Companion Animal Research Review™

Making Education Easy

Issue 6 – 2018

In this issue:

Abbreviations used in this issue
CAD = canine atopic dermatitis
CPV = canine parvovirus
FIC = feline idiopathic cystitis
SC = subcutaneous
UTI = urinary tract infection

Welcome to the sixth issue of Companion Animal Research Review.

Just as the summer weather returns as a balm to warm our hearts, Research Reviews returns as a tonic to invigorate your minds. And in deference to the itchy season, I have chosen four studies of a dermatological nature as a feature of this issue. As always, we have put a hypertext link to the article abstract, summarised the key findings, and attempted to provide some background, criticism, and relevance, which is the height of patronisation to suggest you need me to suggest the relevance of atopic dermatitis. However, I hope you find the window dressing to these exhibits in some way helpful, and in no way distracting. We are as before, as eager as Labrador puppies to hear comments, criticisms and suggestions for future issues of Companion Animal Research Review, and we could not be more hopeful that you find this useful, or at least enjoyable.

Kind regards,

Associate Professor Nick Cave
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Research Review thanks Zoetis for their sponsorship of this publication, and their support for ongoing education for animal health professionals.

Diluted sodium hypochlorite (bleach) in dogs: antiseptic efficacy, local tolerability and *in vitro* effect on skin barrier function and inflammation

Authors: Banovic F et al.

Summary: This study assessed the *in vivo* antibacterial effect of topical application of diluted bleach 0.05% and *in vitro* effects on skin barrier lipids and keratinocytes. Primary keratinocyte cell viability after diluted hypochlorite 0.005% and 0.01% was reduced by 10%; as was the induction of inflammatory genes chemokine ligand-2 (CCL2; p = 0.015) and thymus and activation-regulated chemokine (TARC/CCL17; p = 0.032). Skin lipid ceramide and non-ceramide fractions in stratified epidermal constructs exposed to hypochlorite 0.05% for 17 days were not affected. Topical hypochlorite at 0.05% and tap water applied to both sides of the thorax of four healthy dogs were well tolerated without evidence of skin irritation. The reduction in bacterial counts within 20 min of diluted bleach application was not significant (p = 0.06).

Comment: As new therapies emerge, there is always the risk that we forget the efficacy of the old ones. The excitement that accompanied the emergence of antibiotic therapy after the Second World War, understandably decreased the use of conventional antisepsis. In both human and veterinary medicine we have had to be reminded of both the dangers of over-reliance on antibiosis and of the efficacy of more humble measures. Hypochlorous acid, or bleach, could well be considered a humble and overlooked treatment, and one that is not often considered for topical use. Lest we forget, neutrophils produce large amounts of hypochlorous acid following activation, and of the oxidants produced by neutrophils, hypochlorous acid is the fastest acting and currently thought to be their primary bactericidal compound. We ignore the lessons of evolution at our peril, and perhaps it should not surprise us if the chemical has other physiological effects. In this study by Banovic et al, the authors utilised an impressively thorough, thoughtful, and contemporary *in vitro* cell culture approach for such an old fashioned molecule. In addition to the known bactericidal effects, they found that hypochlorous acid inhibits the expression of two key inflammatory genes: CCL2 and CCL17 which recruit macrophages and T lymphocytes respectively, and it does so at a concentration that does not produce marked cell death. Despite the bactericidal and immunomodulatory effects, the concentration tested did not significantly reduce the production of key ceramides, the lipids that corneocytes secrete to form a critical component of the epidermal barrier. It would certainly not be the only compound produced by leucocytes that has more than one edge to its blade. Thus, the use of dilute bleach baths may act as both anti-inflammatory and anti-bacterial, and its use is a worthy therapy for superficial pyoderma, especially that caused by atopic dermatitis. Old it may be, but as we fail to create new antibiotics and misuse those we have, we do well to learn from the accreted wisdom of the immunological arms race of evolution.

Reference: Vet Dermatol. 2017;Sept 14 [Epub ahead of print]

Abstract

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Evaluation of the correlation between Scoring Feline Allergic Dermatitis and Feline Extent and Severity Index and skin hydration in atopic cats

Authors: Szczepanik MP et al.

Summary: This study examined the correlation between clinical scores measured from the Scoring Feline Allergic Dermatitis (SCORFAD) and the Feline Extent and Severity Index (FeDESI), and skin hydration of European short hair cats (n = 18) with presumed atopic dermatitis. SCORFAD score was positively correlated with skin hydration in the axilla, thorax and forelimb, and for the FeDESI with axilla and lumbar sites. FeDESI was negatively correlated (r = -0.47) with skin hydration in the pinna.

Comment: The last 10 years or so have heralded a change in the understanding of canine atopic dermatitis (CAD), from the perception of an immunological disorder with a cutaneous manifestation, to one where the defect is largely, perhaps solely a cutaneous one, with little reason to suspect a systemic immunological abnormality. Interest has focused on gene variants that affect epidermal cell adhesion, nutrients that affect epidermal cell lipid production, the effects of increased colonisation by bacteria and yeast, and factors such as dust mite proteases that damage the stratum corneum. What links all those disparate components to the pathogenesis of CAD is captured by one word: barrier. A defective barrier allows increased absorption of allergens and inflammatory microbial components, and increased evaporative loss of water. As such, the objective assessment of the cutaneous barrier integrity allows the assessment of disease risk in immature animals, grading of severity, monitoring of response to therapy, and an experimental tool for comparing treatments. The two most widely used methods for assessing cutaneous barrier integrity are the measurement of trans-epidermal water loss (TEWL), and of conductance/capacitance by corneometry. TEWL uses a heated chamber held against the skin into which water evaporates, changing the conductivity of the air trapped inside. The poorer the barrier, the more water evaporates, and TEWL has been shown to correlate with the severity of CAD. The electrical conductance or capacitance of the epidermis correlates reasonably well with the water content, and both TEWL and corneometry have been shown to be fairly reliable when used under highly standardised conditions (Hester SL et al. 2004). Atopic dermatitis in cats, once thought to be a fanciful rarity, is now a common diagnosis for pruritic dermatitis. However, the understanding of its pathogenesis is inchoate, and is as marked by its differences as its similarities to CAD. This study by Szczepanik et al., is the first to have demonstrated an association between the severity of atopic dermatitis in cats and skin hydration as determined by corneometry. Interestingly, although the severity of dermatitis was associated with reduced hydration of the pinna, it was associated with increased hydration in the axilla, thorax and forelimb. The authors suggested that licking behaviour may have increased the water content of those regions, and hence the inside of the pinna was not "protected". That is, at least, a plausible explanation. The alternative is that it may be another example of a difference between cats and dogs.

Reference: Vet Dermatol. 2017;Sept 13 [Epub ahead of print]
Abstract

A double-blinded, randomized, controlled, crossover evaluation of a zinc methionine supplement as an adjunctive treatment for canine atopic dermatitis

Authors: McFadden RA et al.

Summary: This study compared the use of zinc methionine, essential fatty acids (EFA) and biotin product (zinc supplement) to an EFA and biotin product (control) in 27 client-owned dogs with chronic CAD receiving ciclosporin or glucocorticoids. Among dogs receiving ciclosporin plus zinc supplement for 8 weeks, seven (44%) had a reduction in Canine Atopic Dermatitis Lesion Index (CADLI) from 11.9 to 6.0 (p = 0.0002) without a change in the pruritus Visual Analog Scale (VAS). In those receiving glucocorticoids plus zinc supplement for 8 weeks, 6 (55%) experienced a reduction in CADLI from 10.9 to 5.0 (p = 0.0043) and the pruritus VAS decreased from 7.4 to 3.2 (p = 0.0166).

Comment: The second paragraph of the publication by McFadden et al., begins with the sentence, *"Zinc is a constituent or activator of at least 200 known enzymes, including those important for skin and wound healing, cell replication, protein synthesis and immunocompetence"*. I quote that entirely, because it is one of the few sentences in the introduction and discussion that didn't make my own skin crawl, then want to stand, walk, and run its first half marathon. Chronic, incurable, relapsing diseases have long been grist to the mill of those who peddle unproven remedies, often accompanied with highly implausible claims of efficacy. Assertions in support of probiotics and nutraceuticals often lurk on the fringes of belief, whilst claims for herbal remedies cross over into incredulity, and supplication in support of homeopathy is deep into the territory occupied by fairies and wizards. But it pains me when fundamental nutrition is treated with the same lack of intellectual rigor as is given to alternatives to medicine. The association between zinc deficiency and dermatopathies has been recognised for many decades, and zinc is relatively concentrated in the skin, notably in the epidermis. Given the ubiquity of zinc metalloproteins it is not surprising that the continual turnover of the epidermis makes it an organ that manifests deficiency early. Zinc deficiency impairs the proliferation, differentiation, and survival of corneocytes and hence delays wound healing. In addition, corneocytes in zinc-deficient animals take on an inflammatory phenotype, secreting cytokines and chemokines. Hair follicles cease to produce hair (telogen effluvium) and alopecia is a common finding. All of these features would be expected to greatly exacerbate atopic dermatitis. In the study by McFadden et al., the authors aimed to test the hypothesis that clinical signs of atopic dermatitis would be improved in dogs following supplementation with a product that contains zinc, methionine, biotin, and the n-3 polyunsaturated fatty acids (PUFAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The study was designed as a placebo-controlled, blinded crossover trial, and in that respect was of a high quality. However, if you were to run a trial that evaluates the effects of a nutrient on a disease, wouldn't you want to control the amount of that nutrient that the animals ate? Yet amazingly, the diets of the dogs were not controlled, and at no point in the study did the authors consider, or even mention the intake of zinc from their diets. The zinc content of commercial diets varies enormously, and there is no established safe upper limit for dogs, and the amount "supplemented" was approximately 25% that consumed in an average premium diet. So if some dogs respond while others do not, would you not be interested in the amount present in their basal diet? The uncritical suggestion that supplementation was effective for some but not others is more characteristic of motivated reasoning than careful self-critique. While studies like these continue to be published without appropriate criticism, the esteem of nutrition as a scientific discipline is tarnished. Knowing that the supplement manufacturer funded the study, and that one of the company's representatives was a coauthor should not, in itself, be reason for cynicism, but in light of the flaws, it adds an itching sense of skepticism.

Reference: Vet Dermatol. 2017;Jul 23 [Epub ahead of print]
Abstract

The frequency of urinary tract infection and subclinical bacteriuria in dogs with allergic dermatitis treated with oclacitinib: a prospective study

Authors: Simpson AC et al.

Summary: This prospective study in 55 dogs with allergic dermatitis examined the frequency of urinary tract infection (UTI) and subclinical bacteriuria in dogs with allergic dermatitis receiving the selective Janus kinase (JAK) inhibitor oclacitinib. None of the dogs developed UTI while receiving oclacitinib over a mean of 195 days; two dogs developed self-limiting abnormal urinary tract signs without clinical signs of UTI.

Independent commentary by Nick Cave.

Nick Cave is an Associate Professor in small animal medicine and nutrition at Massey University. He graduated from Massey University (NZ) in 1990 with a BVSc, and worked in general practice for 6 years until 1997, when he returned to Massey for a residency in small animal internal medicine, and attained membership in the Australasian College of Veterinary Scientists by examination, and graduated with a Masters in Veterinary Science in 2000. In 2004 he moved to the University of California, Davis, where he attained a PhD in nutrition and immunology. At the same time, he completed a residency in small animal clinical nutrition, and became a diplomate of the American College of Veterinary Nutrition by examination in 2004. In late 2005, he returned to Massey University to lecture in small animal medicine and nutrition. He is a founding member of the WSAVA Global Nutrition Committee, and a founding board member for the Massey University Working Dog Centre.

Comment: Not long after the JAK inhibitor oclacitinib (Apoquel®) became available in the US, Zoetis published a report of its long term (15-672 days) use in 247 dogs (Cosgrove SB et al. 2015). In that retrospective study the most common clinical signs that developed in the dogs during treatment were signs of UTI/cystitis (11.3%), vomiting (10.1%), otitis (9.3%), pyoderma (9.3%) and diarrhoea (6.1%). The rates of otitis and pyoderma were consistent with the study population of dogs with moderate-to-severe atopic dermatitis. The incidents of vomiting and diarrhoea may not be greater than the background incidence of those signs in dogs, but without a control population, it is not possible to be certain. However, the incidence of apparent UTI was more concerning. In humans, JAK inhibitors increase the incidence of clinically significant UTIs, so it was clearly justifiable to conduct a prospective study of UTIs in dogs treated with oclacitinib. The study by Simpson et al., collected urine from 55 dogs at baseline, and again after 58-230 (mean 195) days of treatment. Bacteria were not isolated from any of the 55 end-point urine samples, including two dogs that developed pollakiuria or incontinence during treatment. The conclusion was that treatment with oclacitinib is not expected to lead to UTI. So does the conclusion of this prospective study supersede the conclusion of the previous retrospective study of an 11% incidence? If the true incidence of UTI from treatment is 11%, then a study that includes only 55 dogs will have a 95% confidence interval for the incidence of 0-21%. Or put another way, with an incidence of 0% and a sample size of 55, one is 95% confident that the true incidence is between 0 and 21%. Thus this prospective study cannot conclude that the proportion of UTIs was significantly different from the previous study. However, the concept of asymptomatic bacteriuria is increasingly being investigated. A large population estimate has not been made, but biased sample estimates of asymptomatic bacteriuria range from 8.9% in healthy females (Wan SY et al. 2014) to 13% with increased risk for morbidly obese dogs (Wynn SG et al. 2016). Thus, the incidence of positive cultures in the present study, at worst, falls within that range, but at best probably supports the conclusion that there is no evidence to suspect that oclacitinib treatment increases the risk of either subclinical or clinical bacteriuria.

Reference: Vet Dermatol. 2017;28(5):485-e113
Abstract

Evaluation of mortality rate and predictors of outcome in dogs receiving outpatient treatment for parvoviral enteritis

Authors: Sarpong KJ et al.

Summary: This retrospective case series and case-control study examined mortality rates and prognostic factors in 130 dogs receiving outpatient treatment for parvoviral enteritis. A total of 97 (75%) dogs survived for ≥3 days after initial parvoviral enteritis diagnosis; 33 (25%) dogs did not survive. Chihuahuas, German Shepherds, pit bull–type dogs, and males were over-represented. Dogs receiving a caloric supplement every 2-4 hours had a mortality rate of 19% (16/85); most also received subcutaneous (SC) fluids, an antiemetic, and antimicrobials.

Comment: In Issue 3 of Companion Animal Research Review, I mentioned the blemish on society that is the anti-vaccine movement, and discussed the potential for the emergence of vaccine-resistant subtypes of canine parvovirus (CPV) in New Zealand (Ohneiser Sa et al. 2015). Both of those are threats that increase the risk of CPV enteritis in dogs. However, at the present time we do not have a vaccine-resistant subtype in New Zealand, and although the great majority of dogs with CPV enteritis we currently treat are from un- or inadequately vaccinated dogs, their owners are usually critically short on cash, though usually not short on compassion and concern. The prognosis for CPV enteritis when managed ideally is very good, with up to 75-96% recovery rates reported in large case series. However, ideal management is costly, involving intravenous fluids, parenteral antibiosis, anti-emesis, enteral feeding, monitoring, combined with appropriate isolation and protective clothing to prevent dissemination of the virus. We have all endured the difficult conversations with clients who cannot afford treatment, and most of us have pared-down treatment options for "budget cases". But what of outpatient management? Is it reasonable, or even ethical to attempt management of CPV enteritis on an outpatient basis? In this study by Sarpong et al., we have the first reported series of CPV cases managed as outpatients by a primary accession practice, and the results go a long way to answering those questions. Almost all (95%) were managed with SC fluids administered by the owner, 95% were given maropitant, and 65% were given an oral nutritional supplement (Nutri-Cal®, Vetoquinol). Other treatments used with variable frequency included sucralfate, cefovecin, amoxicillin, metronidazole and pyrantel. A total of 130 dogs had sufficient data for inclusion, and the overall survival rate was 75%. No signalment variable was associated with survival, and although 25% had received at least one vaccination, it was not associated with survival. Of all treatments, including the treatment category "any antibiotic treatment", only the oral nutritional supplement was significantly associated with survival (81% survival with vs 62% without). With only seven patients not receiving SC fluids (who all lived), there were too few to determine if there might have been a small benefit, but in this case series any effect was not massive. All owners were instructed to feed any food that the dog would accept, or to force feed small amounts of canned or baby foods. Despite that, there was a significant effect of dispensing the oral supplement. The supplement is a mixture of simple carbohydrate, oil, a tiny amount of hydrolysed protein, and various vitamins and minerals. At the suggested dose rate it will provide between 20 and 40% of resting energy requirements. No data was available on compliance, fluid administration rate, or feeding success with other foods, and a study of this nature is very limited in its ability to reduce confounders. Whether the supplement in question has truly magical qualities, or that dispensing food with instructions is more likely to result in enteral alimentation, which is so important to recovery, is unknown. None-the-less, this is the first series to describe outpatient mortality, and the conclusions are clear: it is a reasonable alternative for those who cannot afford hospitalisation, and that attention to enteral nutrition, even of very modest intakes, is essential.

Reference: J Am Vet Med Assoc. 2017;251(9):1035-41
Abstract

Risk factors for death in dogs treated for esophageal foreign body obstruction: A retrospective cohort study of 222 cases (1998-2017)

Authors: Burton AG et al.

Summary: This study assessed mortality risk factors and overall outcomes in 222 dogs with oesophageal foreign body obstruction. Most foreign material was osseous (81%), with the distal oesophagus the most common location (49.5%). Risk of death was not associated with duration of clinical signs (OR 1.08; 95% CI 0.99-1.17). Entrapment was treated by endoscopy in 91.8%, surgery after endoscopy in 5.9% and repeat endoscopy after surgery was declined in 2.3%. The in-hospital case fatality rate was 5%; risk of death was higher with surgery (OR 20.1; 95% CI 3.59-112.44; $p = 0.001$), and all five dogs undergoing endoscopy after surgery was declined died. In-hospital risk of death was increased by increased numbers of post-procedural complications (OR 3.44; CI 2.01-5.91; $p < 0.001$), oesophageal perforation (OR 65.47; CI 4.27-1004.15; $p = 0.003$), and post-procedure oesophageal haemorrhage (OR 11.81; CI 1.19-116.77; $p = 0.04$). Oesophageal strictures occurred in 2.1% of survivors.

Comment: In the absence of a national disease surveillance system we do not have any means to easily determine if the incidence of disease related to bone ingestion has increased. A very rough perusal of records at the Massey University Veterinary Teaching Hospital does not suggest a dramatic increase, however, the experience at Veterinary Specialist Group in Auckland suggests it may have been in that region (NZ Herald Article 2017). There are several products available in New Zealand that represent a risk for oesophageal obstruction, and none more so than small meaty bones such as veal neck bones. Dental fracture, vomiting, colitis, and constipation may be the most common problems seen with bone ingestion by dogs, but oesophageal obstruction is the most common serious condition. Several case series of oesophageal obstruction have been published over the years, and although the study of 222 cases by Burton et al., is the largest, it holds few surprises, and has not opened any doors to enlightenment that were previously closed to us. The principle difference to the study, is that the authors did not exclude data from any case that was presented with an oesophageal obstruction, whereas previous case series had excluded cases that had died prior to recovery from anaesthesia, or cases subjected to surgical removal following a failed attempt at endoscopic retrieval. Thus, in the present study the authors were able to more accurately assess the true risk of death, which was 5%. Endoscopic retrieval was attempted in all cases, and was successful in 92%, whereas surgery was required in the remaining 8%, which when declined, was fatal in all cases. Similar to previous studies, oesophageal stricture formation is surprisingly uncommon, occurring in less than 3%, which likely reflects the non-circumferential nature of the lesions induced by the foreign material. The two most common breeds in this study from Queensland were Labradors and West Highland White Terriers. Westies are over-represented amongst cases we have seen at Massey, and they feature as one of the dominant breeds in almost all of the previous case series. The ratio between oral cavity and oesophageal lumen diameter may explain their status, or it may be as a colleague once described them to me, as a small dog that thinks it's a big dog. Also consistent with previous studies, only 16% had the obstruction proximal to the thoracic inlet, and plain cervical or thoracic radiographs were diagnostic in almost every case. What can we take home from this? Firstly, a reminder of the condition. We might see a hundred cases of vomiting to one case of regurgitation, and it is easy to forget to differentiate between them. Secondly, the success of endoscopic retrieval and the lower survival rate when removal is attempted surgically. Finally, full clinical recovery occurs in the great majority, and stricture formation is a very serious, but thankfully a very uncommon sequelae. In that particular case series, I will leave you to guess the cause of obstruction in 81% of cases.

Reference: J Vet Intern Med. 2017;Oct 14 [Epub ahead of print]
Abstract

Epidemiological study of feline idiopathic cystitis in Seoul, South Korea

Authors: Kim Y et al.

Summary: A South Korean case-control cohort study examined risk factors for feline idiopathic cystitis (FIC) in cats (58 FIC and 281 controls) living in a primarily indoor environment (90% had no outdoor access). Estimated FIC prevalence was 1.77% (95% CI 1.36-2.18). A multivariate logistic regression model identified five variables associated with FIC: males versus females (OR 2.34-fold; 95% CI 1.18-4.62; p = 0.015), no vantage points vs vantage points (OR 4.64; 95% CI 2.05-10.49; p < 0.001), apartment versus house (OR 2.53; 95% CI 1.30-4.93; p = 0.006), cohabiting with other cats versus living alone (OR 3.16; 95% CI 1.61-6.22; p = 0.001), non-clumping versus clumping litter (OR 2.62; 95% CI 1.38-4.96; p = 0.003).

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Comment: New Zealand has long been amongst the nations with the highest cat owning rates in the world, which gives credence to the claim we are a cat-loving nation. Nonetheless, the days of unrestricted access of pet cats to the outdoors of New Zealand are surely numbered. In the early 1990's, very few owners housed their cats indoors, and indoor confinement was regarded as a source of stress. In fact a case-controlled study of FIC by Jones BR et al. 1997, undertaken between 1991-1993, found that indoor confinement was a significant risk factor. Several other subsequent studies have similarly found indoor confinement as a risk factor. But what exactly is the causal link between indoor confinement and FIC? A study specifically of indoor-housed cats in urban Ohio emphasised the presence of anxiety or aggression related behaviours as being associated with FIC; however, it did not identify any environmental risk factors (Buffington CAT et al. 2006). The authors concluded that "*lower urinary tract signs in indoor-housed cats may be more closely associated with cat-related factors than with demographic or environmental factors*". Conclusions such as that should be viewed with some scepticism, since the ability to identify risk factors is only as good as the questions asked. In that particular study, questions were limited to variables related to feeding, other animals, and litter boxes, and did not include any descriptive data of the cat's physical environment. Thus this study by Kim et al., being only the second study of FIC in indoor-housed cats, is an important addition to the literature. The study was conducted in South Korea, where the large majority (91% in this study) of cats are confined indoors, and the authors collected descriptive data about the physical environment the cats were housed in, as well as the usual behavioural, feeding, and owner related variables. The final multivariate analysis revealed some familiar risks including male sex and multiple cat households. The novel findings were that a lack of a vantage point for rest or surveillance, and apartment dwelling, were strong risks. The authors suggested that since size of the dwelling was not a risk, apartment dwelling was a risk because in South Korea it is less likely to provide visual stimulation than life in a house. So as we move into an era of increased indoor cat housing in New Zealand, we must pay attention to the construction of environments for the cats that provide unstressful, but visually stimulating lives, with the avoidance of obesity and the ready availability of regularly cleaned toileting facilities. And on the face of it, that sounds enough to relax anyone's urethra.

Reference: J Feline Med Surg. 2017;Sep 1 [Epub ahead of print]
Abstract

Effects of maternal investment, temperament, and cognition on guide dog success

Authors: Bray EE et al.

Summary: To address the question of how important early life experiences are to adult behaviour and the contributions of cognitive skills ("intelligence") and temperament to successful outcomes, these researchers followed 98 puppies from birth to adulthood to determine predictors of success in a guide dog training programme. High levels of maternal behaviour were associated with reduced likelihood of success and maternal nursing styles requiring greater effort by puppies produced more successful offspring. Programme failure was also associated with an inability to quickly solve a multistep task and high levels of perseveration.

Comment: I have often joked, with only tip of tongue in cheek, that the only things I am confident that I am truly responsible for in my kids are their character flaws. The best a parent can do, it seems to me, is provide an environment they can flourish in, and to try not to screw them up. The alternative view – that we can take pride in our offspring because they are the products of our parental endeavours – chips away at their autonomy and robs them of some feeling of pride in themselves. The more smug parents frequently want to believe they are both self-made autonomous individuals themselves, *and* that the success of their children is the direct result of their excellent parenting. Not so much having and eating cake, as an industrial scale patisserie-and-pastry-eating service. But how much influence do early life experiences have on behaviour in adulthood? As messy as observational studies in humans are, there is consensus that early experiences do have lasting effects. Early exposure to significant stress has lasting effects on stress responses in various species. More subtly, children that experience more negative life events (e.g., parents divorcing or losing their jobs, close friends moving away) have lower self-control, and increased symptoms of child and adolescent psychopathology (Duckworth AL et al. 2013). Though such effects seem to be reliable, they are small, non-determinative, and surely very difficult to study. In this paper by Bray et al., the authors suggest that Guide dogs are an excellent model for studying those effects. Several studies have observed that puppies more intensely nurtured by their mothers have lower scores of anxiety and fear. Successful completion of guide dog training is a measure of an excellent temperament, obedience, attentiveness, problem solving, and flexibility in cognition. Thus the authors scored the maternal styles of 21 bitches and followed their litters over 2 years to either completion of or rejection from the training program. Dogs were categorised according to their scores in the three measures that most strongly predicted outcome: level of maternal behaviour, performance in a problem solving task, and speed to vocalise when presented with a novel object as a young adult. Dogs in the top third had an 85% chance of success, whilst those in the bottom third had a 47% chance of success. Whilst it was hardly surprising that the top third category were good problem solvers and slow to vocalise in the presence a strange object (a display of anxiety), it was surprising that the top third category had the lowest level of maternal behaviour. Those mothers were less vigilant, were more likely to suckle while standing up rather than lying down, and spent less time in proximity to and interacting with their puppies. The more attentive mothers, what we would be excused for calling "better mothers", had less successful litters. The horrors of early childhood neglect have long been recognised, but if we can learn from dogs, as the authors suggest we can, it seems that excessive parenting raises individuals who have not benefited from experiences of dealing with stress and autonomous problem solving. Which means I may have some justification to my perception of my role as a parent, and has allowed me to add something else to the list of ways I may have screwed my kids up.

Reference: Proc Natl Acad Sci U S A. 2017;114(34):9128-33
Abstract

Critically appraised topic on adverse food reactions of companion animals (4): can we diagnose adverse food reactions in dogs and cats with *in vivo* or *in vitro* tests?

Authors: Mueller RS and Olivry T

Summary: This systematic review and meta-analysis assessed *in vivo* and *in vitro* tests used to diagnose adverse food reactions in dogs and cats. In total, 22 articles and conference proceeding abstracts provided data on serum tests for food-specific IgE and IgG, intradermal food antigen testing, lymphocyte proliferation tests, faecal food-specific IgE, and patch, gastroscopic, and colonoscopic tests for adverse food reactions. Serum food-specific IgE and IgG testing had low repeatability and highly variable accuracy in dogs. In cats, food-specific IgE testing had low accuracy. Lymphocyte proliferation tests were more accurate, but more difficult to perform and remain a research tool. All other tests were evaluated only in individual studies with small animal numbers. Negative patch test reactions had very high negative predictability in dogs and inform elimination diet selection. Gastroscopic and colonoscopic testing and food-specific faecal IgE or serum IgG measurements were less useful.

Comment: Here's a question that needs to be answered: what percentage of cases that require a dietary elimination and challenge trial in your practice ever actually successfully complete one? Am I being naively harsh to suggest it might be very small? The availability of effective hydrolysed diets largely expunged the need to worry too much about novelty, but how many clients want to put their pets and themselves through properly conducted single protein challenge trials? Does anyone want to study that? It is not for want of understanding that we don't always practice "perfect diagnostic reasoning", it is want of time, compliance, and owner patience that steers us away from that diagnostic path. So it is unsurprising that *in vitro* allergy tests have the appeal of the last few sheets of paper in a public toilet: they provide relief and comfort, but with them the worry they won't quite be enough. One of the most frequent questions I am asked is "can you diagnose food allergy from a blood test?". This review paper, by twin towers of veterinary dermatology, is the definitive answer to that question. Review papers are often enjoyable and untaxing reads, where the conclusion is merely a satisfying culmination of the understanding you accrete along the way. This review, I suspect, will be very heavily cited, but rarely read. After all, for most, it's the punch line and not the set up that the audience wants for this trope. However, at fewer than 2000 words, the authors could hardly be accused of being discursive and straying from the central theme. And the theme is that patch testing has reasonable negative predictive utility in dogs, and lymphocyte proliferation may have excellent positive predictive power, though only one study has evaluated that and it is not a commercially available test. Sadly, intradermal and serum antibody testing are both insensitive and poorly specific in both dogs and cats. One criticism of their analysis was that they did not attempt to weight included studies in order to produce a true meta-analysis. Some of the included studies had very low numbers, and thus had a disproportionate effect on their overall estimated accuracy ranges. As a result, I do take issue with their statement that antibody testing showed "highly variable accuracy", which is the phrase you might use during the orientation week toga party to describe the behaviour of male students at the urinal. Nonetheless, whilst the overall figures of sensitivity and specificity might not themselves be either accurate or precise, it would not change their conclusion one iota. And the punch line could not be more pugilistic: "At this time, the best diagnostic procedure to identify adverse food reactions in small animals remains an elimination diet with subsequent provocation trials." Bugger.

Reference: BMC Veterinary Research 2017;13:275
Abstract

Evaluation of learning curves for ovariohysterectomy of dogs and cats and castration of dogs

Authors: Freeman LJ et al.

Summary: This retrospective study examined learning curves in 4th-year veterinary students undertaking canine and feline ovariohysterectomy and castration in dogs (n = 2945). Surgery time decreased with increasing student experience in a nonlinear manner for castration of adult or paediatric dogs and ovariohysterectomy of paediatric dogs and adult or paediatric cats. For ovariohysterectomy of adult dogs, surgery time decreased in a linear manner as experience increased.

Comment: On the 28th October this year, or "Mentoring Day" in Kansas, the Pratt Tribune newspaper celebrated the efforts of local veterinary clinics to enthuse high school students, with the arousing headline, "Students get first hand job experience". New veterinary graduates are usually greeted with less affectation. In fact it would be fair to say that there was a wide range of experiences in our inaugural employment, from supportive and understanding to neglectful and abusive. Some of that range is explained by the employer, and some by the graduate. A perennial source of employers' frustration is the time it takes for a new graduate to perform routine surgery. How long does it take for a new graduate to spay a bitch? "Too long" might be the answer of cynicism. But the actual answer probably has more to do with the number of surgical opportunities they had as a student than anything relating to ability. So a more informative and relevant question would be, "How many procedures does it take to be fast enough?". In the study by Freeman et al., from the teaching hospital at Purdue, Indiana, the authors timed a staggering 2945 neutering procedures by 88 final year veterinary students. The average surgical time for the first adult bitch spay was approximately 1 hour. Surgical time decreased linearly with experience, such that surgical time was halved after approximately 12 procedures. For adult cat spays, the average surgical time for the first procedure was approximately 37 minutes. Surgical time decreased non-linearly and plateaued at around 20 minutes after 10 procedures. The findings were similar for castrations. The students performed all their surgeries during 3 weeks with close supervision from experienced surgical teachers, including an experienced practitioner who completed adult bitch spays in 11 mercurial minutes, and cat spays in a scorching 6 minutes. Well I was impressed anyway. But are 12 supervised surgical experiences over 3 weeks the same as 12 spread over a longer time period? And what if only the first one or two are supervised? Most Massey graduates will leave university with two spay procedures, some with up to four, and those who participate in the neutering clinic rotation in the Pacific Islands may be lucky enough to do more than 20. From this study it is clear that our term "learning curve" is a good one, and that graduates not fortunate enough to have experienced several supervised procedures will benefit from continued supervision, but can be expected to improve rapidly. The Perdue students certainly deserved a hand, and even a job. Just not both together.

References: J Am Vet Med Assoc 2017;251:322-32
Abstract