

Companion Animal Research Review™

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Issue 5 – 2017

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Abbreviations used in this issue

- CHF** = congestive heart failure
CI = confidence interval
CT = computed tomography
HR = hazard ratio
MMVD = myxomatous mitral valve disease
MPSS = methylprednisolone sodium succinate
PDH = pituitary-dependent hyperadrenocorticism
PEG = polyethylene glycol
US = ultrasound



Welcome to the fifth issue of Companion Animal Research Review.

This review is a unique New Zealand publication providing topical, relevant and accessible information for animal health 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.

I am very pleased to welcome Kat Crosse and Richard Burchell as our guest reviewers for this issue of Companion Animal Research Review. We hope you enjoy our selection of studies and look forward to your feedback.

Kind regards,

Dr Nick Cave

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Research Review thanks MSD Animal Health for their sponsorship of this publication, and their support for ongoing education for animal health professionals.

A placebo-controlled, prospective, randomized clinical trial of polyethylene glycol and methylprednisolone sodium succinate in dogs with intervertebral disk herniation

Authors: Olby NJ et al.

Summary: Sixty-three client-owned dogs with acute onset of thoracolumbar intervertebral disk herniation causing paralysis and loss of nociception for <24 hours were randomised to receive methylprednisolone sodium succinate (MPSS), polyethylene glycol (PEG) or placebo. All of the dogs underwent hemilaminectomy and drug administration was initiated once the diagnosis of intervertebral disk herniation was confirmed. 47.6% of the dogs recovered ambulation and while 17.5% developed progressive myelomalacia, there was no association with treatment group. An open field gait score (OFS) was used to assess neurologic function (primary outcome) at postoperative weeks 2, 4, 8 and 12. A Wilcoxon rank sum test showed no difference in OFS among groups and although full study power was not reached, conditional power analyses indicated the futility of continued case recruitment.

Comment: (KC) Finding that specific treatment to halt the inflammatory cascade initiated by acute intervertebral disc extrusion has become the goal of many a clinical trial. Steroids, non-steroidals, N-acetylcysteine and many others in various forms have all been tested to no avail. Much of our data, however, has been retrospective and difficult to decipher. Evidence from human medicine is often quoted, but despite large studies the jury is still out and the use of steroids in spinal injuries is not currently the accepted standard of care. This paper has given us a specific veterinary study appropriately designed to answer the question of the benefit of MPSS and PEG and found they made no significant difference to outcome. Importantly, the awful adverse events associated with dexamethasone administration in similar patients were not seen. Therefore, we know that dexamethasone has been shown to cause harm, whereas MPSS and PEG appear safe, but that none of these drugs have been shown to be of any benefit. So simply put – is there any evidence that steroids are of benefit to dogs with acute intervertebral disc extrusion? No. Would I ever give steroids in these cases myself? No.

Reference: *J Vet Intern Med.* 2016;30:206-14

[Abstract](#)

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Effect of pimobendan in dogs with preclinical myxomatous mitral valve disease and cardiomegaly: The EPIC Study – a randomized clinical trial

Authors: Boswood A et al.

Summary: This prospective, randomised, placebo-controlled, blinded, multicentre trial in 360 dogs with preclinical myxomatous mitral valve disease (MMVD), examined the use of pimobendan 0.4-0.6 mg/kg/day to delay the onset of signs of congestive heart failure (CHF), cardiac-related death or euthanasia (composite primary endpoint). The median time to the primary endpoint was 1228 days (95% CI 856-not reached [NR]) with pimobendan versus 766 days (95% CI 667-875) with placebo ($p = 0.0038$) with an HR of 0.64 (95% CI 0.47-0.87). Adverse events did not differ between treatments. Median survival time in pimobendan recipients was 1059 days (95% CI 952-NR) versus 902 days (95% CI 747-1061) with placebo ($p = 0.012$).

Comment: (RB) Prior to the publication of this study there were no prospective veterinary therapeutic trials supporting pharmacotherapeutic intervention in preclinical MMVD. In the EPIC trial, patients with stage B2 MMVD ([Atkins C et al. 2010](#)), were randomised to receive either pimobendan (0.2-0.3 mg/kg twice daily) or placebo and the trial was fully blinded. The endpoint of the study was onset of CHF or death. Time to reach the endpoint was significantly longer in the pimobendan group and treatment prolonged the preclinical period by 15 months. Risk of progression to the endpoint was 36% lower in the treatment group at any time, for the duration of the study. The risk of adverse events was not statistically different between the two groups, suggesting that adverse drug reactions are not common, which is relevant given the protracted treatment period. In summary, this study provides good evidence for the treatment of MMVD patients with preclinical heart disease and evidence of cardiomegaly. Practitioners need to be reminded, however, that in spite of this trial, treatment of preclinical MMVD with pimobendan is still considered off-label therapy for MMVD, until the study has been incorporated into the label claim. Lastly, it is worthwhile noting that progression to CHF occurred in about 40% of patients in both groups, which emphasises the fact that many patients with MMVD do develop CHF.

Reference: *J Vet Intern Med.* 2016;30(6):1765-79
[Abstract](#)

Reduction of surgical complications in dogs and cats by the use of a surgical safety checklist

Authors: Bergström A et al.

Summary: A prospective study was conducted in 520 cats and dogs to determine if a surgical safety checklist (SSC) adapted from the WHO surgical checklist would reduce complication incidence after small animal surgery. The frequency and severity of postoperative complications were decreased after versus before SSC adoption (15/220 vs 52/300; $p = 0.0003$). There was also a higher frequency of surgical site infections ($p = 0.045$) and wound healing complications ($p = 0.0006$) prior to SSC adoption.

Comment: (KC) I am borderline evangelical about Atul Gawande's book "The Checklist Manifesto" where simply pausing, communicating and checking reduced mortality rates in hospitals across the USA. In this first veterinary paper, it has been found yet again that checklists – a free and easy addition to clinical practise – decrease post-operative complications in surgical patients. The checklist doesn't tell us to do anything in particular, it is just there to make sure that common human errors are kept to an absolute minimum. In the midst of a busy clinic the checklist allows us to ensure we are keeping to the standards and protocols we have set ourselves. It does mean we have to accept our own fallibility, our tendency to short cut and accept that we all need a safety net. This article includes a copy of the checklist used and the WHO has provided a basic checklist that can be adapted to any practice and a manual on how to implement its use ([WHO surgical safety checklist and implementation manual](#)). If any study showed a drug able to reduce postoperative infections as much as this, we would all put it on our shelves tomorrow. How many will take up a checklist?

Reference: *Vet Surg.* 2016;45(5):571-6
[Abstract](#)

Efficacy of low- and high-dose trilostane treatment in dogs (< 5 kg) with pituitary-dependent hyperadrenocorticism

Authors: Cho KD et al.

Summary: In a prospective observational study the efficacy of two protocols of trilostane administration (low-dose, 0.78 mg/kg every 12 hours [$n = 9$], and high-dose, 30 mg every 24 hours [$n = 7$]) were compared in 16 dogs with pituitary-dependent hyperadrenocorticism (PDH). ACTH-stimulated serum cortisol concentrations and clinical signs improved more slowly in low-dose than high-dose trilostane recipients; however, after 20 weeks two high-dose dogs had clinical signs and abnormal laboratory findings suggesting hypoadrenocorticism. After 24 weeks, all dogs had an improvement in clinical findings.

Comment: (RB) Trilostane has recently received considerable attention in the veterinary literature from which a number of important insights have been gained, most notably that trilostane is not superior to mitotane, but is probably safer ([Barker EN et al. 2005](#); [Arenas C et al. 2014](#)). The current study provides several insights pertaining to trilostane in PDH, namely 1) trilostane is not a benign drug and significant adverse effects DO occur, 2) PDH is a slowly progressing disease that is not usually a clinically severe disease necessitating urgent intervention and thus 3) most patients can be managed with a much lower (ostensibly safer) dose of trilostane. In this study, dogs under 5 kg were dosed with either 0.5-1mg/kg twice daily (low dose protocol), or 30 mg once daily (standard protocol). Notwithstanding the fact that the numbers of dogs per group was small (nine and seven respectively), this study showed that dogs in the low-dose group all achieved remission from PDH, but took longer than the standard protocol (up to 24 weeks in the low-dose group). In two of seven dogs in the high-dose group biochemical evidence of hypoadrenocorticism was present after 20 weeks of therapy. In conclusion, this study suggests that low dose trilostane is an effective alternative to the standard treatment protocol and is likely to be safer, but that patients will take longer to achieve clinical resolution.

Reference: *J Vet Intern Med.* 2013;27(1):91-8
[Abstract](#)

Independent commentary by Kat Crosse.

Kat Crosse is a Senior Lecturer in small animal surgery at Massey University. She graduated from the University of Cambridge in 2006 with an MA and VetMB. After spending four years in mixed practice and emergency clinics, she moved to Massey, New Zealand to complete her specialist training. In 2016 she became a diplomate of the European College of Veterinary Surgery. At Massey, she is the coordinator of charity outreach clinics in Samoa, taking final year students to run desexing clinics across the island. As of this year she will also start a PhD in brachycephalic obstructive airway syndrome.



Independent commentary by Richard Burchell.

Richard Burchell completed a Bachelor of Science degree with an honours year at Rhodes University, and then completed a degree in veterinary science at the University of Pretoria in South Africa. He then spent two years in private practice before enrolling in a residency programme in a private referral practice. He moved to the university of Pretoria as a lecturer in small animal medicine in 2012. During his time there, he completed a small animal medicine residency through the European College of Veterinary Internal Medicine, and is recognised as a small animal medicine specialist by the European Board of Veterinary Specialisation. He has been at Massey for just over a year. He has a passion for teaching and clinics, and his research interests are in endocrinology.



Use of accelerometry to investigate physical activity in dogs receiving chemotherapy

Authors: Helm J et al.

Summary: This preliminary study assessed the effect of single-agent palliative or adjuvant chemotherapy on physical activity in 15 dogs with neoplasia and 15 healthy dogs (controls). ActiGraph™ accelerometer data indicated that chemotherapy-treated dogs were less active than control dogs prior to treatment. Treated dogs were slightly more active at restaging than prior to treatment and similar to control dogs. Activity was slightly lower during chemotherapy in treated dogs versus controls, but there was a slight increase during chemotherapy versus pretreatment. Mean 5-day total physical activity did not change in treated dogs during chemotherapy versus at restaging, but there was a small decrease in sedentary time and an increase in light-moderate activity.

Comment: (KC) This paper highlights some of the important yet rarely studied aspects of cancer treatment in pets. Just because we can treat – should we treat? What effect does treatment have not only on quantity of life (median survival times) but on quality of life? And what advice can we offer clients whose expectations of chemotherapy may be drastically different to our experience? Thankfully this study shows little effect on activity of the treated dogs and allows us to reassure clients that our aims of chemotherapy to prolong life whilst not damaging its quality seem possible with these regimens. Assessing quality of life is difficult and is by nature largely subjective. This doesn't mean though we shouldn't try to assess activity, appetite, willingness to play and other markers that aim to pin down that common client observation "he's just not himself". Being able to do this relatively objectively with accelerometry is great and should encourage us to ask pertinent questions with regard to exercise, play, appetite and sleep patterns when seeing these patients during the course of their treatment.

Reference: *J Small Anim Pract.* 2016;57(11):600-9

[Abstract](#)

Cytologic-histologic concordance in the diagnosis of neoplasia in canine and feline lymph nodes: a retrospective study of 367 cases

Authors: Ku CK et al.

Summary: This retrospective analysis of lymph node reports from 296 dogs and 71 cats assessed the accuracy of cytologic diagnosis based on lymph node sampling versus histology. In 157 (42.7%) non-neoplastic lesions, 62 (16.9%) lymphomas and 148 (40.3%) metastatic neoplasms were observed and cytology was found to have a sensitivity of 66.6% (95% CI 60.0-72.8), a specificity of 91.5% (95% CI 86.3-95.2), and accuracy of 77.2% (95% CI 72.6-81.3) for neoplasia. The likelihood of malignancy after a positive cytologic neoplasia diagnosis was 93.0%. A relatively high proportion of false-negatives were observed for mesenteric T-cell lymphoma (22/35 [63%], mainly in cats), metastatic sarcoma (8/14 [57%]) and metastatic mast cell tumour (15/48 [31%], mainly in dogs).

Comment: (RB) The findings of this study are of great relevance to veterinary practitioners. The authors assessed the diagnostic accuracy of cytology in the detection of neoplasia in lymph nodes. This practice is commonly used to determine nodal involvement in cancer staging. Notwithstanding the limitations and biases associated with retrospective studies, they showed that cytology has poor sensitivity in detecting lymph node neoplasia, particularly in mast cell tumours and feline mesenteric lymphoma. Overall cytology had a sensitivity of 66% which means that neoplasia was missed or incorrectly diagnosed in roughly 1/3 of cases. False negatives were more frequent than false positives, meaning that when cytology was positive it was usually a true positive. The ramifications of this study for the practitioner are immense. 1) veterinarians should be cautious to inform owners that a lymph node is "clear" of cancer based on cytology and should preferably say that the probability is lower based on a negative cytology 2) they should be cognisant of the fact that nodal aspiration is not always reliable in staging and lymph nodes should be monitored when a node is at risk, for example in mast cell tumours.

Reference: *Vet Comp Oncol.* 2016;Aug 15 [Epub ahead of print]

[Abstract](#)

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The use of disposable skin staples for intestinal resection and anastomosis in 63 dogs: 2000 to 2014

Authors: Rosenbaum JM et al.

Summary: A retrospective examination of medical records from 63 dogs receiving intestinal resection and anastomosis (2000-14; most commonly for neoplasia [31.7%] and foreign body removal [30.2%]) was conducted to evaluate the use of disposable skin staples. Overall mortality rate was 12.7% and the overall dehiscence rate was 4.8% (3/63). No difference in mortality was associated with the indication for surgery, multiple procedures, surgeon qualifications or peritonitis at the time of surgery.

Comment: (KC) There are some articles you can read and based on the evidence change your clinical practise with ease. Discontinuing the use of a drug that doesn't work as well as promised, a new approach to improve surgical access or just an understanding that a test may have more false positives than you thought, can be easy to accept. The use of skin staples in gastrointestinal surgery, however, makes me squirm. And for no good reason. The authors have shown it to be quicker and as safe as the method I am comfortable with, yet I cannot imagine adopting this technique tomorrow. Instead I will practise on a cadaver and see for myself. It is a shame that the study did not include a cohort of dogs treated in the same time period, by the same surgeons using accepted suture patterns. This would have added greatly to the conclusions drawn regarding outcomes and safety in my opinion. This paper is a great reminder that a common obstacle to progress is our own perspective, our own academic baggage and that sometimes we need to be objective and leave them behind. And whilst experience is vital in improving clinical skills, we must be ready to embrace new ideas and practises, especially in the face of good clinical evidence.

Reference: *J Small Anim Pract.* 2016;57(11):631-36

[Abstract](#)

Risk factors for coughing in dogs with naturally acquired myxomatous mitral valve disease

Authors: Ferasin L et al.

Summary: A retrospective analysis was conducted on the records of 206 dogs affected by chronic degenerative MMVD to ascertain the relationship between cough and CHF, abnormal radiographic airway pattern and cardiomegaly. In both univariate and multivariate analyses, CHF was not a predictor of cough (OR 1.37; 95% CI 0.72-2.59), but an abnormal radiographic airway pattern (OR 3.65; 95% CI 2.05-6.50) and a radiographic (OR 3.64; 1.90-6.95) or echocardiographic (OR 2.55; 96% CI 1.44-4.54) increase in left atrial size was associated with coughing.

Comment: (RB) Whilst this study is a bit older, I find many veterinarians are still not aware of its findings. In this study, dogs with MMVD that were coughing were assessed for radiographic evidence of CHF and also underwent echocardiography. The authors found no clear association between CHF and coughing, but a strong association between coughing and left atrial enlargement. It was conjectured that the coughing is a reflection of pressure on the left main stem bronchus by the enlarged left atrium. In summary, coughing is not a reliable clinical indicator of heart failure, but usually reflects an enlarged left atrium. Furthermore, in this study the most reliable clinical indicator of CHF was an elevated resting respiratory rate. Respiratory rate and NOT coughing should be used in the clinical monitoring of MMVD patients for the onset of CHF.

Reference: *J Vet Intern Med.* 2013;27(2):286-92

[Abstract](#)

Evaluation of peripheral blood and abdominal fluid variables as predictors of intestinal surgical site failure in dogs with septic peritonitis following celiotomy and the placement of closed-suction abdominal drains

Authors: Guieu LV et al.

Summary: A prospective study was conducted in 26 dogs with septic peritonitis undergoing celiotomy and closed-suction abdominal drain placement to assess the contribution of peripheral blood and abdominal fluid variables in intestinal surgical site failure. Twenty-three dogs had an uneventful recovery while three developed postoperative septic peritonitis. Three days after surgery, the abdominal fluid white blood cell count was lower and the blood-to-fluid white blood cell and neutrophil ratios were higher among dogs with postoperative septic peritonitis versus those with an uneventful recovery.

Comment: (KC) The definitive diagnosis of septic peritonitis can be difficult and ruling it in is often easier than ruling it out. When dealing with postoperative patients this becomes even harder. For example, the presence of free gas on an abdominal radiograph is an easy ticket to surgery, with the big caveat that the patient hasn't recently had abdominal surgery. In recent years, our tools for the diagnosis of septic peritonitis have become more refined with fluid glucose and lactate concentrations providing good support to imaging and fluid cytology. This paper however, indicates that in light of recent surgery all of these tests become less sensitive and specific with the caveat that their sample size was very low. The problem with this article, however, is there is no explanation of how they did in fact identify the dogs with postoperative septic peritonitis that required further surgery. My assumption is the decision to re-operate was surgeon dependent and that holistic clinical evaluation was the difference between those who recovered uneventfully and who that suffered dehiscence. As ever in veterinary medicine there is rarely one golden test that alone can confirm or rule out a condition and this article again shows that all tests should be interpreted in the light of clinical assessment. A larger study is clearly required to try and tease out the differences between these two groups of patients and hopefully this will follow in the not too distant future.

Reference: *J Am Vet Med Assoc.* 2016;249(5):515-25

[Abstract](#)

Comparison of abdominal computed tomography and abdominal ultrasound in sedated dogs

Authors: Fields EL et al.

Summary: This study compared abdominal ultrasound (US) and multidetector helical computed tomography (CT) for lesion detection in 27 sedated dogs. In dogs weighing <25 kg, there was no difference in lesion detection between CT and US; however, in dogs weighing >25 kg, CT detected more lesions ($p = 0.0001$) and more clinically relevant lesions ($p = 0.0277$) than US.

Comment: (RB) This study compared the utility of CT and US in the clinical appraisal of the abdomen of dogs in an attempt to determine whether one modality held an advantage over the other, given the cost differential. The authors found that CT was superior to US in dogs >25 kg and detected more clinically relevant lesions in this group. Simply put, US is comparable in accuracy to CT with the exception of bigger dogs. However, veterinarians should *always* remember that studies such as these are performed by board certified radiologists using state-of-the-art US machines and therefore the sensitivity and specificity of this study cannot be reliably extrapolated to the clinical floor of most general practices. In addition, the real-time nature of US precludes the use of teleradiology or subsequent re-evaluation, whereas CT can be submitted for multiple opinions and interpretation. Consequently, whilst in this study US compared favourably with CT, in many cases CT is likely to be more robust and versatile than US.

Reference: *Vet Radiol Ultrasound* 2012;53(5):513-7

[Abstract](#)

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