Companion Animal Research Review™

RESEARCH REVIEW 10 YEARS
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Issue 3 – 2016

In this issue:

Abbreviations used in this issue

CPV-2 = canine parvovirus type 2
IV = intravenous
MLV = modified live viral
PCR = polymerase chain reaction

Welcome to the third issue of Companion Animal Research Review.

As promised, and in response to requests, this issue of Research Review is a parochial potpourri of science published by researchers and practitioners in New Zealand, or, in one case, about New Zealand, all within the previous 12 months. Whilst the great majority of veterinary science is applicable to practice in New Zealand and across the globe, not all that is pertinent to us here is applicable elsewhere. Thus the collection below includes some very provincial publications, such as the description of feline blood types in NZ, and the survey of vaccination policies in this country. We have also included publications that describe phenomena here but have lessons for elsewhere, such as the description of canine parvovirus in this country. However, it also includes research that, whilst conducted by researchers based here, is as cosmopolitan as anything else you might read, including the assessment of topical methimazole, and the histological description of Bulldog soft palates. Five of the 10 articles were published in the *New Zealand Veterinary Journal*, but it is suspected that many recipients of the journal don't have the time to read through the journal to pick out what is relevant, interesting or useful. So, as with previous issues, it is hoped that you will find this quintessence of veterinary science by and for New Zealanders illuminating. And remember, we appreciate your feedback, if only to assure us this is read, or even that it is useful, or – dare we even dream – enjoyed.

Kind regards,

Dr Nick Cave
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Investigation of cell-free DNA in canine plasma and its relation to disease

Authors: Burnett DL et al.

Summary: This group of researchers measured cell-free DNA in canine plasma by fluorometry without prior DNA extraction in a cohort of 97 client-owned diseased, hospitalised dogs, and in a clinically normal population comprising 9 client-owned dogs presenting for 'wellness screens' and 15 colony-owned Harrier Hounds. The effects of *ex vivo* storage conditions were evaluated in plasma from 2 clinically normal dogs. In all other dogs, plasma was separated within 2 h of collection. cfDNA concentrations were significantly higher in the plasma of the diseased dogs compared with plasma from clinically normal dogs ($p<0.001$). When disease severity was categorised according to the American Society of Anesthesiologists (ASA) status, increasing severity of disease correlated with increasing cfDNA concentrations ($p<0.001$). Dogs that did not survive to discharge had significantly higher cfDNA concentrations than survivors ($p=0.02$).

Comment: When searching for a marker of over-exertion and subclinical injury in working dogs, I came across a description of DNA floating around in plasma not contained within cells. This "cell-free DNA" (cfDNA) increases in concentration in plasma after very heavy exercise in humans. It also increases in diseases associated with inflammation, cell death, and increased cell turnover. Although the exact source of the DNA has yet to be determined, the great majority does not seem to be derived from circulating cells. In fact, DNA from solid tumours can be identified, as can foetal DNA in the plasma of a pregnant female. A couple of previous studies in dogs appeared to demonstrate that there was little association between different diseases and the concentration of plasma cfDNA, but those studies used methods to purify the DNA that lose the majority in the process. We showed that using a very simple and cheap method, you can quickly quantify cfDNA, and that the concentration correlates quite strongly with the severity of several diseases. The technique has been used now in cats, horses, and dolphins, and may be of use for the beach-side prognostication of stranded whales. However, it is unlikely that the simple quantification of cfDNA is going to be an in-clinic assay. The dogs in our study that had increased cfDNA were obviously sick, and a 5-year-old with a plastic Fisher Price veterinarian's kit could have correctly separated the healthy from the infirmed. However, we argue that this study alerts us to the possibility that in plasma, there may be a hitherto unopened mine of diagnostic gold, and that more detailed descriptions of the DNA fragment sizes or sequences may yield useable information. And if nothing else, it emphasises that there is so much more to cellular and systemic physiology than what we learned at vet school.

Reference: Vet Q. 2016:1-25
Abstract

Community attitudes and practices of urban residents regarding predation by pet cats on wildlife: an international comparison

Authors: Hall CM et al.

Summary: These researchers sought to understand international differences in attitudes and husbandry regarding restrictions and desexing of pet cats, as well as interactions between cats and wildlife. They administered a common survey to cat owners and non-owners in Australia, China, Japan, New Zealand, the UK and the USA, to compare the attitudes of both groups in each country to questions such as the desirability of legislation, support for desexing and confinement, and the level of concern over predation by pet cats. The survey was completed by 1720 respondents. In all 6 countries, non-owners were more likely than owners to agree that pet cats killing wildlife were a problem in cities, towns and rural areas. Agreement amongst non-owners was highest in Australia (95%) and New Zealand (78%) and lowest in the UK (38%). Irrespective of ownership, over 85% of respondents from all countries except China (65%) valued wildlife in cities, towns and rural areas. Non-owners were more supportive of cat legislation than owners everywhere other than Japan. Australian non-owners were the most supportive (88%), followed by Chinese non-owners (80%) and Japanese owners (79.5%). The UK was least supportive (non-owners 43%, owners 25%). Many Australian (62%), New Zealand (51%) and Chinese owners (42%) agreed that pet cats killing wildlife in cities, towns and rural areas was a problem, while only 12% of owners and 38% of non-owners in the UK agreed.

Comment: In the last few years, we have seen an increasing number of media discussions surrounding the unfortunate Venn diagram of a) a high rate of cat ownership, b) a large number of owners allowing free outdoor access to their cats, and c) an increasingly endangered endemic fauna. NZ is not alone in having a vociferous community advocating for wildlife preservation, but several studies in different countries have suggested that there might be differences between the countries in the attitudes of their populations to pet cat management. Those differences between countries are important to understand if we are to learn from the successful experiences of others. However, comparisons between studies are difficult when methodologies differ, and thus this study, which surveyed cat owners and non-owners in several countries, is important. The confinement to urban middle-class respondents was a possible source of bias, though the authors argued they represent those most likely to be politically engaged. Of greatest significance to us in NZ was the startling difference in almost all respects between Australia and NZ, or more specifically, Auckland and Sydney. Whereas 67% of cat owners in NZ allow their cats free outdoors access, only 8% in Sydney do. The large rate in NZ was comparable with the UK (64%), where respondents were the least supportive of introducing legislation or restrictions. Unfortunately, the study did not elucidate the reasons why Australian cat owners are more inclined to restrict their cats indoors, although municipal curfews, concern for wildlife, and concern for the welfare of the cat are all likely influences. However, whether good or bad, cat ownership is declining in Australia, and concern for wildlife is the second most common reason for Australians not owning a cat. In contrast, the authors suggest that access to the outdoors is seen as a positive welfare issue for cats in the UK, and argue that changing attitudes there by raising concern for wildlife is unlikely to be effective. To bolster that claim, they cite a recent article by a renowned ethologist who expressed concern for the welfare of cats housed in small communities in "cat cafés" in the UK.* It's not just the Queen's corgis that receive royal treatment in the UK. But what is the best argument for motivating NZ cat owners? Are we best to argue for the welfare of the cat, for the Tui, or for both? For us to be effective in reducing the number of cats hunting and breeding outside in NZ, we would do well to be attentive to what has successfully motivated cat owners across the Tasman, and what the impediments are here.

* Bradshaw J. Are Britain's cats ready for cat cafés? Vet Rec. 2013;173(22):554-5

Reference: PLoS One. 2016;11(4):e0151962

Abstract

Regional variations in percutaneous absorption of methimazole: an *in vitro* study on cat skin

Authors: Hill KE et al.

Summary: A commercial formulation of methimazole (10 mg) was applied to different feline skin regions (the inner stratum corneum of the ear, groin, neck, and thorax regions) *in vitro*, and the receptor medium was sampled up to 36 h postapplication. Absorption was more complete across the pinnal skin as compared with the other regions ($p<0.001$).

Comment: Enthusiasm for the topical delivery of drugs intended for systemic distribution is understandably high for cats, where oral dosing in the short- and long-term can be difficult for many owners. Poor compliance, fears of disturbing owner-animal bonds, failure to dose effectively, and genuine risk of personal injury are all impediments to consistent oral administration. Methimazole has been administered topically for more than a decade, however, topical preparations were for a long time conjured ad hoc by pharmacists, and there was no data in cats to guide formulation, dose, or application. Nonetheless, long-term follow-up of cats treated with one preparation showed an excellent rate of response, a low rate of side effects, and high owner satisfaction, despite less than ideal compliance.* However, the dose required to establish euthyroidism has been found to be highly variable, and reasons for that variation uncertain. The study by Kate Hill et al. provides some answers to these uncertainties. Using skin samples harvested in euthanased cats, the authors showed that absorption of methimazole through the dermis of the pinna is substantially superior to the absorption through the other sites, emphasising that the pinna is the site of choice for topical application. However, the variation in absorption between the samples from the 6 cats was very large, providing at least one reason for the variation in clinical response. Information on the age, sex, and breed of the cats was not available, and the sample size was small, so we remain ignorant of the factors that might affect absorption. Certainly the lipids produced by the stratum corneum are key facilitators of the penetration of lipophilic drugs, and alterations in the lipid secretions affect drug absorption. Thus age, sex, disease, diet, microflora, and the use of detergents may all have important effects that alter the efficacy of topical methimazole. For the right owner and cat, topical methimazole may be the modality of choice, and it can be highly effective. However, this study demonstrates a need to be cognizant of the uncertainties and variability in clinical efficacy.

* Hoffmann G, et al. Transdermal methimazole treatment in cats with hyperthyroidism. J Feline Med Surg. 2003;5(2):77-82

Reference: J Vet Pharmacol Ther. 2015;38(6):616-8

Abstract

Policies for the vaccination of cats and dogs in New Zealand veterinary practices

Authors: Cave NJ et al.

Summary: In February 2012, all 483 listed veterinary practices in NZ were mailed a questionnaire on current practices and attitudes towards vaccination of dogs and cats, the methods used for informing clients on which vaccines to use, and the preferred site for vaccination of cats. 204 completed survey forms were analysed. Vaccines were defined as core when considered essential for every animal and as non-core when recommended for animals whose location or lifestyle placed them at risk. Annual vaccination with modified live viral (MLV) vaccines of dogs was recommended by 54/198 (27.3%) respondents, and of cats by 107/181 (59.1%) respondents. Factors associated with the recommendation of annual administration of MLV vaccines to dogs included being a companion animal practice, a desire for policies on vaccination to be left to individual clinics, and having one veterinarian in the practice. Administration of the final vaccination for puppies was recommended at ≥14 weeks old by 55/185 (29.7%) respondents, and for kittens at ≥13 weeks old by 42/183 (23%) respondents. Of respondents that administered MLV vaccines annually, 62/103 (60.2%) believed reducing the frequency of vaccination would reduce income; 52/103 (50.5%) considered it would have a negative effect on animal health. 181/199 (91%) respondents gave advice to clients for deciding which non-core vaccines were administered. The recommendation to vaccinate considered various factors, including the risk to individual patients (190/203; 93.6%), requirements of boarding kennels/catteries (165/203; 81.3%) and clinic vaccination policy (142/203; 70%). The preferred site for MLV vaccination in cats was the dorsal neck or inter-scapular region (137/198; 69.2%). Eighteen respondents requested disease surveillance information to allow for truly informed decisions to be made about vaccination.

Comment: When we hatched the proposal to ask practitioners their policies on vaccination, I knew that we were pushing on a sore point. When the very first questionnaire was returned with the warm message for us to keep out of the business of others, I wondered if the questions were too much for the hyperalgesic. However, sometimes it is the sore point that reveals where the real point is. In this case, the sore point is that our profession has for some time allowed financial considerations to cloud our policies on vaccination. Yet that appears to be changing, or even to have changed. The large percentage of practitioners (73%) who recommend vaccination of adult dogs with MLV vaccines less frequently than yearly is greater than in the UK, US, and, though not well documented, probably well above Australia. As we discuss in the paper, it could be helpful to establish sharing of business ideas and models between practices to emulate those that have successfully abrogated any negative effect of reducing vaccination frequency. And while we are comparing business models, we would do well to push towards solidarity in our approach to kennels and catteries. A strong message from respondents was the frustration with feeling forced into compliance with recommendations made by misinformed owners of boarding facilities, rather than acting on recommendations made on evidence, and in what we know to be in the best interests of the animals. Several respondents commented that cattery owners, in particular, insisted on recent vaccination before admission, and that may be some of the reason why only c.40% of clinics vaccinate cats less frequently than yearly. Individual clinics talking to local catteries and kennels will achieve something, and might be sufficient, but perhaps we need regional or national initiatives to standardise demands from boarding facilities. And although this survey highlights differences in our practices that are at times stark, for many of the most important questions, we appear to be led by the evidence where it exists, and that is heartening.

Reference: N Z Vet J. 2015;64(3):145-53
Abstract

Histological evaluation of the soft palate in dogs affected by brachycephalic obstructive airway syndrome

Authors: Crosse KR et al.

Summary: These researchers examined tissue samples from the thick rostral portion of the soft palate in 9 severely affected brachycephalic dogs and also from 4 mesaticephalic dogs euthanised for reasons unrelated to respiratory or gastrointestinal disease (controls). Analyses revealed markedly increased acute and chronic muscle degeneration and necrosis, typified by swollen, hypereosinophilic fibres with centralised nuclei, myofibre atrophy, loss of cross striations and fragmented sarcoplasm, in the clinical samples as compared with the controls. In addition, there was a reduction in palatinus muscle ($p<0.001$) and increased proportions of collagenous stroma ($p=0.004$) and salivary gland tissue ($p=0.046$) in the clinical samples, compared to control dogs.

Comment: One of the most illuminating pictorial demonstrations of the changes that have occurred in the Bulldog over the past few decades is the series of photos of the mascot of the University of Georgia college football team: "Uga".* In 1955, the dog had a neck that, by today's standards, looks preposterously long, its antebrachia are strangely straight, and it has a lean, almost athletic torso. Wind forward 50 years, and the appearance is less one of a descendant of a wolf, and more the appearance of a large ball of soft dough that has been fired from a canon against a wall. Whilst the Sharpei has been described as "a disease that became a breed", the Bulldog is certainly a breed that has become a disease. Until recently, the combination of elongated soft palate and stenotic nares were referred to as the primary components of brachycephalic airway syndrome. However, studies of airflow through the upper respiratory tract of affected dogs to document the regions of greatest resistance are only now being conducted, and the relative contributions of the various components have not been carefully defined. The thickened soft palate has, for a long time, been referred to as "muscular hypertrophy", though surprisingly, the histological description of the tissue has been cursory. In this study by Kat Crosse et al., the authors demonstrated that myofibre atrophy and not hypertrophy was present, and that collagenous stroma, salivary gland hyperplasia and oedema were primarily responsible for the thickening. It did not escape the authors' attention that palatal function is likely to be profoundly altered in these dogs, though whether failure of muscle contraction or simple mechanical occlusion from its thickness is more important was not conjectured. Understanding the exact nature of the airflow obstruction is essential for optimal surgical intervention, and functional studies are likely to elucidate that problem. In addition, the mechanisms leading to the histological appearance would be interesting to describe. Are they genetically determined, or the pathophysiological consequence of the airway obstruction and gastroesophageal reflux? Or perhaps the real question is whether the effort we continue to invest in understanding this abominable consequence of misbreeding is disproportional to the effort we invest in preventing these dogs from being bred in the first place?

* Thurston R. History of University of Georgia's "Uga I through VIII" bulldog mascot [PICS]. Available from: http://coed.com/2010/10/29/history-of-university-of-georgias-uga-i-through-viii-bulldog-mascot-pics/

Reference: N Z Vet J. 2015;63(6):319-25
Abstract

Canine parvoviruses in New Zealand form a monophyletic group distinct from the viruses circulating in other parts of the world

Authors: Ohneiser SA et al.

Summary: Over a 13-month period, these NZ researchers collected faecal samples from 79 dogs with suspected canine parvovirus type 2 (CPV-2) infection and screened them by PCR for the presence of CPV-2 DNA. Of 70 positive samples, 69 were subtyped as CPV-2a and 1 as CPV-2. A majority of CPV-2a-positive samples were collected from unvaccinated or not-fully vaccinated puppies aged ≤6 months. A haplotype network of CPV-2 DNA sequences showed no structure when assessed based on location, vaccination status or age of the animals sampled. Data from an international haplotype network indicated that, unlike CPV-2 from other countries, the NZ CPV-2 population appeared to be from a single ancestor.

Independent commentary by Nick Cave.

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Comment: It is still a chilling story for undergraduates today, to learn of a virus that suddenly emerged in the US and elsewhere, to cause fatal disease in dogs in 1978, and within a year, it was found on almost every continent on earth and had made its way to New Zealand. Colin Parrish, a Massey science graduate, left New Zealand just as CPV-2 established here, and enrolled as a PhD student in Cornell University where he has remained. Professor Parish has contributed as much to the understanding of CPV as perhaps anyone else in the world, and is an under-celebrated expat. Amongst the pantheon of contributions that emanated from his laboratory was the description of the virus' early evolution, and the evidence that refuted the story that it was a mutation of feline panleucopenia virus. Whatever the precise origins, it is a reminder that viral mutations can lead to species jumps, and global pandemics of severe and fatal diseases. But it is also a reminder that the virus is new, and prone to further evolution. Within a year of the initial emergence, a variant of CPV-2 had emerged, and CPV-2a subsequently became the dominant subtype, and the original subtype has probably disappeared. Another single nucleotide mutation led to CPV-2b by 1984, and in the early 2000s, another subtype, CPV-2c, was identified in Vietnam.* Then in 2008, the flames of fear were fanned in Italy by reports that disease had occurred in vaccinated dogs infected by CPV-2c.** Although the fear that current vaccines are not protective against CPV-2c was subsequently shown to be unfounded, it occurred to me that we had no idea as to which subtypes are present in NZ. Thanks to the enthusiasm of practitioners around the country to courier leaking pottles of pungent haemorrhagic faeces to me, we collected CPV from more than 70 clinical cases during 2010, and subsequently sequenced and subtyped them, comparing their genetic similarity with viruses from around the globe. Surprisingly, CPV in NZ appears to have had only one major entry into the country, and none of the 70 viruses were 2b/2c variants. In addition, our CPV-2a variants have continued to evolve in a manner that is distinct from elsewhere in the world, including Australia. These facts have two broad implications. Firstly, our current quarantine procedures diligently enforced by MPI appear to have been successful in preventing the reintroduction of globally circulating newer CPV variants. Secondly, the new variants continue to evolve in NZ, and whilst they are likely to be less pathogenic, they may not always be. It is another chilling story, indicating that variants capable of escaping immunity elicited by the current vaccines, or that variants that infect cats despite panleucopenia vaccination, may yet emerge in this country. We should not be surprised if that particular story becomes true.

* Nakamura M et al. A novel antigenic variant of *Canine parvovirus* from a Vietnamese dog. Arch Virol. 2004;149(11):2261-9.

** Decaro N et al. Evidence for immunisation failure in vaccinated adult dogs infected with canine parvovirus type 2c. New Microbiol. 2008;31(1):125-30.

Reference: Vet Microbiol. 2015;178(3-4):190-200
Abstract

Genetic evaluation of the total hip score of four populous breeds of dog, as recorded by the New Zealand Veterinary Association Hip Dysplasia Scheme (1991-2011)

Authors: Soo M et al.

Summary: In this study, estimates of heritability and estimated breeding value (EBV) were used to investigate the genetic trend of the total hip score (to assess canine hip dysplasia) of individual dogs from the German Shepherd, Labrador Retriever, Golden Retriever and Rottweiler breeds recorded in the New Zealand Veterinary Association (NZVA) Canine Hip Dysplasia Scheme database (1991 to 2011). The evaluation included 2,983 NZVA hip score records. Genetic trends of the NZVA total hip score were calculated as the regression coefficient of the EBV (weighted by reliabilities) on year of birth. The estimates of heritability for hip score were 0.32 (SE 0.08) in German Shepherd, 0.37 (SE 0.08) in Labrador Retriever, 0.29 in Golden Retriever (SE 0.08) and 0.52 (SE 0.18) in Rottweiler breeds. In genetic trend analysis, only the German Shepherd breed exhibited a genetic trend towards better hip conformation over time, with a decline of 0.13 (SE 0.04) NZVA total hip score units per year ($p<0.001$). In the remaining 3 breeds, the genetic trends of total hip score did not differ significantly from zero.

Comment: The NZVA canine hip scoring scheme, introduced in the mid-1980s, has been tirelessly supported by veterinarians around the country, and by the long-serving readers of radiographs. With the probable exception of the Huntaway, in this study, Magdeline Soo and Andrew Worth evaluated the scores from the most populous at-risk breeds in this country. The heritability estimates are sufficiently high to make the breeds amenable to genetic selection. Indeed, recent studies of the actual genotypes that increase the risk have shown that selection based on genotyping would significantly increase the rate of improvement. However, there are two less positive views of the findings. Firstly, and obviously, there should be widespread disappointment at the lack of efficacy of the scheme in improving the phenotype of at-risk breeds over the 20-year period. Disappointment yes, but not surprise, and the apparent lack of efficacy of the scheme in this country is not unique, and is similar to the UK. A significant contributor is the insufficient number of dogs being scored. Andrew Worth has previously documented that less than 25% of these breeds that are registered in NZ are scored, and the authors make a strong case for more rigorous enforcement of scoring.* However, the other view of the findings is that they emphasise that the majority of the disease is environmental, and that too little research has focused on identifying the environmental factors, and evaluating the efficacy of manipulating them. Attempts to identify non-genetic factors have invariably relied on retrospective questionnaires with a very limited number of questions, and the very high likelihood of bias, confounding, and error. Intriguingly, the finding by Andrew Worth of a seasonal variation in hip scores in NZ is similar to findings in other countries, even if the exact seasonal pattern differs between studies. What explains seasonal variation is unknown. Epigenetic modifications linked to photoperiods, differences in maternal nutrition, differences in housing, and variations in exercise are all plausible explanations. But this simply calls our attention to the non-genetic factors in the disease. It is important that we question the value of focusing only on the genetic component of this disease, and consider if more aggressive environmental management early in life might be more effective. The NZVA scheme is a tool with which we have been trying to crack the nut of genetic predisposition. Sadly, like scoring schemes elsewhere, it seems that the tool has been ineffective, and worse – that it may be the wrong nut to crack at all.

* Worth AJ et al. Seasonal variation in the hip score of dogs as assessed by the New Zealand Veterinary Association Hip Dysplasia scheme. N Z Vet J. 2012;60(2):110-4.

Reference: N Z Vet J. 2015;63(2):79-85
Abstract

The effect of the canine *ABCB1*-1Δ mutation on sedation after intravenous administration of acepromazine

Authors: Deshpande D et al.

Summary: The *ABCB1*-1Δ mutation results in a severely truncated nonfunctional P-glycoprotein. Dogs homozygous for this mutation (mut/mut) are susceptible to the toxic adverse effects of ivermectin, loperamide, and vincristine. These researchers sought to determine whether *ABCB1* mut/mut dogs have increased depth and duration of sedation after IV acepromazine as compared with normal dogs (nor/nor), in a cohort of 29 rough-coated collies: 10 were *ABCB1* mut/mut, 10 *ABCB1* mut/nor, and 9 *ABCB1* nor/nor. Dogs were administered IV acepromazine 0.04 mg/kg. Level of sedation, heart rate, respiratory rate, and blood pressure were recorded for 6 hours after acepromazine administration. The researchers calculated and compared area under the curves (AUCs) of the normalised sedation score results. Median sedation scores for *ABCB1* mut/mut dogs were higher than in nor/nor dogs throughout the entire 6 hours and were higher in mut/nor dogs for the first 2 hours. These differences were not significant for any individual time point. The median sedation score AUC for mut/mut dogs was significantly higher than nor/nor dogs ($p=0.028$), but the AUC for mut/nor dogs was not ($p=0.45$). There were no significant between-group differences for heart rate, respiratory rate, or blood pressure.

Comment: It is not yet clear how many functional members of the family of membrane transporter proteins known as the "ATP-binding cassette (ABC) family" are present in dogs. The human genome contains 48 genes for members of the family, many of which are duplication-mutation events, but the majority encode for important proteins. The transporters are responsible for moving a large variety of compounds across cell membranes – mostly from inside to outside – and such is their evolutionary importance that versions are found all the way down the phylogenetic tree, from higher mammals to prokaryotes. There are family members that are responsible for transporting simple ions, sugars, amino acids and larger peptides/proteins, and hydrophobic compounds including xenobiotics such as drugs and ingested plant phenolics. Genetic mutations that lead to absence of expression or expression of defective proteins are responsible for several widely different diseases, commensurate with the wide range of functions. In humans for instance, defects in the *ABCB2* or *B3* genes leads to immunodeficiency, whilst *ABCA1* defects prevents cholesterol and phospholipid packaging into HDL causing a deficiency in HDL and atherosclerosis (Tangiers disease). Perhaps the best known genetic defect in the family is a defect in the *ABCC7* gene, which encodes for a chloride channel, and when defective, leads to cystic fibrosis. In dogs, as in people, the *ABCB1* gene encodes for a transporter that functions to remove lipophilic toxic metabolites from cells including drugs, hence its older name "multidrug resistance gene" or *MDR1*. Homozygous mutants are unable to effectively export certain drugs such as ivermectin, doxorubicin, and vincristine. The authors of this paper draw attention to anaesthetic agents normally exported by the transporter which, in homozygous mutants, are expected to reach higher concentrations in the CNS. The difference in sedation between homozygous mutants and normal dogs was clinically rather small when acepromazine was given at the "common" dose of 0.04 mg/kg. However, the authors point out that higher doses, and especially when combined with other drugs also exported by the same transporter which could include opiates, might produce unexpected and possibly adverse levels of sedation in some dogs. Short of being aware of the possibility, it is hard at the present time to know how else to adjust one's practice. The list of anaesthetics, let alone other drugs, that could have different effects in homozygous mutants is long, and there is not yet a unifying chemical or structural understanding that would allow prediction. So for the time being, we will continue to add drugs to the list of those that should be used with greater caution in at-risk dogs, while pushing for genetic testing and selective breeding to eliminate the genetic mutants from the population.

Reference: J Vet Intern Med. 2016;30(2):636-41
Abstract

Distribution of blood types in a sample of 245 New Zealand non-purebred cats

Author: Cattin RP

Summary: This paper reports the results of an analysis of 245 blood typing tests in non-pedigree cats (including domestic short- and longhaired) performed at the New Zealand Veterinary Pathology (NZVP) and Gribbles Veterinary Pathology laboratories nationwide between January 2009 and December 2014. Blood type distribution differed between samples from the two laboratories (p=0.029), but not between domestic short- and longhaired cats, or between the North and South Islands. Gribbles Veterinary Pathology tested 89 cats: 70 (79%) were type A, 18 (20%) type B, and 1 (1%) type AB. NZVP tested 156 cats: 139 (89.1%) were type A, 16 (10.3%) type B, and 1 (0.6%) type AB. It was estimated that 18.3–31.9% of random blood transfusions would be at risk of a transfusion reaction, and neonatal isoerythrolysis would be a risk in 9.2–16.1% of random matings between non-pedigree cats.

Comment: Recent large-scale genotyping studies have confirmed the long-held origin story of the domestic cat as being Mediterranean, or "Near Eastern". The story has now been fleshed out to describe the dispersal of cats along the major trade routes across the steppes of central Asia to the far East, north into Europe, and across the Atlantic to the Americas. As such, North American cats are genetically more similar to European cats than Asian cats. The greatest genetic diversion from their Mediterranean ancestors occurred in Asia, where breeding populations appeared to become isolated.* Domestic cats in New Zealand are thought to have been introduced by European settlers, with no significant migration from Asia, and it is expected that the genetics of cats here would more closely resemble European than Asian genetics. The study by Ryan Cattin doesn't answer this question, but it is of interest that the proportions of major blood types are closer to Japan and China than the UK, or even Australia, where 36% of cross-bred cats are type B.** It is not clear if the regional differences reflect different seeding populations, a consequence of subsequent more recent introductions, or genetic drift. It is also not clear what percentage of incompatible cats will actually experience a detrimental reaction beyond accelerated red cell clearance. The presence of antibodies to red cell alloantigens in a cat not previously transfused is not guaranteed. Indeed, the origin, evolutionary benefit, and variation in the production of alloantibodies is still enigmatic, even in people, and is almost completely unresearched in cats. Nonetheless, the likelihood of some degree of transfusion reactions in untyped donors given untyped blood is still relatively high. Given the availability of both commercial laboratory and in-house red cell antigen typing, the practice of administering unmatched transfusions when not absolutely necessary is, as the author argues, unacceptable.

* Lipinski MJ et al. The ascent of cat breeds: genetic evaluations of breeds and worldwide random-bred populations. Genomics. 2008;91(1):12-21

** Malik R et al. The prevalence of feline A/B blood types in the Sydney region. Aust Vet J. 2005;83 (1-2):38-44

Reference: N Z Vet J. 2016;64(3):154-7
Abstract

Post-vaccinal distemper encephalitis in two Border Collie cross littermates

Authors: Fairley RA et al.

Summary: A 4.5-month-old male Border Collie cross presented with aggression and seizures in October 2006. In September 2007, its littermate, a 16-month-old, female, spayed Border Collie cross presented with hypersalivation and a dropped jaw and rapidly became stuporous. Each dog developed acute neurological signs 5 and 27 days, respectively, after immunisation with different canine distemper MLV vaccines. In both dogs, brain sections showed evidence of encephalitis largely involving the gray matter of brainstem nuclei, consisting of extensive and intense parenchymal and perivascular infiltration of histiocytes and lymphocytes. Intra-nuclear and intra-cytoplasmic inclusions typical of distemper were plentiful and immunohistochemical labelling revealed abundant deposition of canine distemper virus.

Comment: Not long before my maternal Grandmother died, she recounted an experience very shortly after the end of the Second World War, of standing on the streets of London, queuing in the freezing winter rain. The queue she was in snaked around bombed-out buildings, rubble, and desolate streets, and she stood there with her two young daughters for hours. Her destination at the end of the queue was a group of nurses industriously administering Diphtheria vaccines to the children of London. Pre-war England had seen the scourge of diphtheria, measles, polio, and whooping cough, and to my Grandmother, prevention through vaccination was a miracle for which she stood with her crying daughters for hours in the bleak midwinter. Sixty years later, many have forgotten the terrible threats from infectious diseases; and recent measles outbreaks in unvaccinated school children in New Zealand serves as a dreadful reminder to parents about the importance of vaccination. However, in the absence of disease, fear of adverse effects from vaccination becomes disproportionate. The last case of distemper in NZ was probably during the late 1980s, and since then, vaccination and quarantine has successfully prevented disease from the virus in pet dogs. The reservoir for distemper elsewhere is the pool of wild canids such as wolves and foxes. In NZ, it is not clear if there are wild species (e.g. mustalids, pinipeds) that are infected and acting as reservoirs for the virus. An absence of reported sudden death in seals, and the solitary behaviours of mustalids suggest it is not. This should not make us complacent, and it may be that if introduced into NZ, we could see a large number of dogs becoming sick. On the other hand, should we continue to vaccinate against distemper if we have eliminated it from these islands? The report by Rob Fairley et al. of post-vaccinal encephalitis in 2 dogs reminds us that vaccines are not completely benign. The immunohistochemistry compellingly demonstrated the presence of CDV in the brains of the dogs, and the temporal association with vaccination in the absence of a series of cases in other unvaccinated dogs makes the conclusion of vaccine virus-induced encephalitis uncontroversial. The authors point out the high likelihood of a congenital immunodeficiency that prevented normal clearance of the vaccine. But do these events support an argument for ceasing CDV vaccination in NZ? I argue they do not. The phenomenally low risk and the high likelihood of a rare genetic susceptibility in this case do not provide sufficient reasons to discontinue. The absence of disease from these Isles should be reason for celebration, but not carelessness. There may not have been medical wisdom in the sodden, pertinacious queuing of my Grandmother, but there was a deeply felt realisation of what the stakes were.

Reference: N Z Vet J. 2015;63(2):117-20
Abstract