recover. Four cats (23%) without documented resolution of neurological signs were lost to follow up. Mouth gags were identified as a potential risk factor for cerebral ischemia and blindness in cats.

**Canine tissue-specific expression of multiple small leucine rich proteoglycans**


Small leucine rich proteoglycans (SLRPs) are important constituents of extracellular matrix (ECM) and contribute to the production, organization and remodelling of collagen and elastin through complex biological systems. The relative expression and distribution of SLRPs in a variety of different mammalian tissues is poorly characterized. The aim of this study was to map the expression of seven SLRPs (biglycan, versican, prolargin, fibromodulin, osteoglycin, decorin and lumican) in seven tissues (bone, cartilage, cruciate ligament, skin, ventricular myocardium, mitral valve and cornea) in young adult dogs using a combination of quantitative real-time PCR, immunohistochemistry and protein immunoblotting.

Clear and consistent patterns of SLRP expression and distribution were identified for the seven tissues examined, with the greatest SLRP expression in cartilage, skin, cornea and mitral valve, and the least expression in myocardium. In general, lumican and prolargin had the greatest expression across the seven tissues whilst osteoglycin was the least abundantly expressed SLRP. These data provide a SLRP profile for different canine tissues which can inform future studies of SLRP expression in development and disease.

**Comparison of oral robenacoxib and ketoprofen for the treatment of acute pain and inflammation associated with musculoskeletal disorders in cats: A randomised clinical trial**

Tadashi Sano, Jonathan N. King, Wolfgang Seewald, Nobuhiro Sakakibara, Masahiro Okumura

The objective of the study was to evaluate the efficacy and tolerability of robenacoxib, a selective cyclooxygenase-2 inhibitor, for the treatment of acute pain and inflammation associated with musculoskeletal disorders in cats. The study was a prospective, multi-centre, randomised, blinded, non-inferiority design clinical trial comparing robenacoxib to ketoprofen. A total of 68 cats presenting with pain and inflammation associated with acute musculoskeletal disorders were recruited and allocated randomly to receive, orally once daily for 5–6 days, either 1.0–2.4 mg/kg robenacoxib (n = 47) or 1 mg/kg ketoprofen (n = 21). The primary efficacy endpoint was the total clinician score, which was the sum of clinician numerical rating scale scores for pain, inflammation and mobility. Assessments were made at baseline, on day 2, and day 4 or 5. For the total clinician score, non-inferior efficacy of robenacoxib was demonstrated with a relative efficacy of 1.151 (95% confidence interval 0.872–1.494). Non-inferior efficacy of robenacoxib was also demonstrated for the secondary endpoint of the total owner score. Robenacoxib was superior (P < 0.05) to ketoprofen for the owner’s assessment of activity and human/animal relationship. The tolerability of both treatments was good as assessed by monitoring adverse events, clinical signs and haematology and serum biochemistry variables.

**Congenital deafness in Jack Russell terriers: Prevalence and association with phenotype**

B. Comito, K.E. Knowles, G.M. Strain

Congenital hereditary sensorineural deafness is the most common form of deafness in dogs. The objectives of this study were to determine a reliable measure of the prevalence of deafness in Jack Russell terriers, an affected breed, and associations between deafness and phenotypic characteristics. Brainstem auditory evoked response recordings and phenotypic parameters (coat color, coat texture, sex, eye color, sire and dam hearing status) were recorded for 1009 Jack Russell terriers. The prevalence of unilateral and bilateral deafness was 3.57% and 0.50%, respectively, lower by a factor of three to four than in earlier reports based on smaller and closely related kindreds. Significant association with deafness was identified with white coat color and parental hearing status, but not with sex or coat type. Lack of significant sex or coat type associations and the significant association with white coat color are consistent with previous reports. In conclusion the prevalence of deafness in Jack Russell terriers is lower than initially reported. Deafness was associated with white coat color and parental hearing status. The association with parental hearing status supports this form of deafness being a heritable trait in the breed and the association with white coat color supports an inheritance linked to pigmentation genes.
Expression of epidermal growth factor receptor in canine osteosarcoma: Association with clinicopathological parameters and prognosis
Gayathri T. Selvarajah, Monique H. Verheije, Marja Kik, Adri Slob, Peter J.M. Rottier, Jan A. Mol, Jolle Kirpensteijn

Expression of epidermal growth factor receptor (EGFR) is associated with aggressive growth and metastasis of a range of tumours, including osteosarcomas (OS), although some studies have reported no relevance to clinicopathological events or prognosis. The present study evaluated EGFR mRNA and protein expression in a panel of OS cell lines, normal bones, frozen primary OS and tissue microarrays. EGFR expression was significantly elevated in primary OS compared to normal bones and in metastases of OS to the lungs in comparison with extrapulmonary sites. However, there were no clinical or pathological associations with mRNA expression levels in frozen tumours. Tissue microarray analysis demonstrated that a subset of canine OS with high EGFR expression was associated with significantly shorter survival times and disease-free intervals. Cytoplasmic expression of EGFR was present in 75% of metastases and was similar to expression in primary tumours. EGFR expression alone is not a reliable predictor of outcome and other markers are necessary for further prognostic stratification of dogs with OS. However, these findings suggest that a subset of dogs may benefit from anti-EGFR adjuvant therapies.

Acute phase response to Mycoplasma haemofelis and ‘Candidatus Mycoplasma haemominutum’ infection in FIV-infected and non-FIV-infected cats
R.M. Korman, J.J. Cerón, T.G. Knowles, E.N. Barker, P.D. Eckersall, S. Tasker

The pathogenicity of Haemoplasma spp. in cats varies with ‘Candidatus Mycoplasma haemominutum’ (CMhm) causing subclinical infection while Mycoplasma haemofelis (Mhf) often induces haemolytic anaemia. The aims of this study were to characterise the acute phase response (APR) of the cat to experimental infection with Mhf or CMhm, and to determine whether chronic feline immunodeficiency virus (FIV) infection influences this response. The acute phase proteins serum amyloid A (SAA), haptoglobin (Hp) and α-1-acid glycoprotein (AGP) concentrations were measured pre-infection and every 7–14 days up to day 100 post-infection (pi) in cats infected with either Mhf or CMhm. Half of each group of cats (6/12) were chronically and subclinically infected with FIV. Marbofloxacin treatment was given on days 16–44 pi to half of the Mhf-infected cats, and on days 49–77 pi to half of the CMhm-infected cats. FIV-infected animals had significantly lower AGP concentrations, and significantly greater Hp concentrations than non-FIV-infected cats when infected with CMhm and Mhf, respectively. Both CMhm and Mhf infection were associated with significant increases in SAA concentrations, while AGP concentrations were only significantly increased by Mhf infection. Mhf-infected cats had significantly greater SAA concentrations than CMhm-infected animals. Both Mhf and CMhm infections were associated with an APR, with Mhf infection inducing a greater response. Chronic FIV infection appeared to modify the APR, which varied with the infecting Haemoplasma species.

Short-term prednisolone therapy has minimal impact on calcium metabolism in dogs with atopic dermatitis
M. Kovalik, K.L. Thoday, H. Evans, J. Berry, A.H.M. van den Broek, R.J. Mellanby

Glucocorticoids (GCs) are a large group of drugs used to treat a range of inflammatory, autoimmune and neoplastic diseases in dogs. Glucocorticoids have been linked to disturbances in calcium metabolism and skeletal disorders in humans, yet their effects at therapeutically effective dosages in dogs with spontaneous diseases are poorly understood. Serum concentrations of calcium, phosphate, vitamin D metabolites and plasma concentrations of parathyroid hormone and ionised calcium together with urinary fractional excretion of calcium and phosphate, were measured in 16 dogs with atopic dermatitis before and 6 weeks after standard dosage prednisolone treatment (0.93–1.06 mg/kg) every other day after 7 days of treatment with the same dosage once daily. The severity of their physical signs, as assessed by the canine atopic dermatitis extent and severity index version 3 (CADESI-03) and the Edinburgh Pruritus Scale (EPS), decreased in all dogs following prednisolone treatment. There was no significant difference in any of the biochemical parameters measured following prednisolone treatment. This study indicates that prednisolone, used at a therapeutically effective dose, has minimal impact on calcium metabolism in dogs with atopic dermatitis.
Effects of lidocaine constant rate infusion on sevoflurane requirement, autonomic responses, and postoperative analgesia in dogs undergoing ovariectomy under opioid-based balanced anesthesia
Nicolò Columbano, Fabio Secci, Giovanni M. Careddu, Giovanni Sotgiu, Gabriele Rossi, Bernd Driessen
The effects of constant rate infusion (CRI) of lidocaine on sevoflurane (SEVO) requirements, autonomic responses to noxious stimulation, and postoperative pain relief were evaluated in dogs undergoing opioid-based balanced anesthesia. Twenty-four dogs scheduled for elective ovariectomy were randomly assigned to one of four groups: BC, receiving buprenorphine without lidocaine; FC, receiving fentanyl without lidocaine; BL, receiving buprenorphine and lidocaine; FL, receiving fentanyl and lidocaine. Dogs were anesthetized with intravenous (IV) diazepam and ketamine and anesthesia maintained with SEVO in oxygen/air. Lidocaine (2 mg/kg plus 50 μg/kg/min) or saline were infused in groups BL/FL and BC/FC, respectively. After initiation of lidocaine or saline CRI IV buprenorphine (0.02 mg/kg) or fentanyl (4 μg/kg plus 8 μg/kg/h CRI) were administered IV in BC/BL and FC/FL, respectively. Respiratory and hemodynamic variables, drug plasma concentrations, and end-tidal SEVO concentrations (E’SERO) were measured. Behaviors and pain scores were subjectively assessed 1 and 2 h post-extubation. Lidocaine CRI produced median drug plasma concentrations <0.4 μg/mL during peak surgical stimulation. Lidocaine produced a 14% decrease in E’SERO in the BL (P < 0.01) but none in the FL group and no change in cardio-pulmonary responses to surgery or postoperative behaviors and pain scores in any group. Thus, depending on the opioid used, supplementing opioid-based balanced anesthesia with lidocaine (50 μg/kg/min) may not have any or only a minor impact on anesthetic outcome in terms of total anesthetic dose, autonomic responses to visceral nociception, and postoperative analgesia.

Computed tomography findings in portal vein aneurysm of dogs
G. Bertolini, M. Caldin
In this retrospective study, the appearances of extrahepatic and intrahepatic portal vein aneurysms (PVAs) in dogs were evaluated using multidetector computed tomography (CT). Data from 3060 dogs that underwent abdominal CT were reviewed for focal portal vein dilatation. PVAs were detected in 15/3060 (0.49%) dogs. The bodyweights of dogs with PVAs were significantly higher than the bodyweights of dogs without aneurysms (P = 0.0001). Male sex was also significantly associated with PVAs (OR = 6.23). Boxers were predisposed to the development of PVA (OR = 11.88). Extrahepatic PVAs were always located in the portal vein at the level of the gastroduodenal vein insertion and were saccular in 10/15 dogs and fusiform in 5/15 dogs. One dog had an additional intrahepatic aneurysm of the umbilical part of the left intrahepatic portal branch. No dogs had clinical signs related to the PVA(s), although one dog developed a portal vein thrombosis in the site of the aneurysm.

Plasma glucose, insulin, free fatty acids, lactate and cortisol concentrations in dexmedetomidine-sedated dogs with or without MK-467: A peripheral α-2 adrenoceptor antagonist
F. Restitutti, M. Raekallio, M. Vainionpää, E. Kuusela, O. Vainio
Six healthy laboratory Beagles were treated IV with 10 μg/kg dexmedetomidine (DEX) or 10 μg/kg dexmedetomidine combined with 500 μg/kg MK-467 in the same syringe (DMK) in a randomised cross-over design with a 14 day washout. Blood was collected immediately before treatment and 35, 60 and 120 min post-injection through a central venous catheter. The plasma concentrations of glucose, insulin, non-esterified free fatty acids (NEFAs), lactate and cortisol were determined. A repeated-measures ANOVA test was used to compare treatments and effects for each sample time point. Significant differences between treatments were found for plasma glucose (P = 0.037) and insulin (P = 0.009). DEX significantly increased plasma glucose at 120 min, but reduced plasma insulin at 35 and 60 min. NEFA decreased for both treatments at 35 min. This reduction was transient for DMK, whereas it persisted during the follow up period for DEX. Plasma lactate concentrations increased at 35 and 60 min with DEX. Neither treatment altered plasma cortisol concentrations. The addition of MK-467 to dexmedetomidine prevented or abolished most metabolic changes in healthy Beagles.
Phenotypic and genetic evaluation of elbow dysplasia in Dutch Labrador Retrievers, Golden Retrievers, and Bernese Mountain dogs

Canine elbow dysplasia encompasses four developmental diseases: ununited anconeal process, osteochondrosis of the medial part of the humeral condyle, fragmented medial coronoid process (FCP), and incongruity of the elbow joint. Four radiographic views per joint were used to evaluate 2693 Labrador Retrievers (LRs), 1213 Golden Retrievers (GRs), and 974 Bernese Mountain Dogs (BMDs) for the presence of elbow dysplasia between 2002 and 2009 in the Netherlands. The views were also graded for signs of osteoarthritis and sclerosis. FCP was diagnosed most frequently in LRs, GRs and BMDs, with an incidence of 6%, 5%, and 15%, and a heritability of 0.17, 0.24, and 0.06, respectively. Heritabilities were estimated using a sire model and all available ancestors. Sclerosis at the base of the medial coronoid process was the radiographic sign most strongly correlated with FCP (\( r = 0.95, 0.92, \) and 0.95 in LRs, GRs and BMDs, respectively). The sex of the dog was significantly correlated with the presence of osteoarthritis in LRs, but not in GRs and BMDs. Male LRs were 1.7-fold more frequently, but not more severely, affected by osteoarthritis than female dogs. Age at radiographic examination was significantly associated with osteoarthritis in all three breeds. The heritability estimates in Retrievers were high enough to warrant including FCP findings in the breeding policy, but until the biomechanical and genetic background of elbow dysplasia are better understood, correct phenotyping with a sensitive technique is essential.

Aldehyde dehydrogenase activity in cancer stem cells from canine mammary carcinoma cell lines

Increasing evidence suggests that diverse solid tumours arise from a small population of cells known as cancer stem cells or tumour-initiating cells. Cancer stem cells in several solid tumours are enriched for aldehyde dehydrogenase (ALDH) activity. High levels of ALDH activity (\( \text{ALDH}_{\text{high}} \)) were detected in four cell lines derived from canine mammary carcinomas. \( \text{ALDH}_{\text{high}} \) cells were enriched in a CD44+C2D24- population having self-renewal capacity. Xenotransplantation into immunodeficient mice demonstrated that \( 1 \times 10^4 \) \( \text{ALDH}_{\text{high}} \) cells were sufficient for tumour formation in all injected mice, whereas \( 1 \times 10^4 \) \( \text{ALDH}_{\text{low}} \) cells failed to initiate any tumours. \( \text{ALDH}_{\text{high}} \)-derived tumours contained both \( \text{ALDH}^+ \) and \( \text{ALDH}^- \) cells, indicating that these cells had cancer stem cell-like properties.

Canine parvovirus in Australia: The role of socio-economic factors in disease clusters
S. Brady, J.M. Norris, M. Kelman, M.P. Ward

To identify clusters of canine parvoviral related disease occurring in Australia during 2010 and investigate the role of socio-economic factors contributing to these clusters, reported cases of canine parvovirus were extracted from an on-line disease surveillance system. Reported residential postcode was used to locate cases, and clusters were identified using a scan statistic. Cases included in clusters were compared to those not included in such clusters with respect to human socioeconomic factors (postcode area relative socioeconomic disadvantage, economic resources, education and occupation) and dog factors (neuter status, breed, age, gender, vaccination status). During 2010, there were 1187 cases of canine parvovirus reported. Nineteen significant (\( P < 0.05 \)) disease clusters were identified, most commonly located in New South Wales. Eleven (58%) clusters occurred between April and July, and the average cluster length was 5.7 days. All clusters occurred in postcodes with a significantly (\( P < 0.05 \)) greater level of relative socioeconomic disadvantage and a lower rank in education and occupation, and it was noted that clustered cases were less likely to have been neutered (\( P = 0.004 \)). No significant difference (\( P > 0.05 \)) was found between cases reported from cluster postcodes and those not within clusters for dog age, gender, breed or vaccination status (although the latter needs to be interpreted with caution, since vaccination was absent in most of the cases). Further research is required to investigate the apparent association between indicators of poor socioeconomic status and clusters of reported canine parvovirus diseases; however these initial findings may be useful for developing geographically- and temporally-targeted prevention and disease control programs.
Overexpression of P-glycoprotein, STAT3, phospho-STAT3 and KIT in spontaneous canine cutaneous mast cell tumours before and after prednisolone treatment
Shr-Ping Teng, Wei-Li Hsu, Cheng-Yang Chiu, Min-Liang Wong, Shih-Chieh Chang
Prednisolone is a glucocorticoid (GC) commonly used in the treatment of canine mast cell tumours (MCTs); however, resistance to GCs develops in many MCTs following repeated treatment. P-glycoprotein (P-gp), signal transducer and activator of transcription 3 (STAT3) and KIT (CD117) are involved in GC resistance. The aim of this study was to evaluate the response to prednisolone treatment in canine cutaneous MCTs and to investigate the levels of P-gp, STAT3, phospho-STAT3 (pSTAT3) and KIT proteins in MCTs with or without prednisolone treatment. Immunohistochemistry was performed on tumour samples from 41 dogs with cutaneous MCTs. The overall objective response rate (including complete and partial responses) was 51.8% for dogs treated with prednisolone; poorly differentiated or higher stage MCTs had a lower response rate. The median time-span of tumours to reach maximal tumour regression was 14 d (range 3–77 d); 22 (81.5%) reached maximal regression at 21 d. The majority of MCTs overexpressed both P-gp and STAT3 before and after prednisolone treatment. Reduced expression of pSTAT3 and alterations in the KIT expression pattern were observed in MCTs post-treatment. Prednisolone treatment that caused a marked reduction in tumour volume was correlated with reduced pSTAT3 expression. A cytoplasmic KIT staining pattern was correlated with a lower tumour response rate to prednisolone treatment.

Effect of weight loss on inflammatory biomarkers in obese dogs
Asta Tvarijonaviciute, Fernando Tecles, Silvia Martínez-Subiela, José J. Cerón
The objective of this study was to evaluate the effects of weight loss on selected serum inflammatory biomarkers in obese dogs. An experimentally induced bodyweight reduction of approximately 2.5%/week was accompanied by significant decreases in metabolic markers of obesity (lipidic profile, fructosamine, and insulin-like growth factor-1). The concentrations of acute phase proteins and of selected cytokines remained within reference ranges in obese dogs during weight loss, suggesting that significant inflammation was not a major component of this experimental model. However, adiponectin concentrations increased following the period of weight loss suggesting reduced susceptibility of these animals to obesity-related inflammation.

Immunophenotypic evaluation of working Labrador Retrievers and German Shepherd dogs living in the same environment
Alejandra Villaescusa, Mercedes García-Sancho, Alba M. Delgado, Miguel Ángel Tesouro, Fernando Rodríguez-Franco, Ángel Sainz
Multiparametric flow cytometry was used to compare peripheral blood lymphocyte subset distribution between healthy working police Labrador Retrievers (LRs; n = 12) and German Shepherd dogs (GS; n = 11) living in the same environment. The CD4/CD8 ratio was significantly higher in LR than in GS because of the lower percentage of CD8+ T lymphocytes in LR. GS showed the highest relative percentage of CD3−/CD21− lymphocytes, whereas LR had the highest percentages of MHC II+ lymphocytes. Because age, sex, environmental and housing conditions, dietary patterns, and training or working routines were similar in both breeds in the study, differences in peripheral blood lymphocyte subset distribution could be attributed to the influence of breed on the immune system.

Journal of Veterinary Internal Medicine
Recombinant Human Thyrotropin in Veterinary Medicine: Current Use and Future Perspectives
M. Campos, I. van Hoek, K. Peremans, S. Daminet
Recombinant human thyrotropin (rhTSH) was developed after bovine thyrotropin (bTSH) was no longer commercially available. It was approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) as an aid to diagnostic follow-up of differentiated thyroid carcinoma in humans and for thyroid remnant ablation with radioiodine. In addition, rhTSH is used in human medicine to evaluate thyroid reserve capacity and to enhance radioiodine uptake in patients with metastatic thyroid cancer and multinodular goiter. Likewise, rhTSH has been used in veterinary medicine over the last decade. The most important veterinary use of rhTSH is thyroidal functional reserve testing for the diagnosis of canine hypothyroidism. Recent pilot studies performed at Ghent University in Belgium have investigated the use of rhTSH to optimize
Radioiodine treatment of canine thyroid carcinoma and feline hyperthyroidism. Radioiodine treatment optimization may allow a decreased therapeutic dosage of radioiodine and thus may improve radioprotection. This review outlines the current uses of rhTSH in human and veterinary medicine, emphasizing research performed in dogs and cats, as well as potential future applications.

**Drug Hypersensitivity Reactions Targeting the Skin in Dogs and Cats**
K.L. Voie, K.L. Campbell, S.N. Lavergne
Adverse drug reactions (ADRs) can be dose dependent or idiosyncratic. Most idiosyncratic reactions are believed to be immune-mediated; such drug hypersensitivities and allergies are unpredictable. Cutaneous reactions are the most common presentation of drug allergies. In veterinary medicine it can be difficult to assess the true prevalence of adverse drug reactions, although reports available suggest that they occur quite commonly. There are multiple theories that attempt to explain how drug allergies occur, because the pathogenesis is not yet well understood. These include the (pro)-hapten hypothesis, the Danger Theory, the pi concept, and the viral reactivation theory. Cutaneous drug allergies in veterinary medicine can have a variety of clinical manifestations, ranging from pruritus to often fatal toxic epidermal necrolysis. Diagnosis can be challenging, as the reactions are highly pleomorphic and may be mistaken for other dermatologic diseases. One must rely heavily on history and physical examination to rule out other possibilities. Dechallenge of the drug, histopathology, and other diagnostic tests can help to confirm the diagnosis. New diagnostic tools are beginning to be used, such as antibody or cellular testing, and may be used more in the future. There is much yet to learn about drug allergies, which makes future research vitally important. Treatment of drug allergies involves supportive care, and additional treatments, such as immunosuppressive medications, depend on the manifestation of the disease. Of utmost importance is to avoid the use of the incriminating drug in future treatment of the patient, as subsequent reactions can be worse, and ultimately can prove fatal.

**Pathophysiology of Acute Pancreatitis: Potential Application from Experimental Models and Human Medicine to Dogs**
Caroline Mansfield
The cellular events leading to pancreatitis have been studied extensively in experimental models. Understanding the cellular events and inciting causes of the multisystem inflammatory cascades that are activated with this disease is of vital importance to advance diagnosis and treatment of this condition. Unfortunately, the pathophysiology of pancreatitis in dogs is not well understood, and extrapolation from experimental and human medicine is necessary. The interplay of the inflammatory cascades (kinin, complement, cytokine) is extremely complex in both initiating leukocyte migration and perpetuating disease. Recently, nitric oxide (NO) and altered microcirculation of the pancreas have been proposed as major initiators of inflammation. In addition, the role of the gut is becoming increasingly explored as a cause of oxidative stress and potentiation of systemic inflammation in pancreatitis.

**A Multi-Institutional Study Evaluating the Diagnostic Utility of the Spec cPL™ and SNAP® cPL™ in Clinical Acute Pancreatiti in 84 Dogs**
Background: Pancreas-specific lipase is reported to aid in diagnosing acute pancreatitis (AP) in dogs but has not been rigorously evaluated clinically.
Hypothesis/Objectives: To describe variability of disease in dogs with suspected clinical AP, and to evaluate accuracy of 2 pancreatic-specific lipase immunoassays, Spec cPL (SPEC) and SNAP cPL (SNAP), in diagnosing clinical AP. We hypothesized that SPEC and SNAP provide better diagnostic accuracy than serum amylase or total lipase.
Animals: A total of 84 dogs; 27 without AP and 57 with clinical signs associated with AP.
Methods: Multicenter study. Dogs were prospectively enrolled based upon initial history and physical examination, then retrospectively classified into groups according to the likelihood of having clinical AP by a consensus of experts blinded to SPEC and SNAP results. Bayesian latent class analyses were used to estimate the diagnostic accuracy of SPEC and SNAP.
Results: The estimates for test sensitivities and specificities, respectively, ranged between 91.5–94.1% and 71.1–77.5% for SNAP, 86.5–93.6% and 66.3–77.0% for SPEC (cutoff value of 200 μg/L), 71.7–77.8% and
80.5–88.0% for SPEC (cutoff value of 400 μg/L), and were 52.4–56.0% and 76.7–80.6% for amylase, and 43.4–53.6% and 89.3–92.5% for lipase.

Conclusions and Clinical Importance: SNAP and SPEC have higher sensitivity for diagnosing clinical AP than does measurement of serum amylase or lipase activity. A positive SPEC or SNAP has a good positive predictive value (PPV) in populations likely to have AP and a good negative predictive value (NPV) when there is low prevalence of disease.

Evaluation of Arterial Blood Gases and Arterial Blood Pressures in Brachycephalic Dogs

G.L. Hoareau, G. Jourdan, M. Mellema, P. Verwaerde

Background: Brachycephalic dogs (BD) are prone to congenital upper airway obstruction (brachycephalic syndrome, BS). In humans suffering from sleep apnea, upper airway obstruction is known to cause hypertension. There is no information regarding the influence of BS in dogs on cardiorespiratory physiology.

Hypothesis: BD are prone to lower P$_{O_2}$, higher P$_{a}CO_2$, and hypertension compared with meso- or dolicocephalic dogs (MDD).

Animals: Eleven BD and 11 MDD.

Methods: After a questionnaire was completed by the owner, a physical examination was performed. Height and thoracic circumferences were measured. Arterial blood gases, electrolyte concentrations, and packed cell volume (PCV) were measured. Systolic (SAP), mean (MAP), and diastolic (DAP) arterial blood pressure recordings were performed.

Results: A total of 7 French and 4 English bulldogs met the inclusion criteria. The control group consisted in 6 Beagles, 2 mixed breed dogs, 1 Staffordshire Bull Terrier, 1 Parson Russell Terrier, and 1 Australian Cattle Dog. Statistically, BD had lower P$_{O_2}$, higher P$_{a}CO_2$, and higher PCV when compared with controls (86.2 ± 15.9 versus 100.2 ± 12.6 mmHg, $P = .017$; 36.3 ± 4.6 versus 32.7 ± 2.6 mmHg, $P = .019$; 48.2 ± 3.5 versus 44.2 ± 5.4%, $P = .026$, respectively). Also, they had significantly higher SAP (177.6 ± 25.0 versus 153.5 ± 21.7 mmHg, $P = .013$), MAP (123.3 ± 17.1 versus 108.3 ± 12.2 mmHg, $P = .014$), and DAP (95.3 ± 19.2 versus 83.0 ± 11.5 mmHg, $P = .042$). BD with a P$_{a}CO_2$ >35 mmHg were significantly older than those with a P$_{a}CO_2$ ≤35 mmHg (38 ± 16 and 30 ± 11 months, $P = .004$).

Conclusion: Results of this study suggest that some BD are prone to lower P$_{O_2}$, higher P$_{a}CO_2$, and hypertension when compared with MDD. Age may be a contributing factor.

Serum D-Lactate Concentrations in Cats with Gastrointestinal Disease


Background: Increased D-lactate concentrations cause neurological signs in humans with gastrointestinal disease.

Hypothesis/Objectives: To determine if serum D-lactate concentrations are increased in cats with gastrointestinal disease compared to healthy controls, and if concentrations correlate with specific neurological or gastrointestinal abnormalities.

Animals: Systematically selected serum samples submitted to the Gastrointestinal Laboratory at Texas A&M University from 100 cats with clinical signs of gastrointestinal disease and abnormal gastrointestinal function tests, and 30 healthy cats.

Methods: Case-control study in which serum D- and L-lactate concentrations and retrospective data on clinical signs were compared between 30 healthy cats and 100 cats with gastrointestinal disease. Association of D-lactate concentration with tests of GI dysfunction and neurological signs was evaluated by multivariate linear and logistic regression analyses, respectively.

Results: All 100 cats had a history of abnormal gastrointestinal signs and abnormal gastrointestinal function test results. Thirty-one cats had definitive or subjective neurological abnormalities. D-lactate concentrations of cats with gastrointestinal disease (median 0.36, range 0.04–8.33 mmol/L) were significantly higher than those in healthy controls (median 0.22, range 0.04–0.87 mmol/L; $P = .022$). L-lactate concentrations were not significantly different between the 2 groups of cats with gastrointestinal disease and healthy controls. D-lactate concentrations were not significantly associated with fPLI, fTLI, cobalamin, folate, or neurological abnormalities ($P > .05$).
Conclusions and Clinical Importance: D-lactate concentrations can be increased in cats with gastrointestinal disease. These findings warrant additional investigations into the role of intestinal microbiota derangements in cats with gastrointestinal disease, and the association of D-lactate and neurological abnormalities.

**Sensitivity and Specificity of a Blood and Urine Galactomannan Antigen Assay for Diagnosis of Systemic Aspergillosis in Dogs**


Background: Diagnosis of canine systemic aspergillosis requires fungal culture from a sterile site, or confirmatory histopathology from a nonsterile site. Invasive specimen collection techniques may be necessary.

Objective: To evaluate the sensitivity and specificity of a serum and urine Aspergillus galactomannan antigen (GMA) ELISA assay for diagnosis of systemic aspergillosis in dogs.

Design: Multicenter study.

Animals: Thirteen dogs with systemic aspergillosis and 89 dogs with other diseases. Thirty-seven of the 89 dogs had signs that resembled those of systemic aspergillosis and 52 dogs were not suspected to have aspergillosis.

Procedure: The GMA ELISA was performed on serum specimens from all dogs and urine specimens from 67 dogs. Galactomannan indices (GMI) \_ 0.5 were considered positive. Results for dogs in each group were compared.

Results and Conclusions: The sensitivity and specificity of the assay for serum were 92 and 86%, respectively, and for urine were 88 and 92%, respectively. False negatives were seen only in dogs with localized pulmonary aspergillosis. Use of a cutoff GMI of 1.5 increased specificity to 93% for both serum and urine without loss of sensitivity for diagnosis of disseminated infection. High-level false positives (> 1.5) occurred in dogs with other systemic mycoses and those treated with Plasmalyte.

Clinical Relevance: Serum and urine Aspergillus GMA ELISA is a noninvasive, sensitive, and specific test for the diagnosis of disseminated aspergillosis in dogs when a cutoff GMI of \_ 1.5 is used.

**Serum Pepsinogen-A, Canine Pancreatic Lipase Immunoreactivity, and C-Reactive Protein as Prognostic Markers in Dogs with Gastric Dilation-Volvulus**

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Background: Pepsinogens are proenzymes secreted by gastric chief cells. In humans, their serum concentrations reflect gastric mucosal morphological and functional status.

Objectives: To evaluate serum canine pepsinogen-A (cPG-A), C-reactive protein (CRP), and canine pancreatic lipase immunoreactivity (cPLI) concentrations in dogs with gastric dilatation-volvulus (GDV).

Animals: Sixty-six dogs presented with GDV and 79 healthy controls.

Methods: Blood was collected prospectively, and records retrospectively reviewed.

Results: Median cPG-A concentration was higher in GDV dogs (median, 397 lg/L; range, 37–5,410) compared to controls (median, cPG-A 304 lg/L; range, 18–848; P = .07). Mortality rate in GDV dogs was 22.7%. In nonsurvivors of GDV, median cPG-A was higher compared to survivors (median, 746 lg/L; range, 128–5,409 versus median, 346; range, 36–1,575, respectively; P = .003). The proportion of dogs with increased cPG-A increased with gastric wall damage score (P = .007). An ROC analysis of cPG-A as a predictor of death showed an area under the curve (AUC) of 0.75, higher than lactate (AUC 0.66), and corresponded to a sensitivity and specificity of 53% and 88%, respectively. CRP was increased in 48 dogs (75%), cPLI was >200 lg/L in 26 dogs (39.4%) and >400 lg/L in 12 dogs (18.2%) but both analytes had no association with outcome.

Conclusions: Presurgical cPG-A concentration was positively and significantly associated with gastric wall lesion severity, but, based on ROC analysis, it was only a moderate outcome predictor. CRP and cPLI were commonly increased in dogs with GDV

**Effect of Heart Failure on Dipeptidyl Peptidase IV Activity in Plasma of Dogs**


Background: In congestive heart failure (HF), plasma B-type natriuretic peptide (BNP) seems devoid of biological effectiveness. BNP1–32 could be truncated into BNP3–32 by dipeptidyl peptidase IV (DPP4), and BNP3–32 has reduced biological activities.
Hypothesis: Increased DPP4 activity is associated with pathophysiology of HF.

Animals: One hundred twenty-eight client-owned dogs and 9 experimental Beagles from the Clinical Veterinary Unit of the University of Liège.

Methods: We prospectively measured plasma DPP4 activity in 5 groups of dogs: normal growing dogs (n = 21), normal adult dogs (n = 60), healthy Beagle (n = 9), dogs with myxomatous mitral valve disease (n = 35), and dogs with dilated cardiomyopathy (n = 12). The final diagnosis and the severity of HF were determined by Doppler echocardiography. Plasma DPP4 activity was measured kinetically by a fluorimetric method.

Results: In growing dogs, DPP4 activity was higher than in adults (P < .001) and inversely correlated with age (r = -0.57, P < .01). In adults, DPP4 activity increased linearly with body weight (r = 0.39, P < .01), but there was no influence of age or sex. No effect of the circadian rhythm was noted. DPP4 activity was significantly higher in HF ISACHC I (16.3 ± 1.14 U/L) compared with healthy adults (12.4 ± 0.65 U/L, P < .05) and HF ISACHC III (11.0 ± 1.50 U/L, P < .05). Mean DPP4 activity in ISACHC II was 15.1 ± 1.4 U/L.

Conclusion and Clinical Importance: We did not find evidence that plasma DPP4 activity is responsible for the “BNP resistance” in overt congestive HF, but it may be implicated in early stages.

Erythrocytic Pyruvate Kinase Mutations Causing Hemolytic Anemia, Osteosclerosis, and Secondary Hemochromatosis in Dogs

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Background: Erythrocytic pyruvate kinase (PK) deficiency, first documented in Basenjis, is the most common inherited erythroenzymopathy in dogs.

Objectives: To report 3 new breed-specific PK-LR gene mutations and a retrospective survey of PK mutations in a small and selected group of Beagles and West Highland White Terriers (WHWT).

Animals: Labrador Retrievers (2 siblings, 5 unrelated), Pugs (2 siblings, 1 unrelated), Beagles (39 anemic, 29 other), WHWTs (22 anemic, 226 nonanemic), Cairn Terrier (n = 1).

Methods: Exons of the PK-LR gene were sequenced from genomic DNA of young dogs (<2 years) with persistent highly regenerative hemolytic anemia.

Results: A nonsense mutation (c.799C>T) resulting in a premature stop codon was identified in anemic Labrador Retriever siblings that had osteosclerosis, high serum ferritin concentrations, and severe hepatic secondary hemochromatosis. Anemic Pug and Beagle revealed 2 different missense mutations (c.848T>C, c.994G>A, respectively) resulting in intolerable amino acid changes to protein structure and enzyme function. Breed-specific mutation tests were developed. Among the biased group of 248 WHWTs, 9% and 35% were homozygous (affected) and heterozygous, respectively, for the previously described mutation (mutant allele frequency 0.26). A PK-deficient Cairn Terrier had the same insertion mutation as the affected WHWTs. Of the selected group of 68 Beagles, 35% were PK-deficient and 3% were carriers (0.37).

Conclusions and Clinical Importance: Erythrocytic PK deficiency is caused by different mutations in different dog breeds and causes chronic severe hemolytic anemia, hemosiderosis, and secondary hemochromatosis because of chronic hemolysis and, an as yet unexplained osteosclerosis. The newly developed breed-specific mutation assays simplify the diagnosis of PK deficiency.

Concentrations of Noncortisol Adrenal Steroids in Response to ACTH in Dogs with Adrenal-Dependent Hyperadrenocorticism, Pituitary-Dependent Hyperadrenocorticism, and Nonadrenal Illness


Background: Increases of adrenal hormone concentrations other than cortisol have been reported in dogs with hyperadrenocorticism (HAC).

Hypothesis/Objectives: Measuring noncortisol adrenal hormone concentrations will help identify HAC in dogs. The objective was to determine plasma cortisol, androstenedione, estradiol, progesterone, testosterone, and 17-hydroxyprogesterone concentrations during ACTH stimulation testing of dogs with clinical signs of HAC to ascertain their utility in diagnosis of the disease.

Animals: Ninety dogs with clinical findings consistent with HAC had ACTH stimulation tests performed. Results from 29 dogs were excluded from analysis because diagnoses were inconclusive for a variety of reasons. Results from 32 dogs with HAC and 29 dogs with disease other than HAC were analyzed.
Methods: Prospective observational study. Concentrations of adrenocortical hormones were determined before and 1 hour after injecting 5 lg/kg ACTH IM. Diagnoses were determined by response to therapy, histopathology or both.

Results: Post-ACTH cortisol (P < .001), progesterone (P = .001), and 17-hydroxyprogesterone (P < .001) concentrations were associated with a diagnosis of HAC. Sensitivity and specificity, respectively, for diagnosing HAC for post-ACTH cortisol were 84 and 59%, progesterone 88 and 55%, and 17-hydroxyprogesterone 91 and 59%, and for post-ACTH cortisol, progesterone and 17-hydroxyprogesterone combined were 88 and 55%. Of 5 dogs with HAC and normal post-ACTH cortisol concentrations, 5 had increased progesterone and 4 had increased 17-hydroxyprogesterone.

Conclusions and Clinical Importance: Serum progesterone and 17-hydroxyprogesterone concentrations were useful to diagnose HAC in this study, but were not more sensitive or specific than cortisol concentration.

Evaluation of a Quality-of-Life Tool for Dogs with Diabetes Mellitus

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Background: Diabetes mellitus (DM) management primarily focuses on improvement in blood glucose concentrations and clinical signs. A tool to assess the psychological and social impact of DM and its treatment on quality of life (QoL) previously has only been validated for feline DM.

Hypothesis/Objectives: To validate a diabetic pet and owner-centered individualized measure of impact of DM (DIAQoL-pet) for diabetic dogs and their owners.

Animals/Subjects: A total of 101 owners of insulin-treated diabetic dogs were recruited to complete the DIAQoL-pet.

Methods: Discussions and pilot surveys with clinicians and owners of diabetic pets led to the design of 29 specific DM-associated QoL questions. Each item was scored according to impact frequency and perceived importance. An Item-Weighted-Impact-Score (IWIS) for each item was calculated, as was an Average-Weighted-Impact-Score (AWIS) by averaging all IWISs. Principal component analysis and Cronbach’s a calculation assessed the measure’s reliability.

Results: The DIAQoL-pet showed high reliability (Communalities _0.5; Cronbach’s a 0.85). The AWIS was _2.74 ± 1.7 (mean ± SD). Areas reported as most negatively impacting QoL included: “worry” (IWIS ± SD: _5.92 ± 4.3), “difficulties leaving dog with friends or family” (_5.68 ± 5.1), “worry vision” (_5.58 ± 4.6), “boarding difficulties” (_5.18 ± 5.2), “worry hypoglycemia” (_4.95 ± 4.3), “social life” (_4.82 ± 4.4), “costs” (_4.11 ± 4.7), and “future care”(_4.07 ± 4.6). Eighty-four percent of owners reported negative impact of DM on QoL.

Conclusions and Clinical Importance: The DIAQoL-pet proved robust when used by owners of insulin-treated diabetic dogs and identified specific areas most negatively impacting dogs’ and their owners’ QoL. This tool could be used as an additional assessment parameter in clinical and research settings.

Broadly Reactive Polymerase Chain Reaction for Pathogen Detection in Canine Granulomatous Meningoencephalomyelitis and Necrotizing Meningoencephalitis


Background: Granulomatous meningoencephalomyelitis (GME) and necrotizing meningoencephalitis (NME) are common inflammatory conditions of the central nervous system of dogs. Infectious pathogens, particularly viruses, are suspected to contribute to the etiopathogenesis of GME and NME.

Hypothesis: Broadly reactive PCR might aid in the identification of infectious agents in GME and NME.

Animals: Sixty-eight client-owned dogs evaluated by necropsy at 1 university referral hospital.

Methods: A mixed prospective/retrospective case-control study was performed. Brain tissue prospectively collected at necropsy from GME, NME, and control cases was evaluated by broadly reactive polymerase chain reaction (PCR) for adenoviruses, bunyaviruses, coronaviruses, enteroviruses, flaviviruses, herpesviruses, paramyxoviruses, and parechoviruses. In addition, these tissues were retrospectively evaluated for the presence of mycoplasmas by PCR, culture, and immunohistochemistry (IHC).

Results: Brain tissue was collected from 11 GME and 27 NME cases and 30 controls. Viral nucleic acids were not identified in the 6 GME cases, 25 NME cases, and 2 controls evaluated by viral PCR. Mycoplasma canis was identified by Mycoplasma genus PCR in 1/5 GME and 4/25 NME cases and subsequently was cultured.
from 4/5 GME and 4/8 NME cases as well as 2/9 controls. The IHC did not detect M. canis in any of the 11 GME and 27 NME cases or 14 controls evaluated with strain PG14 polyclonal antiserum.

Conclusions and Clinical Importance: The negative results suggest that viral pathogens are not common in the brain tissue of dogs with GME and NME. Further investigation is warranted to determine the importance of M. canis in cases of GME and NME.

Diagnostic Yield and Adverse Effects of MRI-Guided Free-Hand Brain Biopsies through a Mini-Burr Hole in Dogs with Encephalitis

T. Flegel, A. Oevermann, G. Oechtering, and K. Matiasek

Background: The diagnosis of encephalitis is usually presumptive based on MRI, cerebrospinal fluid analysis, or both. A definitive diagnosis based on histopathology, however, is required for optimizing treatment strategies.

Objective: To investigate the diagnostic yield and adverse effects of minimally invasive brain biopsies in dogs with encephalitis.

Animals: Seventeen dogs with suspected encephalitis, based on MR imaging and cerebrospinal fluid analysis.

Methods: Retrospective study. Minimally invasive, free-hand brain biopsy specimens were taken from forebrain lesions through a 4-mm burr hole using a Sedan side-cutting needle. Routine histopathological examination was performed. The adverse effects were assessed by MRI evaluations after biopsy procedure (12/17) and by sequential neurological examinations.

Results: The overall diagnostic yield with regard to a specific type of encephalitis was 82%. Encephalitis was evident in an additional 12%, but a specific disease could not be determined. There were no deaths caused by the biopsy procedure itself, but the indirect case fatality rate was 6%. Morbidity was 29%, including stupor, seizures, tetraparesis, hemiparesis, ataxia, and loss of conscious proprioception. All these signs resolved within 3–14 days.

Conclusions and Clinical Importance: Minimally invasive brain biopsy in dogs with suspected encephalitis leads to a definite diagnosis in the majority of dogs, allowing for a specific treatment. The advantages of a definite diagnosis outweigh potential case fatality rate and temporary neurological deficits.

Effect of Tolfenamic Acid on Canine Cancer Cell Proliferation, Specificity Protein (Sp) Transcription Factors, and Sp-Regulated Proteins in Canine Osteosarcoma, Mammary Carcinoma, and Melanoma Cells

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Background: Tolfenamic acid (TA) is an NSAID currently under investigation as an anticancer agent in humans. TA induces proteosome-dependent degradation of transcription factors Sp 1, 3, and 4. These proteins are known to be overexpressed in many human cancers.

Hypothesis: To evaluate the protein expression of Sp1–4 in canine tissue, and efficacy of TA against several canine tumor cell lines.

Methods: Six canine cell lines (2 osteosarcoma, 2 mammary carcinoma, 2 melanoma) were evaluated. Protein levels of Sp 1–4 and their downstream targets were evaluated using Western Blots. Cell survival and TUNEL assays were performed on cell lines, and Sp1 expression was evaluated on histologic samples from archived canine cases.

Animals: Six immortalized canine cancer cell lines derived from dogs were used. Archived tissue samples were also used.

Results: Sp1 were highly expressed in all 6 cell lines and variably expressed in histologic tissues. TA decreased expression of Sp1–4 in all cell lines. All of the downstream targets of Sp1 were inhibited in the cell lines. Variable Sp1 expression was identified in all histologic samples examined. TA significantly inhibited cell survival in all cell lines in a dose dependant fashion. The number of cells undergoing apoptosis was significantly increased (P < .05) in all cell lines after exposure to TA in a dose-dependent fashion.

Conclusions, and Clinical Importance: Tolfenamic acid is a potential anticancer NSAID and further investigation is needed to determine its usefulness in a clinical setting.
Intensity-Modulated and Image-Guided Radiation Therapy for Treatment of Genitourinary Carcinomas in Dogs

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Background: External beam radiation therapy can be used to treat pelvic tumors in dogs, but its utility is limited by lack of efficacy data and associated late complications.

Hypothesis/Objectives: The objective of this study was to assess local tumor control, overall survival, and toxicoses after intensity-modulated and image-guided radiation therapy (IM/IGRT) for treatment of genitourinary carcinomas (CGUC) in dogs.

Animals: 21 client-owned dogs.

Methods: A retrospective study was performed. Medical records of dogs for which there was intent to treat with a course of definitive-intent IM/IGRT for CGUC between 2008 and 2011 were reviewed. Descriptive and actuarial statistics comprised the data analysis.

Results: Primary tumors were located in the prostate (10), urinary bladder (9), or urethra (2). The total radiation dose ranged from 54–58 Gy, delivered in 20 daily fractions. Grade 1 and 2 acute gastrointestinal toxicoses developed in 33 and 5% of dogs, respectively. Grade 1 and 2 acute genitourinary and grade 1 acute integumentary toxicoses were documented in 5, 5, and 20% of dogs, respectively. Four dogs experienced late grade 3 gastrointestinal or genitourinary toxicosis. The subjective response rate was 60%. The median event-free survival was 317 days; the overall median survival time was 654 days. Neither local tumor control nor overall survival was statistically dependent upon location of the primary tumor.

Conclusions and Clinical Importance: IM/IGRT is generally well-tolerated and provides an effective option for locoregional control of CGUC. As compared with previous reports in the veterinary literature, inclusion of IM/IGRT in multimodal treatment protocols for CGUC can result in superior survival times; controlled prospective evaluation is warranted.

Dirofilarial Hemoptytic Expectoration in 5 Dogs – An Uncommon Manifestation of Canine Heartworm Disease


Trilostane Dose versus Body Weight in the Treatment of Naturally Occurring Pituitary-Dependent Hyperadrenocorticism in Dogs

E.C. Feldman and P.H. Kass

Background: Trilostane is commonly used in the treatment of dogs with naturally occurring pituitary-dependent hyperadrenocorticism (PDH). Dose recommendations have varied from the manufacturer and the literature.

Hypothesis: As body weight increases, dose/kg or dosage/day of trilostane required to control the clinical signs of PDH decreases.

Animals: 70 dogs with naturally occurring hyperadrenocorticism.

Methods: Retrospective study. Each dog must have been treated for at least 6 months and should have shown a “good response” to trilostane, as determined by owners. Statistical comparisons of dose and dosage were made after the dogs were separated into groups weighing <15 or >15 kg; groups weighing _10, 10.1–20, 20.1–30, and _30 kg; and then groups based on body surface area versus dose/kg and total amount of trilostane required to control the condition.

Results: There was no significant difference in trilostane dose in mg/kg of body weight or in the total amount of trilostane required daily to control clinical signs, except when the dose for dogs weighing >30 kg was compared with that for the other groups. However, despite lack of statistical significance when comparing groups, there was a significant trend using polynomial regression analysis, suggesting that as body weight increases, the amount of trilostane (mg/kg/dose as well as mg/kg/daily dosage) required to control clinical signs decreases.

Conclusions and Clinical Importance: Dogs weighing >30 kg, and possibly those weighing >15 kg, might require smaller amounts of trilostane per dose or per day than those weighing less, to control PDH-associated clinical signs.