

# Companion Animal Research Review™

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Issue 1 – 2015

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### Abbreviations used in this issue

**AKI** = acute kidney injury  
**FC<sub>Na</sub>** = fractional sodium clearance  
**FeLV** = feline leukaemia virus  
**FIV** = feline immunodeficiency virus  
**GFR** = glomerular filtration rate  
**IBD** = inflammatory bowel disease  
**ISCL** = intestinal small cell lymphoma  
**IV** = intravenous  
**SC** = subcutaneous

## Welcome to our first issue of Companion Animal Research Review.

This review is a unique New Zealand publication providing topical, relevant and accessible information for animal healthcare professionals with an interest in companion animal health. In essence, the review is a summary of what we consider to be some of the most significant new studies in this area. For each paper we have provided commentary on why the findings are important and, where relevant, have suggested how they can potentially affect local practice.

We hope you find our inaugural selection for Companion Animal Research Review stimulating reading and we welcome your feedback. Furthermore, if you have discovered or been involved with what you think is significant global research, please let us know and we will consider it for inclusion next time.

Kind regards

**Nick Cave**

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## Association between oral health status and retrovirus test results in cats

**Authors:** Kornya MR et al.

**Summary:** A cross-sectional survey of Canadian veterinarians assessed the oral health status of 5179 cats with no history of vaccination against feline immunodeficiency virus (FIV). A total of 237 (4.6%) cats were seropositive for FIV, 186 (3.6%) were seropositive for feline leukaemia virus (FeLV) and 12 (0.2%) were seropositive for both FIV and FeLV. Overall, 40.6% of the cats (n = 2104) had oral disease; gingivitis 1073 (20.7%), periodontitis 576 (11.1%), stomatitis 203 (3.9%), and 252 (4.9%) had other oral conditions. Cats with an inflammatory oral disease (particularly stomatitis) had a higher risk of a positive test result for FIV than those with no disease or other oral diseases. Those with any oral inflammatory disease were also more likely to have FeLV. In retrovirus-seronegative cats, greater age was associated with an increased prevalence of oral disease.

**Comment:** FIV is common in NZ, but the frequency and severity of FIV-associated disease is still not defined. Gingivostomatitis is the disease most frequently associated with FIV, but it has not been previously described how much the risk of gingivostomatitis is increased by either FIV or FeLV. This study enrolled a large number of cats from across the US, and since the investigators tested for both retroviruses, the comparison between FIV and FeLV cats is particularly illuminating. The strongest finding was the hierarchical association between FIV and oral disease, whereby gingivostomatitis was the most strongly associated, followed by periodontitis and finally gingivitis. The strength of association increased with younger cats. The association between FIV and gingival and periodontal disease has not previously been reported. Although assumed by the authors, causality has not been demonstrated, since existing inflammatory oral disease could predispose to retroviral infection through the oral mucosa when an FIV negative cat bites a positive cat. None-the-less, this study emphasises that cats with severe gingivostomatitis and notably young cats with unexpectedly early onset periodontal disease are much more likely to be FIV positive than healthy cats.

**Reference:** *J Am Vet Med Assoc.* 2014;245(8):916-22

[Abstract](#)

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## Risk factors for survival in a university hospital population of dogs with epilepsy

**Authors:** Fredsø N et al.

**Summary:** This retrospective study assessed risk factors for survival and survival duration in 102 dogs diagnosed between 2002 and 2008 with idiopathic epilepsy (n = 78) or epilepsy secondary to a primary intracranial cause (n = 24). The median life span across all dogs was 7.6 years, 9.2 years in dogs with idiopathic epilepsy and 5.8 years in dogs with epilepsy associated with a known intracranial cause (p < .001). The survival time in dogs with idiopathic epilepsy was shorter in dogs euthanased for epilepsy (median 35 months) than in dogs euthanased for other reasons (median 67.5 months; p = 0.0030). Neutered male dogs with idiopathic epilepsy had a shorter survival time after index seizure than intact male dogs (median 38.5 vs 71 months; p = 0.031). Treatment with two antiepileptic drugs did not reduce survival (p = 0.056).

**Comment:** This study found that 52% of dogs with idiopathic epilepsy died or were euthanased because of their disease, compared with 83% of dogs with epilepsy secondary to primary intracranial disease. The median survival time from the index seizure was 4.7 years, and status epilepticus and cluster seizures were associated with a poorer prognosis, similar to another recent study (Arrol L et al. 2012). However, this study did not elucidate the reasons for euthanasia of dogs with idiopathic epilepsy, and cost or inconvenience could have been motivations. Neither did the authors discuss the difference in median survival time in an almost identical study in the same hospital 10 years prior, when the median survival time was only 2.3 years (Berendt M et al. 2007). In both studies, 99% of dogs were treated with phenobarbitone and/or potassium bromide, thus unless management protocols have substantially improved, it seems likely that changes in client attitudes are at play. Therefore, studies are needed to determine owner motivations to euthanase dogs with epilepsy, if we are to maximise their longevity.

**Reference:** *J Vet Intern Med.* 2014;28(6):1782-8  
[Abstract](#)

### Independent commentary by Nick Cave.

Nick Cave is a Senior Lecturer in small animal medicine and nutrition at Massey University. He holds a BVSc from Massey, a Masters in Veterinary Science, a PhD in nutrition and immunology from the University of California, Davis, and is a diplomate of the American College of Veterinary Nutrition. He is a founding member of the WSAVA Global Nutrition Committee, and a founding board member for the Massey University Working Dog Centre.

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## The diagnostic utility of lymph node cytology samples in dogs and cats

**Authors:** Amores-Fuster I et al.

**Summary:** This retrospective study analysed 1473 records to determine common reasons for lymph node fine needle aspirates, cytological diagnoses and the reasons for non-diagnostic sampling from dogs (n = 1274) and cats (n = 199). A total of 928 (72.8%) canine samples and 171 (85.9%) feline samples were diagnostic and 346 (27.2%) and 28 (14.1%) were non-diagnostic. In both species, most samples were for lymphadenopathy assessment or tumour staging. The most common diagnosis in dogs was lymphoma (n = 351; 27.5%); in cats the most common diagnosis was reactive hyperplasia (n = 63; 31.6%). An absence of cells, cellular disruption and a low yield were the most common causes of non-diagnostic samples.

**Comment:** Lymph node cytology is commonly performed in general practice. This is the largest study of cytological specimens from lymph nodes submitted from general practice. It emphasises the need to prepare the smears carefully, and to examine a selection in-house prior to submission. In total, 25% of samples were non-diagnostic for reasons that would have been readily available to the submitting clinician, and submitting more slides increased the chance of a diagnosis. The frequency of small cell lymphoma in cats makes the cytological diagnosis more challenging than in dogs, but this study could not determine the diagnostic accuracy. Although the authors observed that submission of a history with the slides did not increase the rate of diagnosis, this should not be taken as a suggestion of indifference, since it had an unknown effect on accuracy, and it certainly does not expunge the need for submitting histories with other cytological specimens.

**Reference:** *J Small Anim Pract.* 2015;56(2):125-29  
[Abstract](#)

## Glomerular filtration rate, urine production, and fractional clearance of electrolytes in acute kidney injury in dogs and their association with survival

**Authors:** Brown N et al.

**Summary:** In a prospective study, the changes observed in conventional indices of renal function were recorded to define the course of acute kidney injury (AKI; n = 10 dogs) and to identify recovery markers. Six dogs did not survive. Glomerular filtration rate (GFR) did not differ between surviving and non-surviving dogs, but did increase over time in surviving but not non-surviving dogs (p = 0.03). The fractional clearance of sodium decreased over time from 20% to 9.4% (p < 0.0001) in the surviving but not the non-surviving dogs. The excretion ratio and fractional clearance of solutes were highly correlated (r = 0.70-0.95).

**Comment:** Survival following AKI in dogs is less than 50% in most studies, though it is unclear what the best prognostic marker on presentation is. In most studies, urine output is the parameter most consistently associated with survival. This study included 10 oligo-anuric AKI dogs, which are already known to have a poorer prognosis than polyuric dogs. In this study there was no difference at presentation in any of the reported parameters, including serum creatinine, between survivors and non-survivors. Survival was associated with a rise in urine output, a decrease in serum creatinine, an increase in GFR and a decrease in fractional sodium clearance (FC<sub>Na</sub>). Thus, the response to appropriate therapy and not baseline characteristics are most important, and therefore management is worth considering in most cases. This study did not determine if calculating the FC<sub>Na</sub> or GFR out-performs monitoring urine output and creatinine. Until we learn otherwise, accurate monitoring of urine output remains paramount in all cases of AKI.

**Reference:** *J Vet Intern Med.* 2015;29(1):28-34  
[Abstract](#)

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## Management of acute pancreatitis in dogs: a critical appraisal with focus on feeding and analgesia

**Authors:** Mansfield C and Beths T

**Summary:** Despite increases in medical and veterinary knowledge of acute pancreatitis, few studies exist on treatment interventions in dogs. Treatment recommendations are generally based on rodent models or general critical care principles and include replacement of fluid losses, maintenance of hydrostatic pressure, nausea control and the provision of pain relief. In humans the use of neurokinin-1 antagonists for analgesia and early interventional feeding has been recommended. Early feeding is thought to improve intestinal tract health, as unhealthy enterocytes may perpetuate systemic inflammation. Early interventional feeding is not supported by robust clinical trials, although in humans there is evidence that it reduces hospitalisation time. In dogs early feeding is well tolerated.

**Comment:** Acute pancreatitis is a relatively common disease in dogs, and with mortality ranging from 27% to 42%, it is serious and important. Despite advances in the understanding of the pathophysiology of acute pancreatitis, there is still no specific therapy, and many different therapeutic approaches have been recommended over the years, but usually with little to no supportive evidence in clinical patients. In this comprehensive yet accessible review, the authors consider the evidence for the most widely recommended therapies with rigor. Drawing on human and canine clinical, and experimental studies, this is an excellent up-to-date review. The importance of establishing adequate tissue perfusion and maintaining blood pressure, and the control of emesis and pain is emphasised. The growing recognition of the benefits of early enteral nutrition is thoroughly discussed, and will challenge the traditional approach of many practitioners. In contrast, the use of antibiotics, plasma or gastric suctioning is discouraged.

**Reference:** *J Small Anim Pract.* 2015;56(1):27-39

[Abstract](#)

## The effects of diazepam or midazolam on the dose of propofol required to induce anaesthesia in cats

**Authors:** Robinson R and Borer-Weir K

**Summary:** In a prospective, randomised, blinded, placebo-controlled clinical trial in 90 cats (median body mass 4.0 kg), the effects of benzodiazepine (midazolam or diazepam 0.2, 0.3, 0.4 or 0.5 mg/kg) administration on the propofol dose required to induce anaesthesia was assessed. Compared with saline, all doses of midazolam and diazepam reduced the propofol dose required to induce anaesthesia ( $p < 0.001$ ) with no difference between midazolam and diazepam in propofol dose reduction. All midazolam doses reduced propofol requirement; however, the lowest dose of diazepam (0.2 mg/kg) did not reduce propofol requirement compared with saline. All higher doses of diazepam did reduce propofol requirement. Those cats with sedation scores of 3 required less propofol than those with scores of 2 ( $p = 0.008$ ).

**Comment:** Using a combination of induction drugs can reduce the dose of each drug if they function synergistically, and can reduce adverse effects and improve haemodynamic stability. Propofol as a sole agent can decrease heart rate, myocardial contractility, blood pressure and ventilation. Surprisingly, this is the first published study of the administration of benzodiazepines with propofol to induce general anaesthesia in cats. Although it was not surprising that both drugs significantly reduced the dose of propofol required, it was intriguing that neither had a dose-dependent effect, and the lowest dose evaluated for each was equally effective. Although there were no differences in the generally low rate of adverse effects, which differs to dogs and humans, the study did not evaluate differences beyond the point of intubation. None-the-less, this was a nice demonstration of the utility of synergistic anaesthesia to reduce drug dose, and at least cost. Further studies are needed to determine if any other benefit is attained during the anaesthetic and recovery periods.

**Reference:** *Vet Anaesth Analg.* 2015;14 Feb [Epub ahead of print]

[Abstract](#)

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## Cats with inflammatory bowel disease and intestinal small cell lymphoma have low serum concentrations of 25-hydroxyvitamin D

**Authors:** Lalor S et al.

**Summary:** This retrospective study measured serum 25-hydroxyvitamin D ( $25_{OH}D$ ) levels in 20 cats with inflammatory bowel disease (IBD) or intestinal small cell lymphoma (ISCL) and in 23 healthy cats and 41 cats hospitalised with non-gastrointestinal diseases. Serum  $25_{OH}D$  levels overlapped among the 3 groups, but the serum  $25_{OH}D$  levels were lower in cats with IBD/ISCL compared to healthy ( $p < 0.0001$ ) and hospitalised cats ( $p = 0.014$ ). There was a moderate positive correlation between serum albumin and  $25_{OH}D$  levels in the IBD/ISCL cats ( $r = 0.58$ ;  $p = 0.018$ ).

**Comment:** The role of vitamin D in calcium metabolism has been understood for almost 100 years, but the effect of vitamin D on immunity is still surprising, and incompletely understood. The vitamin D receptor is expressed in lymphocytes, dendritic cells and macrophages, and some activated leucocytes produce the active form of vitamin  $D_3$ . Vitamin  $D_3$  can limit dendritic cell function, alters lymphocyte homing, and inhibits T cell proliferation, with a bias away from a Th-2 type response. Low vitamin D status is a risk for allergic disease, as well as immune-mediated disease such as multiple sclerosis in humans. There is little surprising in this study and no surprise that cats with diseases associated with anorexia, malnutrition, and malabsorption/maldigestion have lower serum vitamin D than either healthy cats or cats with other diseases. Indeed, this is consistent with studies of canine IBD and human IBD variants. What remains an intriguing question in human and veterinarian medicine, is whether the hypovitaminosis is simply an effect of the disease, or if it could be more than that. Given the complexity of the association between vitamin D and immunity, it is at least rational to consider whether hypovitaminosis could be exacerbating the inflammatory response, if it could be reducing disease severity, or even if it could be a precedent risk factor. There is much more to be told in the fascinating role of vitamin D.

**Reference:** *J Vet Intern Med.* 2014;28(2):351-5

[Abstract](#)

## Intensive intravenous infusion of insulin in diabetic cats

**Authors:** Hafner M et al.

**Summary:** This randomised comparative trial examined the hypothesis that in newly diagnosed diabetic cats ( $n = 30$ ) an initial IV infusion of insulin that provides tight glycaemic control will decrease subsequent insulin requirements (SC insulin glargine during follow-up for 6 months) and increase remission rate (euglycaemia for  $\geq 4$  weeks without insulin). In 15 cats receiving IV insulin to maintain 90-180 mg/dL blood glucose for the first 6 days, remission was achieved in 10 cats, while in another 15 cats receiving SC insulin glargine for 6 days, seven achieved remission ( $p = 0.46$ ). Good metabolic control was achieved in a further three cats in the first group and one in the second group ( $p = 0.22$ ). Good metabolic control or remission occurred in 13 of 15 cats in the first group and eight of 14 cats in the second. The median insulin dosage during the 6-month follow-up was significantly lower in the first than the second group (0.32 vs 0.51 IU/kg/day;  $p = 0.013$ ).

**Comment:** Prognosis and reasons for death in diabetic cats in primary practice have not been defined. It is highly likely that owner factors are dominant and attempts to decrease the cost and hassle of treatment, and achieve clinical remission will extend life. A recent study reported the median survival time after diagnosis in 59 cats followed to time of death (Callegari C et al., 2013). The median survival time was 24 days in cats that did not reach remission, but was 913 days in those that did. This study by Hafner et al. evaluated a relatively small number of cats to see if, similar to humans, early aggressive maintenance of normoglycaemia significantly improves glycaemic control in the long term, compared with conventional SC injections. Intensive insulin treatment requires surgical placement of a continuous glucose interstitial fluid sensor and close 24 hour care for adjustment of the insulin dose every 15-30 minutes as required for 7 days. Using this intensive care approach, there was no difference in episodes of hypo or hyperglycaemia, or in electrolyte concentrations during hospitalisation. Although the dose of insulin required for the following 6 months was decreased, there was no difference in the rate or duration of remission. If achievement of remission and minimising cost and hassle are key objectives, then the results of this study in light of the expense, ethical cost, and clinical complexity, provide no reason to consider the approach.

**Reference:** *J Vet Intern Med;*2014. 28(6):1753-9

[Abstract](#)

## Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats

**Authors:** Calvo G et al.

**Summary:** To develop a composite pain scale tool for assessment of acute pain in cats, words describing pain in cats were grouped into behavioural categories, ranked and prototype tested. A revised composite measure pain scale and numerical rating scale was then tested in 116 cats using two observers before and after analgesia. The mean decrease in the composite measure pain scale and numerical rating scale scores after analgesia were 2.4 (95% CI 1.21-3.6) and 1.9. Changes in the composite measure pain scale and the numerical rating scale were significantly correlated ( $r = 0.8$ ;  $p < 0.0001$ ). An intervention score of  $\geq 4/16$  was determined for the composite measure pain scale (26.7% misclassification) and  $\geq 3/10$  for the numerical rating scale (14.5% misclassification).

**Comment:** Quantifying pain in others is fraught even in human patients, since the experience of pain is a subjective phenomenon. Yet the recognition and alleviation of pain is one of the most fundamental duties veterinarians are charged with. Thus, a valid, reliable and easily usable means of assessing pain in animals is essential. These researchers present the validation of a new scoring system in cats, based on the answers to six simple questions about the cat's demeanour and responses to stimuli. Although any experienced cat handler would likely find the scoring system intuitive and obvious, that, in itself, is both the basis of its construction, and a testament to its validity. The author's "psychometric approach" began with surveying the opinions of experienced clinical staff, and thus incorporated the biases and anthropomorphic assumptions of the participants. None-the-less, a similar system was developed for dogs in the same teaching hospital in Glasgow. In the ensuing decade, over 50 peer-reviewed published studies have utilised the system in pain-related research, giving resounding support. This is the 4<sup>th</sup> system for scoring pain in cats to have been published in the last decade, but the benefit of having the "Glasgow" moniker, puts it in an esteemed company of widely used clinical scales such that this is likely to become the most used. The scale is simple, quick to use, and would make a worthy addition to hospital walls. Whether it remains a research tool, or garners wider use in general practice remains to be seen.

**Reference:** *J Small Anim Pract.* 2014;55(12):622-9

[Abstract](#)

## 'Four Seasons' in an animal rescue centre; classical music reduces environmental stress in kennelled dogs

**Authors:** Bowman A et al.

**Summary:** This cross-over study examined physiological and psychological changes in dogs exposed to long-term (7 days) of classical music or silence in a kennel environment assessed by measurement of heart rate variability, salivary cortisol and behavior. Changes in heart rate variability and behavioural data suggesting reduced stress levels occurred in dogs in both groups during auditory stimulation with classical music. Behavioural data showed that both groups spent more time sitting/lying and silent and less time standing and barking during auditory stimulation. A General Regression Analysis of changes in heart rate variability parameters suggest that male dogs responded better to auditory stimulation than female dogs.

**Comment:** Stress in hospitalised animals is almost inevitable, but external factors can increase or decrease it. A stressed animal eats and drinks less, and there can be measurable effects on immunity, healing and ultimately recovery. Several simple, economical manipulations of the kennel and cattery environment are available including avoidance of stressful noise, separation of species, provision of toys, grooming, familiar bedding, and the use of aerosolised pheromones. Previous studies have shown that short-term exposure to classical music can increase time sleeping and decrease barking in healthy kennelled dogs. This study, however, is a comprehensive evaluation of the effects of classical music in a rescue shelter, where the authors assessed heart rate variability, behavioural responses and salivary cortisol as the main measures. Again, a positive response in all parameters except salivary cortisol was seen, though the dogs appeared to habituate to the music within a few days. Whether the habituation was to the effect of classical music, or a habituation specifically to the repeated music that could be abrogated with variety, is under investigation. For veterinary clinics, however, the provision of a little Mozart in the wards, might be more than simply music to the ears.

**Reference:** *Physiol Behav.* 2015;143:70-82

[Abstract](#)