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Use Medicines Responsibly (www.noah.co.uk/responsible)
Welcome

Dear colleagues and friends,

It gives me great pleasure to welcome you to the 29th ESVN-ECVN Congress in Edinburgh. The symposium theme is “Applied Translational Neuroscience”. The congress aims to bridge the gap between laboratory and day to day practice: “From Laboratory to Labrador”.

It will feature keynote lectures, short oral presentations of recent research findings, practical orientated lectures and case reports. The programme will include a series of keynote lectures from renowned scientists.

Together with our platinum sponsor, Boehringer Ingelheim, we will offer you all a warm welcome on Thursday September 15 between 19.00 – 21.00 hrs in the Museum. The next day we are holding a special gala dinner in the Caves in Edinburgh for what we promise will be a fun packed evening.

I would like to take this opportunity to acknowledge our organising committee: Head of the Scientific Programme, Professor Holger A. Volk; Head of the Residents’ Day Programme, Dr Rodolfo Cappello and Local Representative for the Edinburgh Symposium, Dr Katia Marioni-Henry. It is due to their support and expertise that we have been able to stage an event of such outstanding quality.

I look forward to welcoming you to the Congress.

Simon Wheeler
Chairman of the 29th ESVN-ECVN congress
**TIMETABLE OF THE SYMPOSIUM**

**FRIDAY 16TH SEPTEMBER**

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INVITED SPEAKERS
Joan Coates  
Professor, University of Missouri

Joan is a Full Professor in the Department of Veterinary Medicine and Surgery at the College of Veterinary Medicine of the University of Missouri. She received her Bachelor of Science degree in General Agriculture in 1987 and DVM degree in 1990 from the University of Missouri. In 1990-1991, she held a small animal rotating internship at Texas A&M University and then from 1991-1994 completed a 3-year neurology and neurosurgery residency at Auburn University, where she also completed a Master of Science degree.

Also in 1994, she became board-certified in veterinary neurology through the American College of Veterinary Internal Medicine. Since, she has served on the faculty at the University of Georgia between 1994 and 1997 and at Texas A&M University between 1997 and 2003.

In 2003, she returned to the University of Missouri as a faculty member. As a clinical neurologist and neurosurgeon, she is Service Leader for the Neurology and Neurosurgery Service and Co-Director for the Physical Rehabilitation Program at the Veterinary Medical Teaching Hospital. As a researcher, she is a member of the Comparative Neurology Program at the College of Veterinary Medicine, which explores the inherited developmental and degenerative diseases of the nervous system and is involved with translational research for treatment of neurodegenerative diseases.

Her area of research focus involves the study of canine degenerative myelopathy as a disease model for translation of therapeutic strategies to amyotrophic lateral sclerosis.

CLINICAL TRIALS ON CANINE DEGENERATIVE MYELOPATHY  
(HOW BASIC SCIENCE CHANGED MY UNDERSTANDING AND CLINICAL PRACTICE)

Joan R. Coates, DVM, MS, Diplomate ACVIM-Neurology  
Professor of Veterinary Neurology & Neurosurgery  
Department of Veterinary Medicine & Surgery  
College of Veterinary Medicine, University of Missouri

Many inherited neurodegenerative diseases in our companion animals share important similarities to human diseases in terms of clinical signs, pathology and genetics and may prove to be excellent models of these conditions. Veterinary clinicians and researchers play a critical role in characterization of the natural history of inherited neurologic diseases in animals. Recent advances in molecular genetics allow for rapid identification of the mutation underlying the disease and correlation with the genetic basis of the corresponding human disease. Disease mutation discovery enables further understanding of pathophysiological mechanisms and ultimately development of rational approaches to therapy. Thus, a naturally-occurring canine disease model offers a ready clinical population where therapies can be evaluated in a setting closely mimicking human clinical trials. We propose that canine DM will permit studies of therapy intervention using similar procedures as those in human ALS patients.

Canine DM in Translation to Human ALS

Based on similarities to SOD1-associated human ALS, canine DM can offer some advantages as compared to existing SOD1 models; albeit not a perfect disease model of human ALS (Table 1). Rodent (mouse and rat) mutants have been established as useful ALS models in understanding disease mechanisms, as similar CNS pathology manifestations and observables are found. However, transgenic studies using transgenic rodent models often fail to predict efficacy and outcome in human patients. The failure of transgenic SOD1 mouse models to predict efficacy in human clinical trials has generated much debate within the ALS community. There are many potential explanations for “failure” of these mouse models, but the most prominent issues are (1) whether the SOD1-related ALS is an adequate disease model of the sporadic disease that represents most ALS patients and (2) whether the mouse is an adequate animal model for testing therapeutics for humans. The size and complexity of the central nervous system, the duration and rate of disease progression, and the pharmacokinetic differences between species further complicate translation of therapeutic interventions. Moreover, the high mutant SOD1 expression levels in rodent ALS models may induce pathologic processes distinct from those in ALS patients with SOD1 mutations. The spontaneous canine E40K mutation lacks the confounding effects of very high expression levels. Without an effective therapy in humans as a benchmark, it is difficult to know which of these issues are representative. We would argue that clinical similarities between SOD1-associated ALS patients and sporadic ALS patients, and recent findings of SOD1 aggregates in pathology in sporadic ALS patients, suggest that further study of SOD1 still is relevant to all ALS. However, it is still unclear whether the failure of drug candidates reflects limitation in the SOD1 rodent models or in the design of clinical trials. Due to heterogeneity of disease onset signs and progression rate, clinical trial success rates might be significantly improved if they were conducted only in those 2% of ALS patients known to have SOD1 mutation.

Canine DM serves to represent another disease model for therapeutic study on ALS because (i) a naturally-occurring SOD1...
mutation (E40K) is causative for canine DM, a common disease of older aged companion dogs, (ii) dogs have a relatively large spinal cord/brain, (iii) DM-affected dogs have a homogeneous pattern of disease progression, and (iv) histopathologic findings and functional deficits in DM share similarities to some forms of human ALS.

Table 1: Characteristics of Canine DM and SOD1-associated Familial ALS

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<th>Clinical Onset</th>
<th>Canine DM</th>
<th>SOD1-associated Human ALS</th>
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<td>Homogeneous UMN onset – pelvic limbs; asymmetric</td>
<td>Heterogeneous; degrees of UMN and LMN signs Onset – limb (most common), bulbar, UMN, frontotemporal degeneration; asymmetric</td>
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| Disease Progression | Homogeneous spread and rate from pelvic to thoracic limbs and eventually bulbar; UMN and LMN involvement Proprioceptive involvement first | Variable rate with spread from site of onset; UMN and LMN involvement No propriocceptive involvement most forms |

| Pathology | Sensory neuron pathology predominates, terminal disease motor neuron soma loss; axonal degeneration/loss in CNS (dorsal portion of lateral funiculus and dorsal funiculus) and PNS; NMJ degeneration does not precede motor neuron soma loss; astroglis; SOD1 intracellular neuronal and astrocytic aggregates; aberrant neurofilament accumulation | Motor neuron loss predominates, axonal degeneration/loss in CNS (dorsal columns) and PNS, astroglis; SOD1 intracellular neuronal and astrocytic aggregates; aberrant neurofilament accumulation |

| Inheritance | Most autosomal recessive | 90% sporadic; 10% inherited – most autosomal dominant |

| SOD1 Genetics | Inherited with variable penetrance; 2 SOD1 mutations: p.E40K and p.T18S | >160 SOD1 mutations; 12% of familial ALS, 2% of sporadic ALS and 2% of all ALS |

| Biochemistry | Detergent-insoluble SOD1 species (enzyme active) in spinal cord | Detergent-insoluble SOD1 species in spinal cord |

When translating therapies for ALS from animals to people or vice versa, establishing disease measures in canine DM will provide sensitive and specific milestones of disease progression and therapeutic response that parallels surrogate markers used in human patients. Reliable methods for measuring progression of damage to upper and lower motor neurons will provide early sensitive and specific milestones of disease progression and therapeutic response that parallels surrogate markers used in human ALS.

**Therapeutic Strategies**

Demonstrating dosing and delivery paradigms and safety of therapy in canine DM as a disease model will provide key supportive data and improve the probability of clinical trial success in human ALS. Target engagement, cerebrospinal fluid penetration, and delivery methods are areas that are undergoing transformation in treatment of neurodegenerative diseases. In ALS, multiple methods are currently being studied for their ability to decrease levels of unwanted proteins, including immunization strategies, small molecules, gene therapy, RNA interference, and antisense oligonucleotides (ASO). Nucleic acid-based therapies offer the promise of modifying or arresting the course of neurodegenerative disease in which down-regulation of a protein is a treatment objective. RNA interference is triggered by short, double-stranded RNA, while ASOs are short, single stranded DNA-like molecules. Recognition of RNA as a regulator of gene expression came with the discovery of interfering RNAs. RNA interference is a collection of small RNA directed mechanisms that result in sequence specific inhibition of gene expression. Both RNA interference and ASOs are posttranscriptional gene down-regulation approaches that destroy messenger RNA (mRNA) in a sequence specific fashion, leads to lower mRNA levels and results in decreased protein production. The use of ASOs and interfering RNA molecules to lower concentrations of mutant mRNA slowed disease progression and increased survival in the SOD1 transgenic rodent models. Nucleic acid-based therapies do not affect a protein that is already expressed; instead they prevent expression of the protein. Thus in ALS, such treatments would reduce synthesis rather than remove aggregated SOD1 protein.

The blood-brain barrier constitutes a challenge for delivering exogenous molecules to the CNS. Parenterally administered ASOs or interfering RNAs do not cross the blood-brain barrier; thus reduced SOD1 expression within neurons and surrounding non-neuronal cells requires direct administration into the CSF via intraventricular or intrathecal (IT) routes. The oligonucleotide or siRNA must then traverse from the cell surface, across the plasma membrane and lastly, to the target RNA. Results suggest that ASOs are transported into cells by endosomal transport mechanisms. To provide continuous down-regulation of mutant mRNA, these RNA interference compounds would need to be administered directly into the CNS through an intrathecal pump from a
reservoir or by repeated bolus injections. We believe therapies that decrease the amount of SOD1 in neurons are likely to reverse or slow the disease in SOD1-related human ALS as well as in canine DM. At the University of Missouri, we are investigating IT administration of ASOs and use of adeno-associated viral (AAV) gene delivered siRNA in therapy targeting SOD1.

References
EEG for the Veterinary Community

With
Lifelines Trackit and the new Lifelines R40

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- Lab quality recording
- Video option

Please contact Paul Wainwright at Lifelines
01264 782226 or 07500 009640
e-mail: paul.wainwright@llines.com
www.llines.com
Natasha Olby
Professor of Neurology/Neurosurgery, North Carolina State University

Natasha gained her veterinary degree from Cambridge University, UK, in 1991, and completed a PhD in spinal cord injury at Cambridge.

Following completion of her PhD and a post-doctoral position, also focused on spinal cord injury, she moved to North Carolina State University to do a neurology/neurosurgery residency and has stayed at NCSU as a faculty member since then.

She is currently a professor of neurology/neurosurgery and leads the Clinical Genomics Core of the Center for Comparative Medicine and Translational Research. Her research interests are spinal cord injury and the genetics of neurodegenerative diseases, with a focus on performing research using naturally occurring disease. She runs clinical trials evaluating novel therapies for the acute and chronic phases of spinal cord injury.

She has published widely on clinical and research topics associated with veterinary neurology and is co-editor of the BSAVA Manual of Canine and Feline Neurology. She is a past president of the American College of Veterinary Internal Medicine Neurology specialty.

How To Unravel The Riddle Of Acute Spinal Cord Diseases

Natasha Olby Vet MB, PhD, DACVIM (Neurology)
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Introduction

Acute paralysis is one of the most common presenting problems to veterinary neurologists, and yet, in spite of the hundreds/thousands of cases we all treat through our careers, there are numerous issues that we completely fail to understand. While we quickly become expert at recognizing clinical patterns of presentation and recovery, probing of our knowledge rapidly results in large voids. For example, here are some of the questions that occur daily - why can extreme compression be tolerated in some instances, while really minor compression results in devastating injury in others? Why do some animals recover walking with no pain sensation while others cannot? Why are withdrawal reflexes so poor at helping us localize the lesion? When should we do decompressive surgery? When should we stabilize? Why do some animals deteriorate so dramatically post operatively? How can animals have a syrinx apparently occupying almost the entire cross sectional area of the spinal cord and yet have no motor deficits? The questions go on and on and while we all have our beliefs and hypotheses, the evidence to support our theories is usually most notable by its absence.

Approach to the riddles

My personal approach clinical questions is systematic. The first step is usually careful clinical observation and definition of the questions. One of my favorite veterinarian observers is Ian Griffiths. One only need to look at his careful descriptions of clinical syndromes and the pathology that accompanied them to understand just how illuminating the careful clinical observation is. The next step is an examination of the literature to find out whether there is an answer to the question. The first place I like to go is the original literature from the turn of the 20th century - this period generated an explosion of physiological and anatomical studies that make really important observations but are easily overlooked. This leads on to review of more recent literature. There are numerous experimental models that allow particular aspects of an injury mechanism to be investigated. The most important fact to realize when reading this experimental literature, or when performing such research, is that this work typically only highlights particular questions, and is extremely unlikely to model the exact clinical scenario you are faced with. Nevertheless, it can provide important information and allow generation of testable hypotheses for your clinical questions. This is where things can become a little more challenging. Typically answering scientific questions requires data that ideally is collected in a very controlled and specific manner that may simply not be possible in a clinical population. For example, if you decide you need RNA to look at gene expression in spinal cord trauma you need to be able to harvest spinal cord immediately after death and you can be pretty sure the opportunity will only present itself on holidays and in the middle of the night! The second challenge is that very specific complex skill sets may be needed. The best way to address this is to collaborate, collaborate, collaborate!

An example of the type of question that may be posed in this way is why do some dogs get progressive myelomalacia? A review of the literature identifies a number of different genes that appear to impact hemorrhage following acute spinal cord injury, and so a plan can be formed to look at their level of expression using immunohistochemistry, quantitative PCR and in situ hybridization! Sounds straightforward but each technique requires canine specific reagents, suitable working protocols and control data, and then last but not least, the spinal cord tissue itself.

These barriers can be insurmountable for even the most enthusiastic person and are best addressed by collaboration. This includes basic scientists, and on the clinical side, forming a group of like minded people who will bank core tissues in the same ways, who will make detailed observations on neurological findings, imaging and surgical findings, and record detailed physiologic observations. One such group, CANSORT SCI, has been formed to work on acute spinal cord injury in dogs. This approach is likely critical for the future progress of discovery in veterinary medicine.
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Richard qualified from Cambridge University in 1994. After two years in private equine practice he moved to the USA and completed a residency in equine internal medicine at The Ohio State University and a Master of Science degree in muscle physiology and disease. He returned to the UK to complete doctoral training in molecular and cellular biology of neuromuscular diseases as a Wellcome Fellow at the Dubowitz Neuromuscular Centre, Imperial College from where he attained his PhD.

Richard is Professor of Comparative Neuromuscular Disease at the Royal Veterinary College. He is an RCVS-recognised specialist in Equine Internal Medicine and a Diplomat of the American College of Veterinary Internal Medicine. He directs the Comparative Neuromuscular Disease Laboratory at the RVC and is currently Director of Research for the Department of Clinical Sciences and Services. His clinical work mainly involves horses with neurological and neuromuscular problems.

New insights into pathophysiology and treatment of laryngeal paralysis (from lab to practice)

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Some of the earliest descriptions of equine recurrent laryngeal neuropathy (RLN) were made by Bouley, and subsequently by Dupuy in the 1820s. Then, during the mid 1800s, atrophy of equine laryngeal intrinsic muscles was commonly identified at necropsy in horses that ‘roared’. Despite these early reports, and considerable interest in recent years, the pathophysiology remains enigmatic, as does the aetiology. A discussion of the pathophysiology of the disease can perhaps best be made in the context of the possible aetiology and for the latter, genetic, acquired and environmental factors have each been proposed. In summary, RLN can be described as a distal axonopathy of (predominantly) the left recurrent laryngeal nerve with secondary neurogenic muscle atrophy of intrinsic laryngeal muscles. The consequence is a reduced size of the rima glottis due to left cricoarytenoideus muscle paresis, which becomes relevant at exercise and manifests as poor performance due to impaired air intake and reduced PaO2. The pathophysiology (and also aetiology) remain very unclear, and so it is helpful to consider certain issues that (currently) remain unresolved – (1) actual disease prevalence; (2) polyneuropathy vs mononeuropathy; (3) selective involvement of specific motor units. These elements will be discussed.

Estimates of RLN prevalence in horses vary widely, largely due to the manner in which diagnosis was made. Historically, horses were diagnosed on the basis of the sound of their inspiratory stridor made at exercise, and subsequently with the slap test. More advanced techniques, in particular exercising laryngoscopy, laryngeal computed tomography and ultrasound reveal that these earlier methods underestimated disease prevalence. Indeed, when examined histologically, it is hard to find a normal horse. Of course, this has profound implications for the search for the genetic cause and for genetic modifiers.

Whilst evidence for the disease has been identified in fetuses and in a few young (draught horse) foals, the disorder is typically recognised as racehorses go into training. There is some evidence supporting disease progression, however such work is likely compromised by difficulties in performing longitudinal studies, variation between and within observers and day-to-day variation in horses and within surgical treatment of affected cases and animals that are lost to follow up.

Histopathological changes within the distal nerves of horses with RLN reveal collapsed myelin sheaths, increased relative myelin sheath thickness, regenerating Schwann cell membrane clusters (Bungner’s bands) and ‘onion-bulb’ formations indicative of demyelination and remyelination thought to be collectively indicative of a primary axonopathy with secondary myelin loss. More specific indicators of a primary axonopathy are the central axon fragments commonly seen within myelin digesting chambers, accumulation of axoplasmic organelles and margination of axonal microtubules. Such defects are seen in human neuropathies with suspected axonal transport defects and given that nerve cell body pathology (in the nucleus ambiguous) is not found in RLN-affected horses, retrograde axonal transport might be most likely to be affected in RLN.

It is conceivable that RLN might have both an acquired and genetic basis: indeed, RLN has long been proposed to be related in some way to stretch-induced trauma of the nerve as it passes around the aorta in the thorax perhaps similar to the induced neuropathy that occurs in humans with hereditary neuropathy with liability to pressure palsies associated with a mutation in peripheral myelin protein (PMP)-22. A combination of both a genetic and acquired component would seem to be necessary, since similar axonopathies are not known to be present in other athletic quadrupeds.

My group is part of a worldwide consortium that is examining pathophysiology, aetiology and in particular, novel treatments for RLN in horses. In collaboration with Mr Justin Perkins at the RVC, and sponsored by MEDel Inc., we have an extensive programme of
work examining use of functional electrical stimulation with and without nerve grafting, for the treatment of RLN. These preclinical trials have led to direct improvement and expedited treatment of laryngeal paralysis in humans. The issues that relate to optimising this novel approach for horses that are galloping at 14 m/sec, will be discussed.

Treatment for neuromuscular disease: how basic science has informed change in clinical practice

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We are entering an exciting age in the treatment of inherited neuromuscular disease. In particular, rapid advancements in cell and molecular biology in the lab are leading to translational therapies that are being tested in animal models before moving into human patients. Whilst early experiments are typically conducted in rodent models, many regulatory authorities require vigorous testing in larger species. Some of these treatments have now reached human trials and it is likely that within the next few years, we will see them being exploits in our veterinary patients.

The artificial selection of modern dog and cat breeds has created an abundance of naturally occurring models of human genetic disorders; many of these disorders are rare in humans, but because of artificial breeding programmes (line breeding for example), certain genetic disorders are common in specific breeds. Recessive diseases are over represented, because breeding from unaffected (but carrier) parents is common, especially when certain pedigrees are popular.

Many of these disorders have a neuromuscular phenotype and increasingly we are aware of the precise genetic cause; indeed, the veterinary profession has benefited hugely from the molecular genetic explosion that hit human medicine about 20 years ago, with development of bioinformatic genetic techniques (such as genome wide association studies) and more recently, with next generation sequencing. Experienced clinicians (veterinary neurologists) are key to identifying novel neuromuscular phenotypes so that geneticists can match the canine disease with its human counterpart: sometimes these phenotypes are readily identified with specific testing and consequently, candidate gene analysis rapidly identifies that causative mutation. Alternatively, sometimes novel disorders are recognised in veterinary patients which informs human medicine.

In this talk, I will discuss some of the exciting treatments that are aimed at human neuromuscular disease, in the context of research and clinical trials that are being conducted in dogs. Such treatments include stem cell-based therapies, gene therapies, exon skipping and gene correction (via CRISPR-Cas9 approaches) sometimes alone and sometimes in combination. I will provide examples using the prototypical disease, Duchenne Muscular Dystrophy, which is the most common, lethal, inherited disease of children worldwide and which has been reported in numerous dog breeds, most notably the Golden Retriever and Cavalier King Charles Spaniel. Further, I will discuss exciting developments in the gene therapy of Myotubular Myopathy, which has progressed from rodent studies to promising work in Labrador retrievers.

Funding bodies are now increasingly recognising the potential for these animals in the search for novel treatments. Interestingly, multinational pharmaceutical companies are also interested in helping develop these forms of therapy - even for rare or orphan diseases - in veterinary patients. The veterinary profession has a huge opportunity (and perhaps responsibility) in helping develop advanced treatment methodologies for humans, and of course, also for pets. If conditions are common, then treatment of client-owned animals is an option (with appropriate legal justification). Alternatively, colonies of such animals can be established, specifically for the investigation of pathophysiology and treatments. This of course creates a dilemma for veterinary clinicians and I will discuss the ethical and welfare considerations associated with establishing a colony for clinical trials in the context of a colony of dogs with muscular dystrophy at the Royal Veterinary College.
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Cold shock – repurposing a single neuroprotective strategy into multiple therapeutic targets

Clinical cooling emerged in the 1940s when it was first used to treat human patients with severe head trauma. Interest in therapeutic hypothermia (TH) has since fluctuated as complications of deep cooling were later sidestepped through realizing the potency of mild hypothermia. The current status quo is ironically lukewarm; TH has become routine for a select group of patients but otherwise lacks a firm evidence base to support its wider use in critical care. Irrespective, mild hypothermia remains the single most effective brain-protecting agent known. How then do we reap the benefits of cooling without cooling patients?

First we must understand what determines brain temperature and which of the many molecular programmes recruited by cooling effect a neuroprotective advantage. As predicted from its rapacious oxidative metabolism, average human brain temperature sits slightly above that of the core. However, brain temperature is not fixed; it varies by brain region, and with neural activity, physical exercise, state of consciousness and pathology. Elevated brain temperature associated with trauma, epilepsy, and stroke is well documented and predicts a poorer prognosis. At the cellular level, hyperthermic insults increase resting membrane potential and calcium levels, reduce pH and incite oxidative stress. The rationale for therapeutic cooling is to minimise the cascade of secondary events that perpetuate neuronal damage after an initial insult.

Clinical efficacy of TH has been demonstrated for neonatal hypoxic-ischaemic encephalopathy, open-heart surgery and acute global cerebral insults after cardiac arrest. Many pre-clinical studies underpinning these techniques were carried out in dogs. Despite this, cooling has failed to translate into the clinic for stroke and traumatic brain injury and its use remains anecdotal in the veterinary referral setting. Partly this reflects the risks and practical challenges of cooling adults. However, the cellular and molecular physiology influenced by temperature reduction remains unexplored and poorly understood. Clinical cooling has essentially been advocated on the basis that it can work, rather than addressing why - tractable pharmacological targets may thus have been overlooked.

The neuroprotective reach of cooling is multifaceted. In cerebral ischaemia, mechanisms of hypothermic neuroprotection include (1) acute effects on cerebral blood flow, excitotoxicity and metabolism, followed by (2) effects on apoptosis, inflammation and the blood-brain barrier and finally, (3) delayed effects on neuroglial differentiation and synaptogenesis. Although primary insults in spinal cord injury, traumatic brain injury, and cerebral ischaemia are diverse, these disorders share secondary pathways that lead to cell death. Ultimately, mechanisms of neurotoxicity and hypothermic protection are determined by the duration and intensity of the insult, the vulnerability of specific neural populations and compartments, and the depth and timing of cooling.

Preconditioning describes the phenomenon in which a subtoxic stress confers resistance to an otherwise lethal injury. It is induced by many and varied stimuli - most classically ischaemia - however rodent studies indicate that hypothermia can also elicit this response. Such homeostatic priming is critical at the level of neural circuitry; extreme hypo- or hyperthermia re-calibrates neuronal circuits so that they can better withstand future temperature shifts. Since preconditioning requires de novo protein synthesis, it has a relatively slow onset and persists over many days. Conceptually, hypothermic preconditioning would seem obsolete for acutely presenting conditions, although postconditioning may offer some protection.

Fundamental to hypothermic conditioning is the cellular cold-shock response - a series of molecular changes that equip the cell for endurance at low temperatures. Mammalian cells respond to cold-stress by switching from a state of growth and division to one of adaptation and survival. This involves cell-cycle arrest and shut-down of gene transcription and protein translation. Conversely, a subset of highly conserved ‘cold-inducible’ RNA chaperones, including RNA binding motif 3 (RBM3) and cold-inducible RNA binding protein are specifically upregulated in response to hypothermia. These glycine-rich binding proteins perform several important functions under stress conditions, including stabilisation and facilitated translation of essential mRNAs. Unsurprisingly,
cold-shock proteins have received attention as proto-oncogenic candidates that promote apoptotic inhibition, an undifferentiated ‘stem cell’ phenotype, and increased proliferation[43]. Several cold-shock protein features are therefore predicted to be useful for neuroprotection – as recently demonstrated for RBM3 in a model of neurodegeneration[49].

Neuronal axons must be maintained for the lifetime of the organism. Microtubule-associated protein tau is upregulated during neuronal differentiation[2]; it is abundant in CNS axons and plays an essential role in cytoskeletal dynamics[52,56]. Tau is also the most commonly misfolded protein in human neurodegenerative disorders[58-61]. Tauopathies are classified by the distribution, morphological and biochemical characteristics of intracellular tau inclusions found in post-mortem brain tissue[60-64]. In Alzheimer’s disease (AD), neurofibrillary tangles (NFTs) composed of paired helical filaments (PHFs) of tau are found in neurons[53,64]. Tau pathology is further recognised in a broader spectrum of degenerative disorders, including prion disease, amyotrophic lateral sclerosis/Parkinsonism-dementia complex and C9ORF72-associated frontotemporal dementia[65]. Across this spectrum, hallmark tauopathic features include hyperphosphorylation, aberrant folding, aggregation and reduced solubility[65].

85 tau epitopes are variably phosphorylated depending on developmental age, neuronal health and physiological state[65-67]. Some of these sites were originally considered disease-specific, however, equivalent epitopes have since been identified in human foetal or healthy adult biopsy-derived brain samples[68-73]. In the disease state, hyperphosphorylated tau sequesters normal tau, and increased phosphorylation prevents tau binding to microtubules, leading to microtubule disassembly[69,74-75]. Hyperphosphorylation also reduces tau turnover, and promotes its misfolding and aggregation. Conversely, a collection of studies have shown that increased tau phosphorylation can proceed independently of tau aggregation[65]. Tau phosphorylation is transiently high in early brain development and reversibly increases during experimental cooling[76,77], thus depending on context, increased tau phosphorylation is not in itself neurotoxic. The dogma of what constitutes ‘pathological tau’ remains controversial.

Retaining plasticity is an effective strategy for managing stressful insults – demonstrated most elegantly in the hibernating brain[78-79]. Hibernation, observed across several mammalian orders, includes a reversible decrease in basal metabolic rate, body temperature, and neuronal activity[68]. Despite radical cerebral ischaemia-reperfusion, most animals emerge from torpor neurologically intact[68]. In ground squirrels, contacts between mossy fibres and hippocampal pyramid neurons undergo regression during hypothermic torpor followed by re-afferentation during euthermic arousal, involving dendritic spine transformation and temporary synaptic loss[80,82-85]. This periodic denervation/re-innervation occurs much faster than that observed during neuronal development or environmental enrichment[86]. Importantly, these ultrastructural and morphological changes are paralleled by fully reversible phosphorylation of tau[87]. Tau becomes hyperphosphorylated during torpor throughout the entorhinal cortex, hippocampus and isocortical areas[80,87]. This enhanced phosphorylation depends primarily on the drop in body temperature and inhibition of tau phasphatase activity[88].

Synaptic regeneration in perfect hibernators appears faithful, explaining why torpid neuronal phenomena do not confer residual cognitive deficits[74,89]. The repeatable nature of tau alterations during torpor also lends itself to the concept of preconditioning; biochemically, the brains of these animals have been likened to a pre-conditioned state[86,90]. The hibernating brain is thus highly resistant to injury, placing ‘foetal-like’ tau at the heart of a neuroprotective adaptation[78,91-92]. Perplexingly, the parts of the brain ‘switched off’ during hibernation are those which retain the highest neuroplasticity in adulthood[93]. In AD, both the course of neurofibrillary degeneration and decline in mental capacity progress along an inverse hierarchy of cortical connectivity[78,94]. In this ‘last in-first out’ model, the latest-maturing regions are least myelinated and structurally most plastic[95-98]. Such plasticity comes at a price however, and its failure may give rise to neurodegeneration[99,100].

Protein aggregation is the most unifying pathological feature of neurodegeneration and is intimately linked to dysfunction of cellular proteostasis[99]. In eukaryotic cells, proteome integrity is maintained by an elaborate network of molecular chaperones and protein degradation factors[100]. Depending on the severity of misfolding, 3 parallel strategies refold, degrade or sequester misfolded polypeptides[101]. These mechanisms are interlinked by a set of chaperones that ‘triage’ the aberrant protein and guide it to the appropriate pathway[102]. Accumulation of misfolded proteins initially triggers induction of heat shock proteins (Hsps) – molecular chaperones which assist in protein refolding[103-104]. If misfolding events are irreversible, Hsps target the substrate to the ubiquitin-proteasome system or the autophagy-lysosomal pathway[105]. Together these represent the major routes for clearance of dysfunctional proteins[106]. Failure of one or more of these pathways perturbs proteostasis and mobilizes cellular stress responses including endoplasmic reticulum (ER) stress and the unfolded protein response (UPR)[106].

Since cooling protects the human neonatal brain[101], molecular effects of clinically-relevant cooling were explored using functional, maturationally-comparable cortical neurons differentiated from human pluripotent stem cells (hCNs)[107-109]. Hypothermia produced an archetypal cold-shock response in hCNs and protected them from oxidative and excitotoxic stress[109-110]. Principal features of human cortical tau development were recapitulated during hCN differentiation, and subsequently reversed by cooling, returning tau transcriptionally and post-translationally to an earlier foetal-like state[110]. Neuroprotective hypothermia further induced mild ER stress in hCNs, with subsequent activation of the UPR[110]. Reciprocal modulation of both tau phosphorylation and the ER-UPR cascade suggested that cold-induced hyperphosphorylation of tau and ER-hormesis (preconditioning) represent significant components of hypothermic neuroprotection[109,110]. Cooling thus modifies proteostatic pathways in a manner that supports neuronal viability[109]. To date, hypothermia has protected hCNs against oxidative, excitotoxic and ER stress, all of which are implicated in acute as well as degenerative processes. This ‘cross-tolerance’ effect places exponential value on molecular cryobiology, with the potential to extract multiple therapeutic targets for an unmet need[111-113].

References
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Amyotrophic Lateral Sclerosis (How basic science has informed change in clinical practice)

Amyotrophic Lateral Sclerosis (ALS) is an adult onset neurodegenerative condition affecting the upper and lower motor neurons that results in progressive muscle wasting and eventual respiratory failure. Death occurs within 2-5 years from symptom onset and the worldwide incidence is about 1 to 3 per 100,000 person/years. About 10% of cases are familial and the rest are sporadic. A wide variety of genes have been identified from the familial cases including C9orf72, SOD1, TARDBP, FUS, TBK1, VAPB, OPTN and a number of others. Most of the proteins encoded by these genes are involved in RNA-binding, nucleocytoplasmic transport or protein quality control. As in many other neuromuscular degenerative disorders, ALS shows abnormal mitochondria and impaired autophagy with cellular aggregates being a common pathological feature.

A number of animal models have been developed to mimic the disease and to test potential treatments. These include genetically modified nematodes, fruit flies, zebrafish, mice, rats and pigs. The only natural non-human ALS equivalent is canine degenerative myelopathy. The most extensively used mouse model is the SOD1 G93A transgenic mouse that expresses a human SOD1 mutation. This model has been highly criticised as therapies that appeared effective in the mouse have uniformly failed to show any benefit in human clinical trials. Indeed, there is only one approved drug for the treatment of ALS and that only adds a few months to patient survival. Careful retrospective analysis of the SOD1 G93A mouse experiments shows that the majority of positive results were due to poor experimental design and inappropriate statistics and guidelines for well-designed experiments are now available. Current therapeutic hopes are centred around stem cells and gene therapies, particularly those using antisense or RNA interference strategies. Recent early success in another disease of motor neurons, spinal muscular atrophy, demonstrates the potential with gene therapy.
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ORAL PRESENTATIONS
ASSESSING THE ROLE OF CANINE AND FELINE ABCG2 AS A MEDIATOR OF PHARMACORESISTANT EPILEPSY.
T. Jukier1; S. Dassanayake2; T. Coffey3; A. Chen1; K. Mealey2; 1Department of Veterinary Clinical Sciences, 2Program in Individualized Medicine, 3Department of Statistics, Washington State University, Collage of Veterinary Medicine Pullman, Washington.

Epilepsy is a chronic condition of recurring unprovoked epileptic seizures. Of the population of idiopathic epileptics, a subset of them fail to respond to medical management. This study investigated whether or not anti-epileptic drugs (AED) are substrates for canine or feline orthologs of the drug efflux transporter ABCG2.

Human embryonic kidney cells that had been stably transfected with plasmids containing either canine or feline ABCG2 cDNA were utilized for these experiments. Levetiracetam, phenobarbital, gabapentin, zonisamide, and lamotrigine were the AED evaluated with a flow cytometry-based competitive transport assay. Mitoxantrone, a classic ABCG2 substrate, is an intrinsically fluorescent molecule. Transfected HEK-293 cells expressing ABCG2 are expected to extrude mitoxantrone from the cell resulting in low intracellular fluorescence. Addition of another ABCG2 substrate results in competition for ABCG2 transport, decreasing mitoxantrone extrusion and increasing intracellular fluorescence. Analysis was performed separately for each AED with either canine or feline ABCG2-transfected cells. One-way ANOVA was used to assess a statistical difference between groups followed by Dunnett’s test for comparisons against control. Statistical significance was achieved for one concentration in the canine zonisamide group. Because fluorescence actually decreased, indicating influx rather than efflux, the clinical significance is unknown.

Results of this study suggest that ABCG2 does not contribute to pharmacoresistant epilepsy for the evaluated AED.

CLINICAL PRESENTATION, MAGNETIC RESONANCE IMAGING FINDINGS AND OUTCOME OF DOGS DIAGNOSED WITH INTRACRANIAL EMPIEYMA. A. K. Forward1, I. N. Plessas2, S. De Decker1. 1Royal Veterinary College, University of London, Hatfield, United Kingdom and 2Davies Veterinary Specialists, Hertfordshire, United Kingdom.

Intracranial empyema is a rare neurological emergency that requires rapid and aggressive intervention. This case series aims to describe the clinical presentation, advanced imaging findings, and short and long term outcomes in dogs with intracranial empyema.

Medical records from two referral hospitals were searched and identified dogs diagnosed with intracranial empyema. Inclusion criteria comprised of an MRI consistent with contiguous infection from adjacent structures, a CSF analysis suggestive of empyema or direct visualization of purulent material during intracranial surgery.

Ten dogs were included, with a median age of 2 years (range 4 months–12.5 years). All presented as emergencies with 8/10 showing neurological abnormalities and 2/10 with retro-bulbar swelling and exophthalmos. 6/10 had surgical intervention, 2/10 were medically managed and the remaining 2/10 were euthanised. Typical MRI findings included extra-axial, T1-weighted hypo-isointense, T2-weighted hyperintense material with varying degrees of contrast enhancement, with 6/9 showing evidence of contiguous infection from adjacent structures on MRI. 6/10 had culture and sensitivity performed with 2/6 returning Enterococcus and Streptococcus species respectively. The median antimicrobial course length was 6 weeks (range 2 – 28 weeks). 8/10 survived to discharge, with a median hospitalisation time of 6.5 days (range 4-10 days). 5/8 are still alive at the time of writing (1 lost to follow up; 2 euthanised for other reasons) with all five considered neurologically normal with a successful long term outcome.

Whilst intracranial empyema in dogs is a rare condition, excellent outcomes are possible in those cases treated appropriately.

THE NOVEL HOMOZYGOUS KCNJ10 C.986T>C (P.LEU329PRO) VARIANT IS PATHOGENIC FOR THE SESAME/EAST HOMOLOGUE IN MALINOIS DOGS.
K. Steel1, M. Van Poucke1, S. Bhatti4, A. Vanhaesebroeck1, L. Bosseler3, L. Peelman2, L. Van Ham1. 1Dept. of Small Animal Medicine and Clinical Biology, Faculty of Veterinary Medicine, Ghent University, Belgium, 2Dept. of Nutrition, Genetics and Ethology, Faculty of Veterinary Medicine, Ghent University, Belgium, 3Dept. of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, United Kingdom, 4Dept. of Pathology, Bacteriology and Poultry Diseases, Faculty of Veterinary Medicine, Ghent University, Belgium.

Sensorineural deafness, Tubulopathy) syndrome is a multisystemic disorder in man. The condition is exclusively caused by homozygous or compound heterozygous variations in the KCNJ10 gene. Here we describe a similar syndrome in the Malinois dog breed. This mutation differs from the already identified KCNJ10 mutation in the Russell group of terriers responsible for spinocerebellar ataxia with myokymia, seizures, or both.

Four 4-month-old Malinois of 2 unrelated families were presented for an uncoordinated gait since the age of 12 weeks. Neurological examination revealed severe generalized hypermetric ataxia in all dogs, involuntary vermicular muscle twitching (myokymia) triggered by excitement in 2 dogs and epilepsy in 2 dogs. Absent patellar reflexes were noted in all dogs. Complete blood count, serum biochemistry, urinalysis, magnetic resonance imaging of the brain and CSF analysis did not reveal any abnormalities. Electromyography showed neuromyotonic discharges in the clinically affected muscles. Results of motor nerve conduction and repetitive nerve stimulation did not differ from two age-matched Malinois control dogs, however, brainstem auditory evoked potentials showed disappearance of wave components and mildly prolonged latencies in the affected dogs. Histopathology revealed bilateral myelopathy with predominant axonopathy and myelin vacuolization in the central nervous system. Genetic analysis detected a novel pathogenic KCNJ10 c.986T>C (p.Leu329Pro) variant, which is inherited in an autosomal recessive way.

Conclusively, these mutant Malinois dogs may serve as a promising animal model to elucidate the pathogenesis and treatment of this disorder in man.

SeSAME (Seizures, Sensorineural deafness, Ataxia, Mental retardation, and Electrolyte imbalance) or EAST (Epilepsy, Ataxia, Sensorineural deafness, Tubulopathy) syndrome is a multisystemic disorder in man. The condition is exclusively caused by homozygous or compound heterozygous variations in the KCNJ10 gene. Here we describe a similar syndrome in the Malinois dog breed. This mutation differs from the already identified KCNJ10 mutation in the Russell group of terriers responsible for spinocerebellar ataxia with myokymia, seizures, or both.

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Conclusively, these mutant Malinois dogs may serve as a promising animal model to elucidate the pathogenesis and treatment of this disorder in man.
Inherited juvenile-onset polyneuropathy with laryngeal paralysis has been reported in several breeds of dogs such as Dalmatian, Alaskan Malamute, Leonberger, Russian Black terrier, Rottweiler and Pyrenean mountain dogs, with a suspected autosomal recessive inheritance pattern.

Eight young American Staffordshire Terriers were presented for inspiratory stridor and dyspnoea (7/8), locomotor weakness (8/8) with palmpadle and plantar gait stance (5/8), with an age of onset ranged from two to six months. Neurological evaluation revealed four limbs ataxia with high stepping pelvic limb gait (8/8), limb muscles atrophy (6/8), cutaneous hypoesthesia (5/8) and decreased spinal reflexes (5/8).

Laryngeal paralysis was diagnosed during laryngoscopy in seven dogs. Electrophysiological investigations showed abnormal spontaneous electrical activities in the laryngeal muscles (7/8) and appendicular muscles (8/8), marked attenuation of compound muscle action potentials amplitude (8/8), reduced motor nerve conduction velocities (7/8), decreased or absent sensory nerve action potentials (8/8).

Muscle biopsies were performed in six cases and histologic analysis was consistent with neurogenic atrophy and intramuscular nerve branches myelinated fiber loss. Fibrilar nerve biopsy analysis, when performed (four cases), was consistent with chronic and severe extensive nerve fiber loss resulting from axonal degeneration.

To the authors’ knowledge, this is the first report of a juvenile-onset polyneuropathy with laryngeal paralysis in American Staffordshire Terrier. One of the dogs is a backcross and an autosomal recessive mode of inheritance is suspected. If pedigree analysis and genotyping are consistent with this hypothesis, the American Staffordshire Terrier polyneuropathy could be considered as a new spontaneous animal model of inherited axonal neuropathy (Charcot-Marie-Tooth disease). Genotyping could lead to the discovery of new genes involved in axonal degeneration.

Tissue mechanical properties vary over several orders of magnitude in the disease state and elude current veterinary neuroimaging modalities. Magnetic Resonance Elastography (MRE) combines conventional MRI with acoustic wave propagation to generate high-resolution viscoelasticity or ‘stiffness’ data and is emerging as a valuable, non-invasive diagnostic tool in human neurology. The purpose of this study was to establish whether MRE could be applied to the canine brain.

Post-mortem brain scans were performed on canines euthanized on welfare grounds with approval of the R(D)SVS Veterinary Ethical Review Committee. A standard cartesian Echo Planar Imaging sequence with additional motion encoding gradients was used for multiple frequency (30-100Hz) acquisition on a 3T Verio MRI system (Siemens Medical Systems), with vibrations generated by the Resoundant actuator and head pillow (http://resoundant.com/). Raw phase images were analysed with the Elastography Software Pipeline to produce maps of viscoelastic parameters.

Our protocol readily propagated waves into the specimens enabling construction of high-resolution elastograms of the canine brain. Variation in tissue stiffness across different brain regions was observed, as noted in the human brain in situ. Mean whole brain tissue viscoelasticity ± standard error was 2.99 ± 0.30 kPa (n=3).

This is the first demonstration that acoustic waves can be propagated into the canine brain in situ. Our follow-on objective is to construct a reference atlas of canine brain stiffness against which to test the sensitivity of MRE for detecting and differentiating age-related and pathological changes. ‘Virtual palpation’ of the brain with MRE has the potential to revolutionize veterinary neuroimaging.

Brain damage causes profound and prolonged ATP loss. Prior in vitro studies showed that supplementation of ischaemic brain slices with precursors of ATP synthesis, Dribose&Adenine (RibAde), restores ATP levels. We aimed to assess the therapeutic potential of RibAde&Allopurinol in a rat model of transient focal cerebral ischaemia. Allopurinol should potentiate the effect of RibAde by preserving hypoxanthine, also used in the purine salvage pathway.

This study conforms to the UK Animals (Scientific Procedures) Act. Male Wistar rats were randomised to three groups and the investigator was blinded to treatment. After 1-hour transient focal ischaemia, RibAde group received at reperfusion an intravenous infusion of ribose (200 mg/kg/h) and adenine (10 mg/kg/h) over 6 hours. RibAde&Allopurinol group also received allopurinol (10 mg/kg, IP). Saline group received intravenous and intraperitoneal injections of saline. Acute ischaemic injury and subsequent infarction were assessed by MRI immediately prior to reperfusion (diffusion weighted imaging) and 7 days after reperfusion (T2-weighted imaging).
Intervertebral disc extrusion (IVDE) is a common cause of severe spinal cord injury, and an accurate prognosis remains challenging. Hemorrhage in the spinal cord or in the subarachnoidal space may have an important impact on damage of the spinal cord parenchyma and outcome, and thus, may be relevant for the prognosis of dogs with IVDE. Therefore, the aim of the study was to evaluate if blood degradation products and ferritin are measurable in the CSF of dogs with thoracolumbar IVDE, and if there is an association to clinical parameters.

Measurements of net oxyhemoglobin absorption (NOA), net bilirubin absorption (NBA) and ferritin concentration were prospectively performed in the CSF of 34 dogs with thoracolumbar IVDE, 21 dogs with idiopathic epilepsy either native (IE) or artificially contaminated with blood (IEc), and 9 dogs with steroid responsive meningitis arteritis (SRMA).

The NOA was significantly higher in the IVDE group compared to the IE ($P = 0.001$) and SRMA ($P = 0.001$), but not to the IEc group ($P = 0.89$). The NBA was significantly higher in the IVDE group compared to all control groups ($P < 0.001$, respectively). Ferritin concentration was significantly higher in the IVDE compared to the IE group ($P = 0.03$). In dogs with IVDE, there was no association between NOA, NBA and ferritin concentration and severity and duration of clinical signs, and outcome.

It is possible to quantify blood degradation products and ferritin in the CSF. However, larger case numbers are needed to evaluate their relevance as prognostic indicator in dogs with thoracolumbar IVDE.

**THE ODDS OF DEMOGRAPHIC, SOCIAL AND ENVIRONMENTAL FACTORS INFLUENCING THE DEVELOPMENT OF ACUTE CANINE POLYRADICULONEURITIS IN THE UK.**

Immune-mediated diseases, in animals and man, have been linked to factors and triggers that contribute to the pathogenesis of disease. The aim of this study was to identify if the development of acute canine polyradiculoneuritis (ACPRN) is associated with recent vaccination, breed, season, rural/urban habitation, sex, neuter status or age.

A retrospective case-control study with conditional logistic regression analysis was performed. Dogs were selected from a referral hospital population in the UK and controls were matched for year of presentation. 43 cases were identified with ACPRN and 86 controls were selected. Jack Russell Terriers ($P = 0.003$) and West-Highland White Terriers ($P = 0.021$) were found to have a significantly greater odds of developing ACPRN compared to ‘other breeds’ in our population of dogs. The odds of developing ACPRN were greater in the autumn ($P = 0.043$) and winter ($P = 0.032$) compared to spring. Vaccination, rural/urban habitation, sex, neuter status and age were not found to increase the odds of developing ACPRN.

In conclusion breed and season were found to increase the odds of developing ACPRN. This may be important in further understanding the pathogenesis of disease. This may allow identification of triggers or genetics that play a role in ACPRN and allow us to develop breeding programs, avoid triggers or even produce preventative treatments to reduce the prevalence of the disease.

**ACCURACY OF A PATIENT-SPECIFIC 3D-PRINTED DRILL GUIDE FOR VERTEBRAL PEDICLE SCREW PLACEMENT.**

The aim of this study was to develop a patient-specific 3D-printed drill guide for placement of caudal cervical bicortical pedicle screws as part of the treatment of disc-associated wobbler syndrome and to validate its accuracy.

CT scans of the cervical vertebrae from two patients were acquired. These data were exported to medical image processing software and virtual 3D models of the vertebrae created for processing in computer aided design (CAD) software. This was used to determine the optimal trajectory and size of the pedicle screws. For each patient virtual drill guides were created, 3D-printed, and used intraoperatively. Locking titanium screws were used to reduce metal artifact on post-operative CT; screw heads were bonded with polymethylmethacrylate cement to stabilise affected vertebral segments. Post-operative CT was performed for each patient; the degree of vertebral canal violation was subsequently graded as 0 (no violation), 1 (<2mm), 2 (2-4mm) and 3 (>4mm). For each screw CAD files were analysed to yield a screw-diameter-to-pedicle-width-ratio (SDPWR) at the narrowest point of the pedicle; this was expressed as a percentage.

A total of 22 screws were placed; 11 screws were 3.5mm, nine were 2.7mm and two were 2.4mm. 20 screws (90.9%) were grade 0, 2 (9.1%) were grade 1 and no screws were grade 2 or 3. This was achieved despite a mean SDPWR of 73.6 % (range 57.9 – 93.3%).

The use of a 3D-printed patient-specific drill guide permitted accurate placement of bicortical pedicle screws in the caudal cervical
Feline infectious peritonitis (FIP) is the most common infectious central nervous system disease in the cat, and is invariably fatal. Improved means of ante mortem diagnosis are required to facilitate clinical decision-making. Information regarding the magnetic resonance imaging (MRI) findings in cases of FIP is currently limited, resulting in the need for better descriptions to optimize the use of this imaging modality as a diagnostic tool in suspected cases.

The aim of this study was to describe the MRI findings in cases of confirmed neurological FIP. Archived records from 4 institutions were retrospectively reviewed to identify cases with confirmed neurological FIP that had undergone MRI of the brain and/or spinal cord. Signalment, clinical, clinicopathological, histopathological findings and outcome were evaluated.

MRI abnormalities were detected in all 20 cases, including periventricular contrast enhancement (17), leptomeningeal contrast enhancement (18), ventriculomegaly (17), syringomyelia (14) and foramen magnum herniation (12). CSF was analysed in 10 cases, all of which demonstrated a marked increase in both total protein and total nucleated cell count.

All 20 cases were euthanized due to the grave prognosis. The median survival time from onset of clinical signs to euthanasia was 14 days (range 2-105).

Histopathological analysis revealed perivascular pyogranulomatous and/or lymphoplasmacytic infiltrates affecting the leptomeninges in 13 cases, the choroid plexus in 13 cases, periventricular infiltrates in 11, the spinal cord parenchyma in 7 and the brain parenchyma in 3.

MRI provides a sensitive means of detecting neurological FIP, particularly in combination with consistent signalment, clinical presentation and CSF analysis.

SAFETY AND EFFICIENCY OF AN INCREASED STANDARDISED PROTOCOL FOR THE TREATMENT OF MENINGOENCEPHALITIS OF UNKNOWN ORIGIN IN DOGS. C. Ricco, L. Cauzinille. Centre Hospitalier Vétérinaire Frégis, Arcueil France.

Despite being a common diagnosed disease in veterinary neurology, treatment options in literature for méningo-encephalo-myelitis of unknown origin are quite variable and poorly standardised. The use of Cytarabine Arabinoside (CA) (50mg/m² at repeated injections) in combination with prednisolone has been previously reported with variable success rates. The aim of the paper was to determine the efficiency and safety of high dosage CA (100mg/m²) protocol in conjunction with prednisolone and the outcome for dogs according to previously reported variables. These were assessed through a repeated cerebrospinal fluid collection obtained around the 6th CA administration (average - 3,4 months) after the initiation of protocol, records of survival, relapse rates and side effects.

The Chihuahua appeared statistically over-represented in this study in regard to our regular hospital population. Eighty seven percent of dogs (77/89) were alive by the completion of the protocol, 61% were considered to have a positive outcome and 46% of dogs did not require any further CA administration. Thirty percent of dogs (27/89) relapsed during the protocol period and 15% after its completion. Cerebrospinal fluid analysis did not allow to predict relapse in this study. Dogs with a forebrain lesions and a higher initial dose of glucocorticoids had increased odds of a positive outcome. Brainstem lesions appear to carry a worse outcome. The degree of pleocytosis and protein contents at the first CSF collection was not a prognostic factor of outcome.

This (100 mg/M2 SQ for 48h every 3 weeks, 6 times) protocol of CA appears safe and enabled to reduce faster the initial immunosuppressive dosage of prednisolone with lower risks of heavy side effects and a better short term outcome.

GENETICALLY MODIFYING CANINE OLFACTORY ENSHEATHING CELLS FOR SPINAL CORD INJURY REPAIR. D. Carwardine1, E. Muir2, L.F. Wong2, N. Granger1. 1School of Veterinary Sciences, 2School of Clinical Sciences, University of Bristol.

A multitude of factors must be overcome following spinal cord injury. Chondroitin sulphate proteoglycans (CSPGs) of the glial scar present a significant block to axonal regeneration. Digestion of CSPGs by the bacterial enzyme chondroitinase ABC (ChABC) leads to axonal regeneration, neuronal plasticity and functional improvement in rodent spinal cord injury models. However, the enzyme degrades within 24-72 hours at body temperature, limiting its application. Another therapy for spinal cord repair, the olfactory ensheathing cell (OEC) transplant, has been shown to be beneficial in numerous rodent spinal cord injury paradigms and in naturally occurring spinal cord injury in canine patients. OECs support and guide axonal regeneration across the lesion gap. We have genetically modified canine OECs to produce a mammalian ChABC using a lentiviral vector thereby combining these two promising therapies.

We have demonstrated digestion of CSPGs with OECs expressing ChABC in vitro using an enzyme assay and western blotting. In nude rats with dorsal column crush injury, we also observed digestion of CSPGs following transplantation of OECs expressing ChABC. To improve the safety and clinical applicability of the system, we have developed a tetracycline regulated lentiviral vector (Tet-On) capable of switching ChABC production ‘on’ when oral doxycycline is given to the animal. We have achieved efficient lentiviral transduction of neurons and regulatable digestion of CSPGs in vitro and in vivo with the addition or removal of doxycycline.

In conclusion, we have generated a novel cell therapy that we plan to develop further using dogs with naturally occurring spinal cord injury.
KINEMATIC MEASURES FOR ASSESSING GAIT IN DOGS WITH DEGENERATIVE MYELOPATHY. H. Williams,3, S. Sanchis,2, H.A. Volk,2, L. Pelligand4, J. Murrell3, N. Granger.1 1The School of Veterinary Sciences, University of Bristol, Bristol, U.K. 2Queen Mother Veterinary Hospital, The Royal Veterinary College, Hatfield, U.K.

Only 35% of Cavalier King Charles Spaniels (CKCS) with syringomyelia display pain-associated behaviours, but we suspect that a greater proportion experience pain. An objective means of detecting pain in these dogs is lacking. Electronic von Frey aesthesiometer (eVF) testing consists of applying pressure onto the skin via a plastic tip. The pressure value is displayed electronically. Exceeding a certain pressure, defined as the skin sensitivity threshold, triggers a behavioural response from the dog.

We conducted an ethically-approved, two-centre prospective observational study to assess whether the eVF could differentiate, based on cervical skin sensitivity threshold, CKCS with: (i) syringomyelia and clinical signs (syringomyelia-symptomatic – SM-S); (ii) syringomyelia without clinical signs (syringomyelia-asymptomatic – SM-A); and (iii) no syringomyelia (syringomyelia-free - SM-F). All dogs had cervical and caudal fossa magnetic resonance imaging.

Following acclimatisation, the eVF was applied by an investigator blinded to the eVF display and skin sensitivity threshold recorded at C2 and C4 vertebrae bilaterally (three measures per site) and at the right dorsal metatarsal (RH). Data were analysed with multiple analysis of variance including fixed factors (centre, medication, group) and covariates (RH, age, clinical signs duration).

Seventy CKCS were recruited into: SM-S (37), SM-A (15), SM-F (18). No difference in sensitivity was found between groups, except for the RH when analysed as a covariate (p=0.031) but not post-hoc as a dependent variable (p=0.885). Split plot analysis of variance demonstrated differences between cervical sites, independently of syringomyelia group (p<0.001).

In conclusion, eVF assessment of skin sensitivity does not differ significantly by syringomyelia status.

Equine motor neuron disease (EMND), a degenerative polyneuropathy, is characterised by an insidious onset of generalised muscle atrophy, and mild elevations in plasma muscle enzyme activities. Affected horses are paretic and present with an ‘elephant on a drum’ stance and intermittent muscle fasciculation. Ante-mortem, gold standard diagnosis is achieved by biopsy of the sacrocaudalis dorsalis muscle.

In this study, we hypothesised that these classic clinical signs are a manifestation of various neuromuscular problems, rather than being specific for EMND. We retrospectively examined muscle biopsy submissions from horses with suspected EMND and compared them with the final diagnosis.

Of a total of 85 biopsy samples from horses with possible EMND, 24 had neuropathic histological features, of which EMND was diagnosed in 18 (21%). 28 (33%) had various myopathic features, of which 9 (11%) had polysaccharide storage myopathy (PSSM). 24 (28%) biopsy submissions were considered normal and 9 (11%) had an open diagnosis. Of the 9 PSSM cases, 3 were homozygous for the R309H GYS1 mutation responsible for PSSM1, 2 were heterozygotes, 1 was wild type and therefore diagnosed with PSSM2. Genotyping was unavailable for the remaining 3.

This study reveals the high prevalence of primary myopathies in horses suspected to have EMND, in particular of PSSM. It emphasizes the need for additional testing, because the final result would likely influence prognosis and disease management.

BOVINE DORSAL ROOT GANGLIA CULTURE AS AN IN VITRO MODEL FOR LISTERIA MONOCYTOGENES BRAIN INVASION. A. Fadda 1, 3, M. Bärtschi 1, H.R. Widmer 2, A. Zurbriggen 1, A. Oevermann 1

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Listeria monocytogenes (LM) causes rhombencephalitis in humans and ruminants associated with high mortality rates. Previous studies indicated that Schwann cells are a port of entry for brain invasion of LM. The aim of this study was to characterize primary dorsal root ganglia (DRG) cultures from calves slaughtered for food consumption and to assess their suitability as a host specific model for LM infection of peripheral nerves and brain invasion.

Dissociated DRG cultures consisted of neurons, Schwann cells and satellite cells. Neurons survived for more than 4 weeks. Growth factor (GF) supplementation was not required for neuronal survival but promoted neurite outgrowth and branching. Cultures were susceptible to infection with a LM bovine rhombencephalitis isolate (JF5203) from sequence type 1 (lineage I). Bacterial invasion of DRG cells was similarly efficient as that of cell lines, but replication was lower and reached an early plateau phase. Bacteria showed tropism for Schwann and satellite cells and were rarely observed in neurons and axons. Inactivated bacteria were not internalized indicating that invasion of satellite cells involves an active receptor-mediated invasion mechanism rather than phagocytosis. The isogenic InlA-deletion mutant of JF5203 was less efficient in invasion than the parental strain JF5203 suggesting that the bacterial virulence factor Inl-A is involved in satellite cell invasion.

DRG cultures from slaughtered calves represent a useful host specific model for the mechanistic study of peripheral nervous system invasion by LM. Results indicate that neurons are not the primary target and are invaded by non-receptor dependent spread from Schwann/satellite cells.

THE DOG MODEL OF HUMAN BRAIN AGING AND EARLY ALZHEIMER’S DIESASE: A TRANSLATIONAL STUDY OF NEUROPATHOLOGICAL MARKERS. T. Schütt 1

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Canine cognitive dysfunction (CCD) or “canine dementia” is a neurobehavioural syndrome in aged dogs characterized by varying degree of progressive cognitive decline and with certain similarities to the clinical and neuropathological changes associated with Alzheimer’s disease (AD) in humans.

The present study investigated specific markers of brain pathology related to aging and cognitive dysfunction in dogs and compared these findings to human AD neuropathology. The neuropathological investigations included evaluation of amyloid-β (Aβ) plaque deposition (including N-terminally truncated and pyroglutamyl-modified Aβ) and tau pathology in the prefrontal cortex from fifteen aged dogs with normal cognitive function, mild cognitive impairment or CCD and compared with findings in the prefrontal cortex from two young control dogs and human AD sections from human AD subjects.

Cortical Aβ deposition was found to be only of the diffuse subtype as no dense-core or neuritic plaques were found. The Aβ deposition followed a progressive pattern in four maturation stages. Accumulation of the Aβ peptide was also extensively observed in the vessel walls. Both immunohistochemically and biochemically measured levels of Aβ pathology in the prefrontal cortex showed a consistent positive correlation to age but not to cognitive decline. No evidence of neurofibrillary tau pathology was found.

In conclusion, the findings support the senescent dog with spontaneous cognitive dysfunction as a valuable non-transgenic model for further investigations of the molecular events involved in the neurodegenerative processes associated with aging and early stage AD, especially the Aβ-related pathology.

BIDIRECTIONAL BENEFITS OF A NATURALLY OCCURRING CANINE MODEL FOR TESTING AND
Compounds for status epilepticus (SE) have exclusively been developed from drugs for chronic therapy. With 20–40% mortality for SE in both people and dogs, there is a need to develop novel drugs with unique properties. The purpose of these studies have been to validate the canine model of SE via RCTs, and to utilize 4-6 research dog with naturally occurring epilepsy to initially test compounds.

Pharmacokinetic analysis of IV levetiracetam, and IV fosphenytoin was performed in 4-6 research dogs with modeling simulations that led to RCTs for SE of 30-60mg/kg of IV levetiracetam and 15mg/kg phenytoin equivalent of fosphenytoin in 19 and 31 client owned dogs respectively. 10-20mg/kg of a novel formulation of IV topiramate was studied for pharmacokinetic and EEG pharmacodynamic parameters.

The RCT for levetiracetam resulted in a response rate of 56% vs 10% for placebo, and for fosphenytoin of 63% vs 23%. Pharmacokinetic modeling of topiramate indicated that 20mg/kg IV for dogs not on phenobarbital, and 25-30mg/kg for dogs on chronic phenobarbital might potentially be effective for SE. EEG analysis during topiramate administration indicated it had similar spectral changes to 0.5mg/kg IV diazepam. We will be performing similar studies of up to 4 mg/kg IV of allopregnanolone, a novel neurosteroid, over the summer of 2016. In addition, in testing novel IV formulations in the canine model, there is hope for new future therapies of SE for both species.

In conclusion, pharmacokinetic and EEG pharmacodynamic testing of established drugs validated the utility of the canine model. In addition, in testing novel IV formulations in the canine model, there is hope for new future therapies of SE for both species.
Sellar-based masses including pituitary tumors are common in veterinary medicine. Large pituitary masses with a high pituitary/blood (P/B) ratio have historically been difficult to remove and have poorer outcome as compared to tumors with lower P/B ratios. This retrospective and ongoing clinical series is evaluating the intra-operative complications, post-operative care and long-term follow-up of dogs with large sellar masses. The goal is to assimilate this information into an algorithm to aid in surgical decision-making.

The surgical protocol is based on Meij’s original work with the addition of a novel telescope and high-definition camera for excellent magnification and illumination of the surgical field. Our pituitary team consists of a surgeon, neurosurgeon and critical care specialist which all play an integral part in each aspect of the patient’s care.

Twenty-two of 34 dogs (65%) evaluated have a P/B ratio of > 0.70 (normal canine P/B ratio < 0.32) with a mean P/B ratio of 0.95. Preliminary results have been very encouraging with some dogs living greater than 2 and 3 years after surgery, either with complete or incomplete resection of their tumor. Those dogs surviving surgery have improvement in their neurologic status and those with hormonally functional tumors show improvement in their hormonal status. Surgical debulking has been followed with radiation therapy in some dogs with promising results. Median long-term survival is currently being investigated.

Our ongoing evaluation has been encouraging for those dogs with large sellar masses and we have had success removing tumors with a P/B ratio of > 0.70.

TREATMENT OF CANINE FRONTAL AND OLFACTORY LOBE MENINGIOMA WITH EITHER SURGICAL DEBULKING ALONE, SURGERY AND METRONOMIC CHEMOTHERAPY OR SURGERY AND DEFINITIVE RADIATION THERAPY. D. Faissler¹, T. Bentley ², A. Bilderback ³, A. Sato ³, Cummings School of Veterinary Medicine at Tufts University, North Grafton, MA, USA, ² Purdue University, Department of Veterinary Clinical Sciences, Purdue University College of Veterinary Medicine, West Lafayette, IN, ³ Long Island Veterinary Specialists, Plainview, NY, USA.

The goal of this retrospective study was to examine outcome in dogs with frontal lobe meningiomas undergoing transfrontal cranietomy alone (group 1), surgery and metronomic chemotherapy (group 2) or surgery followed by definitive radiation therapy (group 3). In order to examine the influence of tumor location a control group with temporal, parietal, occipital and cerebellar meningiomas treated with surgery alone was enrolled.

Criteria of inclusion were access to complete medical history and information of final outcome. Only dogs discharged from the hospital and free of concurrent disease at the time of diagnosis were included.

Forty dogs with an average of 9.9 years were enrolled. Seizures (n=36) were the most frequent clinical sign. Eight dogs were assigned to group 1, 8 to group 2, and 18 to group 3. The control group included 6 dogs. In group 2 CCNU (n=3) and hydroxyurea (n=5) was used. The median total radiation dose was 48 gray. Life-threatening peri-surgical complications (n=3) included pneumoencephalus, brain herniation and aspiration pneumonia. Two dogs developed histologically proven radiation necrosis. Four dogs are alive, 15 were euthanized for disease progression and 21 for other reasons. Median survival times were the following; Group 1: 9.5 months, group 2: 14.9 months, group 3: 27.6 months and control group: 30.5 months.

In frontal lobe meningiomas surgery and radiation therapy have the best survival (p=0.049) similar to non-frontal cases treated with surgery alone, most likely due to the more complete tumor removal in this group. Metronomic chemotherapy does not significantly extend survival time.

PACLITAXEL RELEASING MESENCHYMAL STROMAL CELLS TREATMENT IN CANINE GLIOMAS. O. Zeira¹, E. Ghezzi¹, M. Aralla¹, N. Asig¹, M. Konar¹, A. Pessina², G. Alessandrini³. ¹San Michele Veterinary Hospital, Tavazzano, Italy; ²Dept. of Medical Science, University of Milan, Italy; ³Stroke Unit, Ist. Neurologico Besta, Milan, Italy.

Mesenchymal stromal cells (MSCs) are able to upload and release drugs. MSCs preloaded by paclitaxel (MSCsPTX) have a strong anti-tumor activity, both in vitro and in vivo, due to their homing capacity towards the tumor and its microenvironment.

Our study evaluates safety, feasibility and efficacy of MSCsPTX as growth inhibitor of canine gliomas.

After harvesting bone marrow (BM) from dogs and generating BM-MSCsPTX, we evaluated, in vitro, their activity on canine gliomas by means of binding the tumoral cells and their anti-angiogenesis activity.

Three dogs with brain gliomas, diagnosed by clinical signs, MRI characteristics and histologic exam, underwent treatment schedule consisting of: day 0- MSCsPTX administrated intrathecally; day 5- temozolomide (100 mg/m² for 5 days every 28 days); day 15- MSCsPTX administrated intravenously. Schedule has been repeated for 5 months. Other three dogs were treated with temozolomide only. All patients had no other treatments. Follow-up included neurologic exam and MRI 3 months after the beginning of treatment.

In vitro results showed a considerable killing activity of BM-MSCsPTX; no adverse effects followed BM-MSCsPTX administration. Neurologic exams were normal. MRI showed no further tumor development in the first group.

The results suggest that BM-MSCsPTX may be a safe and feasible optional treatment for canine gliomas.

EVALUATION OF A MODIFIED TRANSFRONTAL CRANIOTOMY TECHNIQUE IN 8 DOGS. R.T. Bentley¹, S.A. Thomovsky¹. ¹Dept. of Veterinary Clinical Sciences, Purdue University College of Veterinary Medicine, West Lafayette, IN, USA.

The study purpose was to evaluate a modified transfrontal surgical approach providing greater rostral cerebral and falceine access. Medical records were searched for dogs undergoing transfrontal craniotomy, and data retrieved regarding signalment, surgical procedure, complications, histopathologic diagnosis and outcome. Patients were predominantly large mixed-breed dogs, median age 9.5 years (range 3.6 – 14.3), including 7 spayed females and 1 castrated male.

A sagittal saw used to create a diamond-shaped opening in the frontal sinus. The rostral portion of the diamond was conventional in
shape and design. Caudally, the bony opening was enlarged laterally compared to the conventional approach, via exposure enhanced by temporalis elevation. This afforded 68% (95% CI, 42 – 93%) wider access to the mid-frontal lobes when pre-operative imaging was assessed.

The procedure was easily combined with rostrotemporal craniectomy (n=2). Median surgical time was 280 minutes (first 4 cases) or 170 minutes (subsequent 4 cases). Five dogs suffered complications but recovered fully: CSF rhinorrhea, cutaneous infection, subcutaneous emphysema, aspiration pneumonia, prolonged neurological recovery. There was 1 peri-operative death. Median hospitalization was 6 days. Magnetic resonance imaging confirmed complete resection (n=5). Diagnoses were meningioma (n=4), oligodendroglioma (n=3) and granuloma (n=1). Euthanasia occurred due to recurrence (n=2; 9 and 12 months) and unrelated disease (n=1; 8 months). Four patients remain alive (1–10 months). Median survival (Kaplan-Meier analysis) was 22 months.

A diamond-shaped opening of the frontal sinus, made wider caudally via elevating temporalis musculature, provides excellent access to the mid-caudal frontal lobes. Despite short-term complications, long-term outcome can be excellent.

**IL-6 IS INCREASED IN CSF AND PLASMA OF DOGS WITH ACUTE ISCHAEMIC STROKE.** H. Gredal1, B. Thomsen1, A. Boza-Serrano2, L. Garosi1, C. Rusbridge4, D. Anthony5, A. Möller6, B. Finsen7, T. Deierborg1, K. L. Lambertsen2,8, M. Berendt1.

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Inflammatory cytokines are potential modulators of infarct progression in acute ischaemic stroke. They are therefore possible targets for new treatment strategies in humans. From a translational research perspective, dogs with spontaneous ischaemic stroke offer an opportunity of studying the cytokine response in a non-invasive setup, and thus may complement current experimental stroke models.

The aim of our study was to investigate cytokine concentrations in plasma and cerebrospinal fluid (CSF) in dogs with acute ischaemic stroke, and to search for correlations between infarct volume and cytokine concentrations.

Blood and CSF were collected from dogs less than 72 hours after a spontaneous ischaemic stroke. Infarct volumes were estimated on magnetic resonance images. IL-2, IL-6, IL-8, IL-10 and TNF in plasma, CSF and brain homogenates from the infarct core were measured employing a canine-specific multiplex immunoassay and compared to healthy control dogs. IL-6 was significantly increased in plasma \((P = 0.04)\) and CSF \((P = 0.04)\) in stroke dogs compared to healthy controls. The concentrations of other cytokines, such as TNF and IL-2, were unchanged. Plasma IL-8 levels correlated significantly with infarct volume (Spearman \(r = 0.8, P = 0.013\)).

The findings of increased concentrations of IL-6 in CSF and plasma in dogs compare to previous findings in humans. This suggests that the inflammatory response in dogs with spontaneous stroke resembles that in humans, and that dogs could provide alternative opportunities for studies of the inflammatory processes that accompany stroke.
POSTER PRESENTATIONS
No updates for canine peripheral nerve sheath tumors (PNST) appeared in recent literature. The aim of this study was to evaluate the correlation between clinical aspects and MRI findings of tumors involving a major peripheral nerve, plexus or root and to determine the survival time in dogs treated with palliation, surgery or stereotactic radiotherapy (SRT).

Records of dogs with PNST evaluated from 2000 to 2014 were reviewed to determine signalment, duration of clinical signs, neurological examination, MRI features, treatment option (palliation, surgery, stereotactic hypo fractionated radiotherapy). Time to first event, survival times and statistical differences across categories were calculated by the Kaplan-Meier product limit method and log-rank test.

Forty-seven dogs (median age 9 years, male:female ratio 1.76) were included, with Labrador retrieveroverrepresented (17%). Roots lesions were the most frequent (46.8%), with C5-T1, V nerve and left side more involved (25.5%, 19.1% and 61.7%). Presenting sings were lameness, paresis and pain. Mean duration of clinical signs was 90 days. MRI findings comprises increased diameter, hyper intense and contrast enhancing nerve roots (57.1%), plexus or peripheral nerve (42.9%), focal hypomiotropy and muscle hyper intensity (73%). The time to first event was 30 days after surgery and 240 days after SRT. Overall mean survival was 97, 144 and 371 days with palliation, surgery and SRT. A predilection for Labrador retriever is observed.

Comparing our results with published data, SRT seem to promise better results than palliation or surgery and warrant further evaluation.

**CONTRAST-ENHANCING EXTRA-AXIAL CENTRAL NERVOUS SYSTEM MASSES IN DOGS: MAGNETIC RESONANCE IMAGING DIFFERENTIAL DIAGNOSES FOR MENINGIOMA.** R.T. Bentley1, S. Carrera-Justiz2, S.A. Thomovsky1. 1Dept. of Veterinary Clinical Sciences, Purdue University College of Veterinary Medicine, West Lafayette, IN, USA, 2Dept. of Small Animal Clinical Sciences, University of Florida College of Veterinary Medicine, Gainesville, FL, USA.

Limited information is available to inform differential diagnoses for meningiomas on canine magnetic resonance imaging (MRI). A retrospective study and a literature review of lesions with similar imaging appearance to meningioma was performed. Inclusion criteria were contrast-enhancing intra-dural extra-parenchymal MRI mass lesions and histologic confirmation. Brain and spinal lesions were eligible. Meningiomas and ventricular lesions were excluded. We investigated radiologic criteria that could aid in differentiating other etiologies from meningiomas.

Nineteen cases were retrospectively identified. Brain histological diagnoses included: histiocytic sarcoma (n=2), granuloma (n=2), glioma (n=2), and craniopharyngioma (n=2). There were single cases of granular cell tumor, hemangioblastoma, hematoma, esthesioneuroblastoma, gliomatosis cerebri and germ cell tumor. Spinal lesions included two intradural-extraduralmyelopathy nerve sheath tumors, two nephroblastomas and an undifferentiated sarcoma. Irregular or indistinct margins were useful in discriminating from meningioma. Craniopharyngioma and germ cell tumors were seen in the sella turcica region only. Otherwise, these lesions could not be readily distinguished from meningioma.

Literature review identified 93 cases, highlighting the frequency with which the following lesions are described as contrast-enhancing extra-axial masses or preliminarily diagnosed as meningiomas: pituitary adenoma, nerve sheath tumors (trigeminal and spinal), granular cell tumor, lymphoma, glioma, fungal granuloma and histiocytic sarcoma. Sarcoma, metastasis and various sporadic pathologies were rare.

Many neoplasms and granulomas can have similar or identical MRI appearance to meningioma. A poorly defined or irregular margin on MRI might decrease the suspicion of meningioma. Differential diagnoses for sella turcica masses should include craniopharyngioma and germ cell tumor.
Gliomas are among the most vascularized human solid tumours and are related with their poor prognosis. While neovascularization occurs by vasculogenesis in embryonic stages, angiogenesis is mostly related with adult tissue development. However, there are five different mechanisms by which gliomas achieve neovascularisation: vascular co-option (CO), angiogenesis, vasculogenesis, vascular mimicry (VM) and glioblastoma endothelial cell transdifferentiation. The objective of this study is to evaluate the neovascularization features of spontaneous canine gliomas.

Eighteen spontaneous canine gliomas were retrospectively selected from the databases of the Mouse and Comparative Pathology Unit of the Universitat Autònoma de Barcelona, including 12 anaplastic oligodendrogliomas, 3 oligodendrogliomas and 3 glioblastomas. Vascular features were evaluated by slides stained with Hematoxylin-Eosin. The immunohistochemical study was performed by a semiquantitative evaluation of representative fields using CD31 as a mature endothelial cell adhesion protein marker and VEGFR-2 as an angioblast plasmatic membrane receptor cell marker.

The morphological study showed that low-grade gliomas (LGG) mostly display a generalized capillary proliferation and high-grade gliomas (HGG) mostly contains capillary glomeruloid formations (GC) in peripheral areas. Self-organization of neoplastic cells with presence of CO mechanisms were present in LGGs while MI was only present in HGGs. No expression of vascular markers was observed in CO or VM areas, confirming that they occur independently of endothelial proliferation. GC showed a variable CD31+/VEGFR-2+ cells, indicating their high angiogenic potential in HGG. These results are similar than those described in human gliomas indicating that vascular markers are useful for to localize neurogenic areas as therapeutic targets.

Transsphenoidal hypophysectomy (TSH) is an effective therapy for functional pituitary corticotroph adenomas; however, little is known about the clinical presentation and outcome of non-functional sellar masses following TSH. The purpose of this study was to characterize the clinical features and outcome post-TSH in dogs with non-functional sellar masses.

Medical records were retrospectively reviewed for historical and neurological findings, histopathological diagnosis, and outcome. Ten dogs had TSH performed as therapy for their non-functional sellar masses. The Bulldog was the most common breed represented (4 dogs) and all but one breed represented were brachycephalic. Median body weight was 22.5 kg and median age at time of diagnosis was 8.8 years. Six dogs had a history of progressive dullness, 3 dogs had behavior or personality changes, 2 dogs had head or generalized tremors, and 2 dogs had vision loss. Neurologic findings included: dull mentation (7 dogs) with the other 3 dogs reported to be obtunded, delayed or absent conscience proprioception (5 dogs), and ataxia (3 dogs). Histopathology revealed that 4 dogs had chromophobe pituitary adenomas, 2 dogs had meningiomas, and one each of the following tumor types was seen: pars intermedia adenoma, ependymoma, cranioopharyngioma, and chromophobe pituitary adenocarcinoma. Overall median survival post-TSH was 232 days (range 0-1190 days). Median survival for dogs with adenomas was 847 days (range 182-1190 days).

Peripheral nerve sheath tumors (PNST) affecting the trigeminal nerve are relatively uncommon in dogs and few literature data regarding the best treatment are available.

The aim of this work was to evaluate the feasibility and effectiveness of curative high dose hypo fractionated frameless Volumetric Modulated Arc Radiotherapy (VMAT). The primary endpoints were the recurrence or the progression of the tumor, the death from any cause and the death from the considered disease.

A prospectic clinical trial was conducted from February 2010 to December 2013 on client-owned dogs with presumptive imaging-based diagnosis of trigeminal PNST. The treatment was performed using a 6 MV linear accelerator equipped with an external beam micro-multileaf collimator. The plans were computed with Montecarlo algorithm. Overall survival was estimated using the Kaplan–Meier product method.

Seven dogs were enrolled and treated with 37 Gy in 5 fx. MRI follow-up examinations revealed complete response in 1 dog, partial response in 4 dogs, stable disease in 2 dogs as the best treatment results. No major complications occurred. One dog develop disease progression at 483 days and deceased for proven relapse at 523 days. Considering all deaths, mean and median overall survival were, respectively, 609 days (range, 313-952) and 952 days.

Comparing the obtained survival with previously published studies, VMAT appears to be safe, effective and offer the best median survival time in dogs suffering from trigeminal PNST. Due to the rarity of intracranial canine PNST, further multi center cooperative trials are advisable.
RE-OPENING THE WINDOW ON USE OF FENESTRATION FOR TREATMENT OF ACUTE THORACOLUMBAR DISC HERNIATION IN DOGS. P. Freeman¹ & N. Jeffery². ¹Department of Veterinary Medicine, University of Cambridge, Cambridge, UK. ²Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University, Ames, USA.

Acute thoracolumbar intervertebral disc herniation in dogs is a common cause of ‘back’ pain, pelvic limb paresis or paralysis and incontinence. Treatment of this condition has long been a source of controversy, especially since the introduction of surgical interventions in the 1950s. Unfortunately, formal clinical trials to compare efficacy of conservative and surgical interventions have never been carried out and the current lack of clinical equipoise on this subject now precludes such a trial on ethical grounds. In this presentation we re-examine and discuss previously published data on recovery associated with the various therapies, focusing on evidence suggesting that decompressive surgery and fenestration may be equally efficacious. The results of this study cast doubt on the currently perceived superiority of decompressive surgery for the treatment of Hansen type 1 herniations in dogs, and may pave the way for a prospective clinical trial comparing fenestration and decompression.

MULTISLICE COMPUTED TOMOGRAPHY FOR THE DETECTION OF COMPRESSIVE HYDRATED NUCLEUS PULPOSUS EXTRUSION IN DOGS. E. Royaux¹, I. Gielen², K. Kromhout³, E. Van der Vekens³, B.J.G. Broeckx¹, L. Van Ham¹, V. Martlé³. ¹Department of Small Animal Medicine and Clinical Biology, Faculty of Veterinary Medicine, Ghent University, Belgium. ²Department of Veterinary Medical Imaging and Small Animal Orthopedics, Faculty of Veterinary Medicine, Ghent University, Belgium. ³Laboratory of Pharmaceutical Biotechnology, Faculty of Pharmaceutical Sciences, Ghent University, Belgium.

Compressive hydrated nucleus pulposus extrusion (HNPE) is defined as an acute extradural compressive lesion consisting of hydrated nucleus pulposus material, occurring at the level of the associated intervertebral disc in dogs. Magnetic resonance imaging (MRI) is the imaging modality of choice to diagnose HNPE. This study examines the possibility to detect compressive HNPE with computed tomography (CT). A first objective of the study was to determine the capability of CT to detect HNPE and to describe the CT characteristics. The second objective of the study was to determine the sensitivity and specificity of CT to detect HNPE.

A retrospective analysis of the clinical and imaging data of dogs diagnosed with compressive HNPE on MRI was performed. Both CT and MR images had to be available to be included. The CT images of MRI confirmed cases were assessed by a non-blinded image reader to define the CT characteristics. The sensitivity and specificity of CT to detect a cervical HNPE was determined by 2 blinded observers using a control group of dogs with acute type 1 disc disease.

HNPE was characterized on CT as a hypodense extradural compressive lesion dorsal to the intervertebral disc space with rim enhancement on postcontrast images. The sensitivity and specificity to detect HNPE with CT was respectively very good (91%) and excellent (100%). CT is a useful technique to detect compressive HNPE in dogs. However, if no clear lesion is identified with CT or if information about intramedullary changes is needed, MRI still needs to be performed.

ENGINEERING CANINE OLFACTORY CELL GRAFTS USING MAGNETIC PARTICLE MEDIATED DELIVERY OF THERAPEUTIC GENES: IMPLICATIONS FOR CANINE SPINAL INJURY. C Adams¹, A Delaney¹, D Carwardine², A Fernandes¹, A Al-Shakli¹, N Granger¹, D Chari¹. ¹Cellular and Neural Engineering Group, Institute of Science and Technology in Medicine, Keele University, Keele, UK. ²School of Veterinary Sciences, University of Bristol, Bristol, UK.

A clinical trial in spinal cord injured dogs demonstrated that implantation of autologous canine olfactory mucosa cells (cOMCs) lead to recovery of some motor function. However, not all dogs responded to cOMCs and there was no improvement in long-tract functionality. One strategy to enhance transplant-mediated regeneration is genetically engineering cOMCs to release therapeutic biomolecules. To achieve this clinically, magnetic particle (MP) based vectors are emerging as key non-viral alternatives for genetically engineering therapeutic cell populations. In particular, magnetofection with various magnetic fields has been shown to safely and efficiently transfect a range of neural cells.

Here, we optimised MP mediated gene delivery to cOMCs and demonstrated delivery of Brain Derived Neurotrophic Factor (BDNF; shown to promote repair in spinal injury) encoded by the advanced minicircle vector platform. Along with MPs, minicircles have significant advantages for translation compared to conventional plasmids, resulting from bacterial backbone removal. Therefore, they can incorporate larger genes, do not undergo transcription silencing and do not elicit immune responses, leading to higher safety.

Under the no-field condition, 86 +/- 0.8% of cells displayed MP uptake and 34.9 +/- 2.9% expressed the reporter gene. These values were significantly enhanced by application of all tested magnetic fields to ca. 95% (MP uptake) and 55% (transfection efficiency) whilst maintaining high cOMC viability. Minicircle encoded BDNF was successfully delivered to cOMCs (transfection efficiency of 8.1 +/- 0.3%) resulting in a fourfold concentration increase of BDNF in conditioned media (transfected cells versus controls)

This is a major refinement of the cOMC therapy now requiring testing in the clinic.

URODYNAMIC CHARACTERISTICS OF NEUROGENIC BLADDER DYSFUNCTION IN THE CANINE CLINICAL MODEL OF SPINAL CORD INJURY. Granger, NJ; Hu, HZ; Kichler, V²; Marko, C; Jeffery, ND. ¹School of Veterinary Sciences, University of Bristol, Bristol, UK. ²Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University, Ames, USA.

Supra-sacral spinal cord injury, common following intervertebral disc herniation in dogs, causes dysfunction of urine storage and
voiding leading to urinary incontinence and retention. Severe dysfunction of this nature is currently incurable and may lead to serious, even fatal, secondary complications.

Our objectives in this study were to characterise lower urinary tract dysfunction in chronic supra-sacral spinal cord injury in dogs and analyse the relationship of bodyweight, chronicity and severity of injury with bladder compliance, to serve as baseline data for future clinical trials using this natural animal model.

After receiving ethical permission, we prospectively recruited dogs as part of randomized clinical trials on treatment for severe chronic (>6 weeks) thoracolumbar spinal cord injury for cystometric evaluation. Relationships of bodyweight, chronicity and severity of injury with compliance were analysed using logistic regression. In 84 dogs, mean bladder capacity was 73% of that expected for bodyweight. 58 dogs (69%) had premature urine leakage. Of 38 dogs in which it was measured, 21 (55%) had unprovoked involuntary detrusor contractions (median=3 contractions/cystometry – range= 1-11) during bladder filling with bladder pressure reaching a mean of 32.2cmH\textsubscript{2}O (range=10-54cmH\textsubscript{2}O). 58/84 dogs had reduced bladder compliance (defined as <12.5mL/cmH\textsubscript{2}O) with a median of 5.8mL/cmH\textsubscript{2}O (range=2.8-16.5mL/cmH\textsubscript{2}O). Compliance was not associated with bodyweight, chronicity or severity of injury.

This population of spinal cord-injured dogs exhibited many features of lower urinary tract dysfunction also found in injured humans. It constitutes an available model to test putative therapies for abrogating the loss of bladder control caused by severe spinal cord injury.

**SPONTANEOUS REGRESSION OF LUMBAR HANSEN TYPE1 DISK EXTRUSION DETECTED WITH COMPUTED TOMOGRAPHY IN A CAT.** H. Ueno\textsuperscript{1}, S. Tsubakishita\textsuperscript{2}, A. Hori\textsuperscript{1}, K. Miyoshi\textsuperscript{1}, T. Uchide\textsuperscript{3}, 1) Department of Small Animal Clinical Sciences, School of Veterinary Medicine, Rakuno Gakuen University 2) Department of Veterinary Nursing Sciences, School of Veterinary Medicine, Rakuno Gakuen University, Ebetsu, Hokkaido, 069-8501 Japan.

Case Description—Age-indeterminate sexually neutered male Japanese short hair domestic cat was evaluated because of acute signs of back pain and paraparesis of pelvic limbs.

Clinical Findings—Neuroanatomic localization indicated a lesion in the T3-S3 spinal cord segment from the results of neurological examinations. Computed tomography (CT) revealed extradural spinal cord compression at the ventral aspect (from center to the right) of the intervertebral disk space L6-7. On the basis of these findings, a diagnosis of sequestrated Hansen type 1 disk extrusion was made.

Treatment and Outcome—Cauda equina decompression was achieved by dorsal laminectomy. The extruded disk material could not be removed completely. Although postoperative CT showed the decrease of the nerve root pressure compared with pre-operation, CT also revealed the remains of approximately 90% of intervertebral disk materials in comparison with pre-operation. Therefore, the cat was treated conservatively with cage rest and NSAIDs. Following surgical decompression, the cat was also received physical rehabilitation protocols such as passive range of motion exercises, massage of limb muscles and supported standing exercises during hospitalization. The rehabilitation activities were allowed to continue this activity after discharge. Results of follow-up examination 7 weeks later indicated complete resolution of clinical signs, and results of repeated CT indicated complete reduction of the herniated disk material.

Clinical Relevance—Findings for the cat of this report indicated spinal cord compression attributable to extruded intervertebral disk material resolved. Functional improvements in the cat with such problems may be partly attributable to spontaneous regression of intervertebral disk extrusions.

**ELECTROPHYSIOLOGICAL EVIDENCE OF SPINAL CORD PLASTICITY IN DOGS WITH CHRONIC SEVERE SPINAL CORD INJURY.** Granger, N\textsuperscript{1}, Hu, HZ\textsuperscript{2}, Jeffery, ND\textsuperscript{2}. 1 School of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University, Ames, USA, 2 Department of Veterinary Clinical Sciences, College of Veterinary Medicine, University of Bristol, Bristol, UK.

Estimation of the severity of thoracolumbar spinal cord injury (SCI) following canine intervertebral disc herniation relies on neurological examination. Cases lacking conscious pain perception (CPP) are problematic because: (i) many will recover but predicting an individual’s prognosis is not possible; and (ii) assessing CPP is not standardised or truly objective. Having a means of objectively teasing out different severities of SCI within the ‘deep pain negative’ group would be useful.

Our objective in this study was to describe the presence/absence of ascending somatosensory evoked potentials (SSEPs) and descending transcranial magnetic motor evoked potentials (TMMEPs) in the chronic phase of SCI in dogs.

After receiving ethical permission, we prospectively recruited 82 dogs as part of randomized clinical trials on treatment for severe (lacking CPP) chronic (>6 weeks) thoracolumbar SCI for electrophysiological evaluation under sedation. In 31 dogs in which brain recording was done, SSEPs could be detected over the left cortex in 9 (29%) (latency=25.5 +/-2.9ms, amplitude=0.318 +/-0.196μV) and over the right cortex in 5 (16%) (latency=27.9 +/-3.0ms, amplitude=0.523 +/-0.323μV) with 5 dogs having detectable waves bilaterally. In 51 dogs, we attempted to record sensory evoked spinal potentials but no wave could be recorded above the lesion. Of 82 dogs, TMMEPs could be detected in the left pelvic limb in 16 (19%) (latency=57.4 +/-23.0ms), in the right pelvic limb in 13 (16%) (latency=54.0 +/-16.7ms), and bilaterally in 9 dogs.

Dogs lacking CPP can be divided into 2 groups based on the presence/absence of SSEPs/TMMEPs. This distinction might help case selection to test putative therapies for SCI repair.

**DIFFERENTIAL DIAGNOSIS BETWEEN PRESUMED SPINAL GRANULOMATOUS MENINGOENCEPHALOMYELITIS AND INTERVERTEBRAL DISK DISEASE IN THE DOG.** H. Ueno, A. Hori, K. Miyoshi. Department of Small Animal Clinical Sciences, School of Veterinary Medicine, Rakuno Gakuen University, Ebetsu, Hokkaido, 069-8501 Japan.
OBJECT—The dogs with granulomatous meningoencephalomyelitis (GME) in spinal cord often show hyperesthesia and/or ataxia. Therefore, the differentiation between GME and ambulant intervertebral disk disease (IVDD) would be difficult. The aims of the present study are to clarify the differentiation between spinal GME and IVDD and to let treatments of spinal GME succeed.

RESEARCH OUTLINE—Medical records of client-owned 8 suspected spinal GME dogs were reviewed. Signalment, clinical symptoms, treatment before diagnosis, CSF analysis, MRI, treatment after diagnosis, period from the onset to clinical diagnosis, survival time after diagnosis were reviewed. Mann-Whitney U-test was used, where applicable.

RESULTS—Six of eight dogs were chondrodystrophoid breed, and the referral veterinarians presumed IVDD. Although MRI detected only a spinal lesion in 4/8 dogs, the symptoms and complete neurological examination indicated the abnormalities of both spinal cord and brainstem. CSF analysis revealed a mononuclear pleocytosis and/or increased protein level. The treatments before diagnosis were divided into two groups (steroid-based [ST1] group; 4/8, non-steroid-based [NST] group such as NSAIDs or AED administrations; 4/8). The period from the onset to clinical diagnosis of ST1 was longer than NST significantly. The treatments after diagnosis were divided into two groups (ciclosporin-based [CS] group; 5/8, steroid-based [ST2] group; 3/8). The survival time of CS was longer than ST2 significantly.

CONCLUSION—Because the symptoms referable to both spinal cord and brainstem were seen in all 8 dogs, the veterinarian should perform the prudent and complete neurologic examination even if the dogs show only hyperesthesia and/or ataxia. When the ambulant dogs suspecting IVDD do not show any improvement with medication, the veterinarian should consider MRI and CSF analysis for the differential diagnosis and for beginning of immunosuppression.


An 8-week-old intact female Chihuahua was evaluated for acute tetraparesis progressing to non-ambulatory paraparesis. On neurologic examination, the patient was non-ambulatory tetraparetic with subtle motor and ataxia in the thoracic limbs and mild motor in the pelvic limbs. There was increased extensor tone with normal reflexes in all four limbs. Placing responses were absent in all four limbs and hopping was decreased to absent in all four limbs. The dog demonstrated discomfort over the calvarium and cervical spine. The neuroanatomic localization was to the cervical spine, with or without the involvement of the brain, based on the hyperesthesia.

Ultrasound assessment of the cranium ruled out hydrocephalus and was used further to assess the craniocervical junction. A small curvilinear ultrasound probe was applied to the cranial neck and the C1 and C2 vertebrae were visualized in extension and with mild flexion. There was repeatable distraction of these bony landmarks and visualization of the spinal cord revealed kinking at the level of the atlanto-axial articulation. Radiographs and CT were performed to corroborate the suspected ultrasound diagnosis of atlantoaxial subluxation.

The relative safety of this procedure makes it more favorable than traditional radiography that usually requires flexion of the neck and can require general anesthesia. This imaging modality may be limited in its success to very young animals which are skeletally immature. Ultrasound can also potentially provide a more cost-effective preliminary diagnostic tool prior to pursuing more expensive diagnostics such as CT and MRI.

PHENOBARBITAL OR POTASSIUM BROMIDE AS AN ADD-ON ANTI-EPILEPTIC DRUG FOR THE MANAGEMENT OF CANINE IDIOPATHIC EPILEPSY REFRACTORY TO IMEPITOIN. E. Royaux1, L. Van Ham1, B. Broeckx2, I. Van Soens3, I. Gielen4, D. Deforce2, S. Bhatti1. 1Department of Small Animal Medicine and Clinical Biology, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium, 2Laboratory of Pharmaceutical Biotechnology, Faculty of Pharmaceutical Sciences, Ghent University, Ghent, Belgium, 3Companion Animal Internal Medicine Section, Faculty of Veterinary Medicine, Liège University, Liège, Belgium and Orion Veterinary Clinic, Noorderwijk, Belgium, 4Department of Medical Imaging of Domestic Animals and Orthopaedics of Small Animals, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium.

Imepitoin has recently been registered for the management of dogs with idiopathic epilepsy (IE). Currently, there is no evidence-based information available on which antiepileptic drug (AED) to add to the treatment of dogs with IE that are not well controlled with imepitoin.

The goal of this study was to evaluate the efficacy of phenobarbital (PB) or potassium bromide (KBr) as an add-on AED for controlling dogs refractory to a maximum dose of imepitoin. The study was performed as a prospective, randomized, controlled clinical trial. The efficacy of PB or KBr was evaluated by comparing monthly seizure frequency (MSF), monthly seizure day frequency (MSDF) and the presence of cluster seizures during a retrospective 2-month period with a prospective follow-up period of 8 months. The 50% responder rate (RR) was investigated. Twenty-seven dogs were included in the study, 14 dogs in the PB group and 13 dogs in the KBr group. A significant decrease in median MSF and MSDF was found in the PB group (P=0.001 and P=0.001, respectively) and in the KBr group (P=0.004 and P=0.003, respectively). Overall, the number of dogs with cluster seizures decreased significantly (P=0.0005). The RR was 79% vs. 69% in the PB and KBr group, respectively.

We conclude that PB or KBr add-on treatment efficiently decreases median MSF and MSDF in dogs refractory to a maximum dose of imepitoin. Combination therapy was generally well tolerated and resulted in an improvement in seizure management in the majority of the dogs.

THE MR VOLUMETRIC BRAIN ASSESSMENT IN CANINE EPILEPTIC PATIENTS – A PILOT STUDY. M. Wrzosek, P. Podgórski, P. Drobot, W. Bodys, J. Nicpoń. Department of Internal Medicine and Clinic for Horses, Dogs and Cats, Center of Experimental Diagnostics and Innovative Biomedical Technology, The Faculty of Veterinary Medicine, Wroclaw University of
Canine epilepsy MR imaging is still a diagnostic challenge for veterinary professionals. MR volumetry is technique of non-invasive volume measurement of the selected anatomical structures, that could allow to determine a possible structural changes in a CNS. Quantitative MR imaging in humans exceeds the findings of visual inspection of clinical MR imaging studies. The aim of the work is to study the canine brains in terms of its volumetric construction designed to demonstrate the possible brain volume changes in canine epileptic patients as a possible model for human patients.

The study was carried out on 22 MRI scans (1.5T Ingenia Philips), 13 dogs with diagnosed idiopathic epilepsy (according to IVETF guidelines), 9 normal control. All dogs were patients of the Department of Internal Medicine and Clinic for Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Poland. Analyzed MRI research dimensional sequence were T1-weighted (sTIW_3D, TE 5.2, TR: 25.0, FOV: 220, layer thickness: 0.8 mm, GAP: -0.4 mm, voxel size: 0.75x0.75x0.375). The analysis was conducted by using Slicer software (version 4.5.0). A ratio of ventricular system to brain tissue (V-B) was counted with special reference for white to gray matter (W-G) comparison. There was a significant difference in a V-B ratio in between the IE and control groups (respectively, 0.0056 to 0.0153) found, and no difference in the W-G ratio (0.261 to 0.232). These preliminary results suggest a possible reduce of the brain volume in epileptic patients with a preservation of the white-to gray matter ratio.

EPILEPSY AND COMPULSIVE DISORDERS IN DOGS. C. Escriou, M. Garrone. Unité de neurologie, VetAgro-Sup, Université de Lyon, Campus vétérinaire de Lyon, Marcy L’Etoile, France

There is a long-recognized association between obsessive–compulsive disorder (OCD) and chronic epilepsy in humans, most notably refractory temporal lobe epilepsy (TLE). In dogs, neurobehavioral comorbidities associated with development of epilepsy have been recently demonstrated. Compulsive disorder (CD) are well described in dogs with breed specific CD like breed specific idiopathic epilepsy. Our aim was to assess the association between CD and idiopathic epilepsy in a comparative design.

50 dogs diagnosed with idiopathic epilepsy in the neurology unit of a university referral center between the 01/01/2010 and the 31/12/2014 were enrolled. All dogs completed Tier 1 and Tier 2 diagnostic approach proposed by the “international veterinary epilepsy task force”. 100 healthy non-epileptic dogs (2 healthy dogs (same breed, same age) for one epileptic dog) chosen in the referral center clinical database were enrolled as control. Owners were asked to complete a questionnaire designed to assess the presence or absence of all CD described in dogs during a telephone conversation conducted by always the same investigator.

Significant association were found between the CD pacing, head bobbing, self-biting, face- rubbing, self-licking, inanimate objects aggression, whining, chewing or eating objects, and polyphagia – polydipsia. Head bobbing and inanimate objects aggression was neither reported in control dogs.

Although antiepileptic drugs can induce some CD like polyphagia-polydipsia, our study is the first to assess comorbidities between CD and idiopathic epilepsy in dogs. As some CD remains infrequent behavior, our results probably underestimate their link with idiopathic epilepsy and increasing statistical strength of the study with larger population is mandatory.

AN ASSESSMENT OF NEURONAL CELL BODY AND SYNAPTIC TERMINAL DENSITY IN THE SPINAL CORD AND RED NUCLEUS OF CANINE DEGENERATIVE MYELOPATHY. L.Henderson1, P.E.Johnston1, L.Stevenson1, J.Leach1, T.J.Anderson1, M.McLaughlin1. 1School of Veterinary Medicine, College of MVLS, University of Glasgow.

Canine degenerative myelopathy (DM) is a late onset disorder characterised by progressive general proprioceptive ataxia and paresis of the pelvic limbs which progresses to affect the thoracic limbs. A missense mutation (118G>A) in the superoxide dismutase 1 gene (Sod1) is associated with DM but it is unclear how this mutation leads to the disease.

The purpose of this study was to determine if pathology in specific anatomical regions could account for clinical features of the disease. Specifically, we investigated whether the accumulation of SOD-1 in neurons impacted on the density of neuronal cell body and synaptic terminals in the thoracic and cervical regions of the spinal cord and the red nucleus. Immunohistochemistry was performed on paraffin embedded sections from both control and DM cases and staining intensity was quantified using Image J software. SOD1 staining was higher in spinal cord regions of DM dogs compared with controls but the density of neuron cell bodies was comparable. The synaptic density was unchanged in both the thoracic or cervical spinal cord. However, in the red nucleus, SOD1 staining was comparable between control and DM but synaptic density was significantly decreased in DM.

In conclusion, the results of this study suggest the accumulation of SOD1 does not alter neuronal density, however it has an impact on synaptic density in the red nucleus, one of the brainstem nuclei involved with motor co-ordination and may relate to clinical features associated with DM. Ethical approval was granted for use of all tissues in this study.

VISUALIZATION OF INTRACRANIAL VESSELS IN TOY-BREED DOGS USING THREE DIMENSIONAL TIME-OF-FLIGHT MAGNETIC RESONANCE ANGIOGRAPHY. C. Ishikawa, D. Ito, N. Tanaka, S. Ohta, M. Kitagawa. School of Veterinary Medicine, Nihon University, Kanagawa, Japan.

Accurate visualization of canine intracranial vessels using three dimensional time-of-flight magnetic resonance angiography (3D TOF MRA) have been reported, which were evaluated dogs with more than 9 kg. We hypothesize that image quality of intracranial vessels between small-sized (toy-breed) dogs and large-sized dog might be different, as vessels in small-sized dog would be thinner than those in large-sized dog. Therefore, the aim of this study was to evaluate image quality of intracranial vessels in small-sized dogs...
CEREBROSPINAL FLUID MOVEMENT USING MAGNETIC RESONANCE SPIN LABELING IN 3 DOGS WITH CONGENITAL HYDROCEPHALUS. N. Tanaka1,2, , D. Ito1, C. Ishikawa1, S. Ohta1, M. Kitagawa1. 1School of Veterinary Medicine, Nihon University, Kameino, Fujisawa, Kanagawa, Japan, 2Grace animal hospital, Ogikubo, Suginamiku, Tokyo, Japan

Diagnosis of hydrocephalus is to obtain image observation of the ventriculomegaly. In human, time spatial labeling inversion pulse (time-SLIP) is used to research about cerebrospinal fluid (CSF) dynamics. In dogs, it is thought that common causes of congenital hydrocephalus are flow obstacles of CSF, but actual CSF dynamics in dogs was not understand. Therefore, we investigate CSF dynamics in dogs with hydrocephalus using time-SLIP.

This study was approved by Nihon University Animal Medical Center ethical committee. Two dogs that diagnosed stenosis/obstruction at outlet of the forth ventricle on conventional MRI and one dog with aqueduct stenosis/obstruction was underwent further images, time-SLIP. We observed CSF dynamics at the aqueduct and pre-pontine cisterns on mid-sagittal brain.

In all dogs, CSF flow (one direction movement) was observed in the aqueduct and the pre-pontine cisterns. It is conceivable that CSF flow in the aqueduct and CSF circulation of outside of the ventricular system would stop when CSF flow in the aqueduct is obstructed completely. However CSF flow was observed in the aqueduct and the pre-pontine cisterns. Therefore the cause of hydrocephalus might be stenosis of the aqueduct, not obstruction.

CSF flow at the pre-pontine cisterns might be affected in dogs with stenosis/obstruction at outlet of the forth ventricle. Because dilatation of the fourth ventricle compress the brain stem and space of the cistern would be getting thinner. But again, CSF flow was observed at both pre-pontine cistern and aqueduct, this mean the isle of CSF at exit of the fourth ventricle was not closed.

CSF flow was visualized by time-SLIP in all dogs with congenital hydrocephalus. This method might be help for explication of CSF dynamics in hydrocephalus.

CSF AQUAPORIN-4, -1 AND INTERLEUKIN-6 IN DOGS WITH NATURALLY OCCURRING COMMUNICATING INTERNAL HYDROCEPHALUS BEFORE AND AFTER VENTRICULO-PERITONEAL SHUNTIG. M.J. Schmidt 1, C. Rummel 1, J. Hauer 1, M. Kolecka 1, N.Ondreka 1, V. McClure2, J. Roth 3, 1 Small Animal Clinic Dept. Of Small Animal Surgery, JL University, Giessen, Germany, 2 Institute for Veterinary Physiology and Biochemistry, Justus-Liebig-University, Frankfurter Strasse 100, 35392 Giessen, Germany, 3 Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110, Republic of South Africa.

Studies in animal models, in which internal hydrocephalus has been induced by obstructing the cerebrospinal fluid pathways, have documented an up-regulation of the concentrations of aquaporin-4 (AQP4) in the brain. In this study, the concentrations of aquaporin-1 (AQP1), AQP1, AQP4 and Interleukin-6 (IL-6) were determined in the CSF of dogs with idiopathic communicating hydrocephalus before and after the reduction of intraventricular volume following ventriculo-peritoneal shunt (VP-shunt) treatment. The concentrations of AQP4 and IL-6 were increased in the cerebrospinal fluid of dogs with hydrocephalus compared to controls. Both parameters significantly decreased after surgical treatment, accompanied by decrease of ventricular size and the clinical recovery of the dogs. AQP1 was not detectable in CSF.

Brain AQP4 up-regulation might be a compensatory response in dogs with hydrocephalus. Future determination of AQP4 at the mRNA and protein level in brain tissue is warranted to substantiate this hypothesis.

SOUND LOCALISATION IN DOGS WITH VESTIBULAR DISEASE: A PRELIMINARY STUDY. P. Gardiner1, P. Freeman1.

1Department of Veterinary Medicine, University of Cambridge, UK.

Vestibular disease is a common neurological presentation in small animal practice and has many possible aetiologies. An important step in the investigation of vestibular disease is to determine whether the signs are caused by a peripheral or central lesion, as this informs both the prognosis and the most appropriate diagnostic investigations. In human medicine determining whether there is any hearing loss associated with the vestibular signs is part of the initial assessment. This information aids in localisation of the lesion as unilateral deafness is common in peripheral vestibular disease but rare in central disease. Demonstrating unilateral deafness in dogs relies on specialist equipment to investigate brainstem auditory evoked potentials (BAEP), and the equipment required for this is not widely available in first opinion practice.

This study used a simple test involving a squeaky toy suitable for use in first opinion practice to demonstrate localisation of sound in dogs.
The preliminary component of the study establishes a baseline of responsiveness in 39 healthy dogs with which to compare animals with vestibular disease. It also establishes and validates the test protocol as a practical way of measuring this response to sound.

**NOISE INDUCED HEARING LOSS IN A POLICE DOG.** D.W. Hague. Veterinary Clinical Medicine Dept., University of Illinois, Urbana, Illinois

A four year old intact male Belgium Malinois was evaluated for acute hearing loss. The dog was a working police dog involved in a training exercise where a gun was fired five times on his right side. The estimated noise level was approximately 140 decibels. Later that day, the dog was involved in bite work and the handler noted the dog was not responding to verbal commands. He presented three days later for evaluation of hearing. There was no evidence of any abnormalities on neurologic or physical examination.

Brainstem auditory evoked response (BAER) testing was performed in both ears with a 70 and 90 decibel click stimulus using a mastoid reference and masking tone in the opposite ear. There was evidence of an absence of waveforms. Based on the history, the patient was diagnosed with a noise-induced hearing loss. Two weeks later, a repeat BAER test showed evidence of intact waveforms (I-V) in both ears. The handler reported the dog was responsive to oral commands. This case represents the risk of noise-induced hearing loss in working dogs. Therefore, hearing protective devices should be considered in working dogs exposed to episodic or chronic loud noises.

**AUTOPHAGY VERSUS APOPTOSIS - MYOFIBRE DEATH IN CANINE IMMUNE MEDIATED MYOSITIS (CIMM).** M. Rosati, M. Leipig, K. Matiaszek. Section of Clinical & Comparative Neuropathology, Ludwig-Maximilians University, Munich, Germany

Muscle fibre death in immune-mediated inflammatory myopathies is poorly understood. MHC-II myocytic expression in CIMM represents a shift towards an antigen presenting cell phenotype and breaking of immuno-tolerance. Autophagy can impact the immune response through its role on antigen delivery to the MHC. In order to unravel myofibre death mechanisms we investigated autophagy and apoptosis in CIMM.

34 CIMM dogs (11 MMM and 23 PM), 10 dogs with non-inflammatory myopathy, 10 dogs with neurogenic muscle atrophy and 4 dogs without neuromuscular disorders were evaluated immunohistologically for the expression of MHC-II, LC3 and Cleaved Caspase-3 in muscle biopsies. Their expression was semiquantitatively scored and sorted for subcellular distribution (MHC-II) after which group specific data were obtained according to standard algorithms.

CIMM presented with significantly higher (p<0.05) scores for MHC-II and LC3 if compared to the other diseases and controls, while Cleaved Caspase-3 was not expressed by myocytes throughout the groups. There was no difference in MHC-II and LC3 expression in MMM and PM. No correlation could be found between MHC-II and LC3 in CIMM.

MHC-II regulation seems to be driven by inflammation rather than be triggered by autophagy with subsequent exposure of self-antigens to T helper cells. However increased expression of LC3 with activation of macroautophagy might be responsible for sarcopenia in course of CIMM together with direct destruction of myofibres by inflammatory infiltrates. Lack of Cleaved Caspase-3 expression on the other hand suggests that myocytes do not undergo apoptosis and T-cells exert their lethal hit by a different mechanism.

**1H NMR CEREBROSPINAL FLUID PROFILE IN DOGS WITH POLYRADICULONEURITIS – CASE SERIES.** M. Musteata1, A. Nicolescu1, A. Wessmann2, N. Carmichael 3. Carmichael Torrance Veterinary Diagnostic Laboratory

The aim of this study was to describe the cerebrospinal fluid (CSF) metabolites identified and quantified by 1H NMR spectroscopy in four dogs with polyradiculoneuritis (PRN). The diagnosis was fixed based on clinical appearance (acute flaccid tetraparesis, dysphonia) and electrodiagnostic tests (positive sharp waves and complex repetitive discharges on EMG, and slow NCS). The CSF samples were harvested from altantoccipital space under general anaesthesia and they were analyzed for proteins and cells. The 1H NMR spectra were recorded from four dogs with PRN and were compared with those obtained from 10 healthy dogs, 13 metabolites being identified and quantified. The data were analyzed with PASW Statistics 18.

On routine examination, the CSF samples were characterized by a normal number of cells (< 5 cells/ul) with normal or a moderate increase of protein amount (< 40 mg/l). Using 1H NMR examination, a decreased concentration of pyruvate (0.058 ± 0.361 mmol/l vs 0.234 ± 0.011 mmol/l, p < 0.001) and myo-inositol (0.408 ± 0.023 mmol/l vs. 0.499 ± 0.017 mmol/l, p = 0.012) and an increase concentration for glucose (0.467 ± 0.028 mmol/l vs 0.398 ± 0.013 mmol/l, p = 0.03) were observed when compared with normal group. Citrate was found in ¼ dogs and ascorbic acid was absent in all PRN cases.

Our results may suggest that in PRN CSF reflects a major alteration in the energetic metabolism of the neurons, similar with those reported in humans’ central nervous system chronic demyelinating diseases.

**ALPHA-CHLORALOSE POISONING IN A CAT.** L. Grau-Roma1, A. Stephens1, A. Wessmann2, N. Carmichael1, S. de Brot1. 1University of Nottingham, School of Veterinary Medicine and Sciences, 2Pride Veterinary Centre, Neurology, 3 Carmichael Torrance Veterinary Diagnostic Laboratory

A five-year-old domestic cat presented with acute onset of ataxia, depressed mentation, hyperaesthesia, hypothermia, and continuous twitching/seizure activity in the morning after having been outside overnight. Despite immediate treatment, the cat progressed within twenty-four hours to a comatose state, opisthotonus and severe miosis unresponsive to light. Given a poor prognosis, euthanasia was
A six-year-old, neutered male Scottish Terrier was referred for progressive lethargy and anorexia of a week duration. Neurological examination confirmed the presence of mild brain oedema, but failed to identify a cause for the severe clinical symptoms. In a final attempt to solve the case, a urine sample was tested for toxic substances and it was found to contain a significant amount of alpha-chloralose.

Alpha-chloralose (AC), a chlorinated acetate derivative of glucose, is used as a rodenticide, avicide and repellent, often in form of hypnotic baits to immobilize and live-capture pest animals. It is moderately toxic to mammals and fish, and highly toxic to birds. In animals, accidental AC poisoning is only poorly reported. The most common clinical signs are seizures, muscle tremor, hyperaesthesia, hypothermia, salivation, miosis, stupor, coma and ataxia. Coma and hypothermia was more common in cats, whereas salivation, ataxia and hyperthermia was more frequently seen in dogs.

AC poisoning in pet animals within Europe or the United States is poorly reported and no case has been described within the UK, as far as the authors are aware.

GENOME SEQUENCING REVEALS A SPlice DONOR SITE MUTATION IN THE SNX14 GENE ASSOCIATED WITH A NOVEL CEREBELLAR CORTICAL DEGENERATION IN THE HUNGARIAN VIZSLA DOG BREED. J. Fenn1, M. Boursnell1, R.J. Hitti1, C.A. Jenkins1, R.L. Terry2, S.L. Priestnall2, P.J. Kenny1, C.S. Mellersh3, O.P. Forman3, 1Department of Clinical Science and Services, 2Department of Pathology and Pathogen Biology, Royal Veterinary College, Hawkshead Lane, North Mymms, Hertfordshire, AL9 7TA, UK, 3Kennel Club Genetics Centre, Animal Health Trust, Kentford, Newmarket, Suffolk, CB8 7UU, UK.

Cerebellar cortical degeneration (CCD) is a neurodegenerative disease affecting many dog breeds. Typical presentation consists of progressive cerebellar ataxia, with variable onset ages and rates of progression. Causative genes have been identified associated with CCD in several breeds, allowing screening for selective breeding to reduce disease prevalence. There have been no previous reports of CCD in Hungarian Vizslas.

Two full-sibling Hungarian Vizsla puppies from a litter of nine presented with progressive ataxia, starting around three months old. Clinical signs included cerebellar ataxia, truncal sway, intention tremors, absent menace responses and nystagmus in one dog. Routine diagnostic investigations were unremarkable, and magnetic resonance imaging in one dog demonstrated cerebellar atrophy. Euthanasia was elected shortly after the onset of signs. Histopathological examination revealed primary Purkinje neuron loss consistent with CCD. Whole genome sequencing identified a disease-associated splice donor site variant in the sorting nexin 14 gene (SNX14) as a strong causative candidate. An altered SNX14 splicing pattern was demonstrated by RNA analysis, and no SNX14 protein could be detected in CCD case cerebellum by western blotting. Genetic screening of 133 unaffected Hungarian Vizslas revealed three heterozygotes, supporting the presence of carriers in the wider population.

SNX14 is involved in maintaining normal neuronal excitability and synaptic transmission, and a mutation causes autosomal recessive cerebellar ataxia and intellectual disability syndrome in humans. This is the first report of CCD in Hungarian Vizsla dogs and identifies a splice donor site mutation in SNX14 as the likely cause, with an autosomal recessive mode of inheritance suspected.

ASPARTOACYLASE DEFICIENCY IN A DOMESTIC CAT WITH LEUKODYSTROPHY. M. Kohyama1-2, T. Fujimura3, N. Matsuki3, K. Uchida4, A. Yabuki4, M. Shima-Sawa3-4, O. Yamato1. 1Laboratory of Clinical Pathology, Joint Faculty of Veterinary Medicine, Kagoshima University, Kagoshima, Japan, 2Research Fellow of Japan Society for the Promotion of Science, Tokyo, Japan, 3Minnie Animal Hospital, Chiba, Japan, 4Laboratory of Veterinary Clinical Pathology and 3Laboratory of Veterinary Pathology, The University of Tokyo, Tokyo, Japan.

Aspartoacylase (ASPA) deficiency, also called Canavan disease in humans, is a rare autosomal recessive neurodegenerative disease and is a type of leukodystrophy. The deficiency is caused by mutations in the ASPA gene. Absence of ASPA activity results in accumulation of N-acetylaspartate (NAA) in the brain, visceral organs, and urine. In animals, naturally occurring ASPA deficiency has not been reported yet. Recently, ASPA deficiency was diagnosed in a domestic cat with leukodystrophy, and a candidate causative mutation was identified in the feline ASPA gene.

A 4-month-old female domestic cat weighting 1 kg was presented with frequent vomiting, head tremors, and frequent falling due to body imbalance. Magnetic resonance imaging showed T2-weighted hyperintensity and T1-weighted hypointensity in the brain stem and cerebellum. Gas chromatography-mass spectrometry analysis of the urine revealed unusual excretion of NAA, which is indicative of ASPA deficiency. The cat finally died at 7 months of age, and histopathological spongy degeneration was observed in the cerebrum and cerebellar region. Direct sequence analysis identified a homozygous missense mutation in the coding region of the feline ASPA gene. A genotyping survey using real-time PCR did not detect this mutation in approximately 1,000 domestic cats, thereby suggesting that this mutation is most possibly a causative mutation in this disease. Ethical approval for this study was obtained from the Animal Research Committee at Kagoshima University (approval number VM15041).

In conclusion, this is the first report of naturally occurring ASPA deficiency in animals, and the cat represents a model of human Canavan disease.

HYPOPHYSISIS IN A SCOTTISH TERRIER WITH ASSOCIATED PANHYPOPITUITARISM AND HYPOTHALAMITIS MIMICKING A PITUITARY GLAND NEOPLASIA. M. Oliveira1, L. Polledo2, J. Adamany2, A. Wessmann1, P. Graham1, M. Dhumeaux2, K. Baiker1. 1Department of Neurology and Neurosurgery, 2Department of Internal Medicine, Pride Veterinary Centre, Derby, UK, 3School of Veterinary Medicine and Science, University of Nottingham, UK.

A six-year-old, neutered male Scottish Terrier was referred for progressive lethargy and anorexia of a week duration. Neurological
examination revealed a low head carriage, hind limb ataxia, and decreased bilateral nasal sensation localising the lesion to the forebrain. MRI of the brain revealed a rounded, well-defined, central mass measuring 12mm in diameter located dorsally and slightly rostrally to the pituitary fossa. The mass was slightly hypointense to cortical grey matter on T2W, hypointense on T1W and without T2* signal void. There was a central fusiform enhancement of the mass after contrast administration suggestive of neoplasia. T4 and TSH levels raised the suspicion of secondary hypothyroidism. The cortisol ACTH ratio was < 0.0132 suggestive of primary hypoadrenocorticism. During hospitalisation, the dog developed an acute severe hypernatremia and died. Post mortem examination showed a severe lymphocytic panhypophysitis with extension to the hypophalumus; most lymphocytes were CD3 positive T-cells. Immunohistochemistry for *Neospora caninum* antigen was negative.

To the authors' knowledge, a lymphocytic panhypophysitis with extension to the hypophalumus has never been reported. Hypothalamic involvement in autoimmune hypophysitis has rarely been described in people and usually manifests with central Diabetes Insipidus as suspected in our case due to the sudden onset of severe hypernatremia. This is the first MRI description of autoimmune hypophysitis in a dog. Like in humans, the clinical and MRI findings can be difficult to differentiate from other more common pituitary masses. Therefore, transsphenoidal biopsies may be required for conclusive histopathological diagnosis and prompt institution of adequate treatment.

**BRAIN ABSCESS DIAGNOSIS VIA ULTRASOUND-GUIDED ASPIRATION THROUGH THE ORBIT IN AN ENUCLEATED IMMUNOCOMPROMISED MIXED-BREED DOG.** MPF1, MBB2, RGR2, DCA1, IG2, CPD2 1Hill’s resident. Emergency and ICU Service-Veterinary Teaching Hospital, Veterinary Faculty, Complutense University Madrid, Spain, 2Neurology and Neurosurgery Service. Animal Medicine and Surgery Department. Veterinary Teaching Hospital, Complutense University Madrid, Spain, 3Imagine Diagnosis Service. Animal Medicine and Surgery Department. Veterinary Teaching Hospital, Complutense University Madrid, Spain. 4Medical Imaging and Surgery Department. Veterinary Teaching Hospital, Complutense University Madrid, Spain.

A 14-years old mixed-breed dog presented with history of seizures, circling and behavioural changes of short duration. Two years earlier the left eye had been removed due to phthisis bulbi, and immunosuppressive therapy with cyclosporine and prednisone for atopy established. Neurological examination showed depressed mental status, left circling, dragging right forelimb, slight right eye ventral positional squint and neck pain.

MRI(Siemens 0.23T) showed a cystic lesion in the left olfactory lobule with large vasogenic oedema and mass effect destroying the left orbital bone. Differential diagnosis included neoplastic event or brain abscess. Ultrasound-guided aspiration of the mass content was performed through the enucleated orbit draining 0.7 ml of opaque liquid that was cultured obtaining positive *S. aureus* growth. The antibiogram identified sensitivity to enrofloxacin and doxycycline. Treatment with enrofloxacin(5mg/kg/BID), doxycycline(10mg/kg/SID) and levetiracetam(10 mg/kg/TID) was established. Cyclosporine was suspended and prednisone reduced(0.5 mg/kg/SID). Follow-up MRI acquired 41-days after therapy identified lesion persistence with minimal size reduction and lower vasogenic oedema. A new ultrasound-guided aspiration yielded an acellular aseptic aspirate. The patient is currently asymptomatic and stable.

Brain abscess is an uncommon and rarely reported medical condition in veterinary medicine. The more common causes are bites, foreign bodies and immunosuppression. Elective therapy is generally surgical removal, although in the present case this was not the best option considering the age of the patient. Alternatively, the prior enucleation allowed us to make an aspiration of the mass content and decide on a successful conservative course thanks to the performed antibiogram.

**COMPUTER TOMOGRAPHY (CT) GUIDED DRAINAGE OF A BRAINSTEM ABSCESS IN A CAT AS A LIFE SAVING PROCEDURE.** E. Bersan1, T. W. Maddox1, G. Walmsley1, R. Burrow1 1School of Veterinary Sciences, University of Liverpool, Small Animal Teaching Hospital, Neston, UK

A 3-year-old male neutered domestic short haired cat was presented with progressive lethargy and abnormal behaviour. Clinical exam found cardiovascular signs suggestive of raised intracranial pressure. Neurological examination found obtunded mentation, non-ambulatory tetraparesis with left sided pleurothorotonus and intermittent decerebrate rigidity. The postural responses were reduced in all four limbs, worse on the right. Cranial nerve evaluation found absent menace response and reduced facial sensation on the right, vertical positional nystagmus, anisocoria (right sided mydriasis) and an absent pupillary constriction on the right in response to direct and indirect PLR. Neurolocalisation was to multifocal lesions involving the right brainstem and forebrain.

Magnetic resonance imaging of the brain revealed a large, well-defined, predominantly fluid-filled extra-axial mass causing severe dorsal displacement of the pons and the medulla oblongata and cerebellar vermis herniation through the foramen magnum. These findings were most consistent with an intracranial abscess.

Emergency CT-guided needle drainage of the space-occupying lesion was performed through the soft palate and basioccipital bone. Bacteriology revealed heavy growth of *Arcanobacterium haemoliticum* and mixed growth of pleomorphic, mainly Gram-negative rods (*Cl.hastiforme, Cl.Septicum, Cl.perfringens and Treponema/Serpulina spp*). At discharge the cat had normal mentation and mild ambulatory tetraparesis. Broad-spectrum antibiotics based on culture and sensitivity were continued for 8 months and repeat imaging prior to withdrawal found complete resolution. Follow-up examination 16 months later found only mild right sided postural reaction deficits that did not affect quality of life.

CT guided drainage of a brainstem abscess is not without risk however in this case it reduced intracranial pressure and provided a diagnostic sample.

**EVALUATION OF THE PROPRIOCEPTIVE POSITIONING RESPONSE AND PATELLAR TENDON REFLEX IN DOGS WITH NO NEUROLOGICAL CLINICAL SIGNS.** E. Daniell1, S. Gomes1, A. Jeandel2, P. Freeman1 1The Queen’s Veterinary School Hospital, Department of Veterinary Medicine, University of Cambridge, UK, 2Davies Veterinary Specialists, Hitchin, UK
The proprioceptive positioning response (PPR) and patellar tendon reflex (PTR) are clinical tests commonly used to assess and localise neurological conditions in dogs. The primary aim of this study was to investigate the specificity of these tests by evaluating test outcomes in the hindlimbs of a population of dogs showing no overt signs of neurological disease. The secondary aim was to investigate the influence of age on these tests.

Twenty-nine dogs without evidence of neurological or hindlimb orthopaedic disease were selected and divided into two groups: A (<10 years-old, n=20) and B (≥10 years-old, n=9). A European Specialist in Veterinary Neurology, blinded to the age of the dogs, performed the tests.

The PTR was considered normal in all of the study population, while the PPR was abnormal in 17% of the dogs. The proportion of dogs with an abnormal PPR in one or more hindlimb was 10% in group A and 33% in group B; this difference was not statistically significant (p=0.29). Only dogs in group B had bilateral PPR deficits (22%), but this difference between groups was not statistically significant (p=0.089).

The finding that some dogs had PPR deficits despite having no overt neurological disease has implications for neurological examination interpretation: deficits should be interpreted with caution. There was no statistically significant difference in the proportion of PPR deficits between the two age groups. The PTR was normal in all cases, suggesting a lower prevalence of absent patellar reflexes in the general population than recorded in previously published literature.


Canine Degenerative Myelopathy (DM) is associated with a substitution mutation of a glutamic acid (E) to lysine (K) residue in SOD1 (E40K) which increases its tendency to aggregate in cells. E40 is highly conserved across mammalian species with the exception of horses, which naturally express a K residue. We hypothesised that normal horse SOD-1 has the same tendency to aggregate as mutant DM-affected dog SOD1 in contrast to its E40 counterpart.

cDNAs from wild-type (E40) and mutant (K40) canine SOD1 and wild-type (K40) equine SOD1 were amplified by PCR and cloned with N-terminal GFP-tags. PCR-mutagenesis was used to create an equivalent equine E40 SOD1 variant. Inserts were sub-cloned and transduced, alongside a GFP-only vector as lentiviral particles into human neuroblastoma cells (SHSY-5Y). Aggregates (nuclear or cytosolic) were quantified following fluorescence microscopy, in a blinded fashion (n=3 coverslips per variant, on 3 separate occasions; minimum of 1500 cells counted per condition).

There were significantly more cytoplasmic SOD1 aggregates in the GFP-mutant dog SOD1 expressing cells (mean %±SEM; 23%±5), compared to the wild-type dog (6.7%±1.3) or GFP-only vector (1.7%±0.5) (p<0.05); there were significantly more nuclear aggregates in both GFP-horse SOD-1 variants (K40: 50.4%±5.2, E40: 68.1%±4.9) compared to the GFP-only vector (8.2%±1.2) (p<0.05).

These results suggest that there are species-differences in vitro in the tendency of mutant and normal SOD1 proteins to aggregate and localise.

COGNITIVE DEFICITS AND PATHOLOGICAL FEATURES OF CEREBRAL AMYLOID ANGIOPATHY IN 27 ELDERLY DOGS. R. A. Marcasso¹, J. R. Moreira², M. V. Bahr Arias³, A. P. F. R. L. Bracarense⁴, ¹Laboratory of Animal Pathology, UNOPAR, Arapongas, Paraná, Brazil, ²Laboratory of Animal Pathology, Universidade Estadual de Londrina, Paraná, Brazil; ³Department of Veterinary Clinics, Universidade Estadual de Londrina, Paraná, Brazil

Cerebral amyloid angiopathy (CAA) is defined as the deposition of beta amyloid proteins within leptomeningeal and cortical vessels, being associated to Alzheimer disease and canine cognitive disease.

This study aimed to evaluate in elderly dogs the association between cerebral amyloid deposition and pathologic lesions in the development and clinical manifestation of cerebral dysfunction. Local ethical permission was obtained for this study.

Gross evaluation of 44 brains of elderly dogs revealed cortical atrophy and ventricular widening in 22.7% (10/44) specimens. Congo red stain was utilized to classify the 61.4% (27/44) positive dogs (9-19 years old, mean 13.9 years old) to CAA. CAA were graded in mild (13/27 dogs), moderate (3/27 dogs) and severe (11/27 dogs). In all groups the most common clinical sign was disorientation. By the immunohistochemistry using polyclonal anti-beta amyloid 1-42 antibody, the average of positive vessels to beta-amyloid increased with age. Association of cortical atrophy, neuron loss and micro hemorrhages contribute to the developing of cognitive deficits.

The consistent presence of this change in a variety of dogs above the age of 13 years, the correlation with intracerebral hemorrhage, and the similarity of the affected regions between dogs and humans, all uphold the utility of aged dogs as a natural model for studies about cerebral amyloid angiopathy.

3 YEARS AFTER CLINICAL ONSET OF CEREBELLAR CORTICAL DEGENERATION IN A JUVENILE COTON DE TULEAR - WHAT COMES AFTER INFLAMMATION? C. Ricco¹, A Fouhetti¹, M Rosati², K Matiashek², L. Cauzinille¹. ¹Centre Hospitalier Vétérinaire Frégis, Arcueil France, ²Ludwig-Maximilians-University, Munich Germany.

Cerebellar disorders in dogs can be subclassified into congenital, developmental and abiotrophic/degenerative types. Among the abiotrophies, the term cerebellar cortical degeneration (CCD) has been introduced lately, which includes an uncommon form mainly affecting granular cells. This variant has been described in several breeds including the Coton de Tulear. In this specific breed an immune-
mediated disease process has been suggested. In this case report we describe a late stage presentation of a cerebellar granuloprival degeneration.

A 7-month-old, Coton de Tuléar was presented with a history of progressive ataxia. The puppy was clear of the breed specific neonatal cerebellar ataxia.

Neurological examination revealed generalised ataxia, hypermetric gait, head tremors, decreased proprioception in the hind limbs and an inconstant bilateral menace response.

MRI revealed a cerebellum mildly decreased in size and a normal cerebrospinal fluid analysis. Clinical signs progressed over time and the dog was euthanized at the age of three years.

Histopathology confirmed diffuse, chronic and severe granuloprival cerebellar cortical degeneration accompanied by severe gliosis of the cerebellum. Signs of inflammatory infiltrates were not detected on conventional stains and immunohistochemistry.

This Coton de Tulear appears as the first report of a chronic form of granuloprival CCD in this breed. Although the lack of inflammatory cells could suggest the absence of an immune mediated disease, these findings are most likely stage related and might reflect successful removal of the immunogenic target.

Further studies should focus on the research of a genetic mutation associated with these histologic findings.

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**EVALUATION OF GFAP LEVELS IN SERUM AND CEREBROSPINAL FLUID IN DOGS. D. Kostic, R. Carlson, S. Wicha, A. Tipold.**

Glial fibrillary acidic protein (GFAP) is the main intermediate filament protein in astrocytes and a potential biomarker for intracranial disorders. The hypothesis should be proven that severe brain tissue destruction leads to measurable GFAP serum levels independent of the cause of the disease. Furthermore, it should be proven that GFAP levels in cerebrospinal fluid (CSF) are reflecting disease categories.

Six healthy Beagles and patients (n=198) with the clinical diagnoses idiopathic epilepsy, brain tumor, inflammation, spinal cord injury (SCI) and traumatic brain injury (TBI) were included. GFAP concentrations were determined by ELISA. In serum, GFAP was only measurable in single cases. However, all CSF samples were positive for GFAP. Using Wilcoxon test, significant differences were found between GFAP CSF levels of dogs with tumor and epilepsy (p<0.0004) and between inflammatory diseases and epilepsy (p<0.0408).

There was no correlation between GFAP values and severity, type and seizure frequency and severity of neuroparenchymal damage. In TBI patients high GFAP levels had a strong correlation with the Glasgow Coma Scale score. In dogs with SCI no significant difference between chronic and acute cases and severity of clinical signs could be detected.

In conclusion, GFAP cannot be recommended as a marker for a specific disease. However, serum levels in TBI patients may have predictive value for the outcome.

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**8 CASES OF EOSINOPHILIC MENINGOENCEPHALITIS (EME) IN DOGS FROM 2009 TO 2015. S Guo, D Lu**

Idiopathic eosinophilic meningoencephalitis (EME) is a rare condition of unknown etiology and has been described in different breeds such as Golden Retriever, Rottweiler, Yorkshire Terrier, etc. When the eosinophils in the cerebrospinal fluid (CSF) is <5%, this finding is considered nonspecific; it is recommended that an eosinophilia of 10% of the total white cells in the CSF should be used as a minimum criteria for the diagnosis of EME in people.

This retrospective study described 8 cases of EME seen in a private referral practice in Hong Kong from 2009 to 2015, affecting several breeds of dogs.

EME is a rare condition and makes up to 4.6% of all the MUE cases seen in a Hong Kong referral clinic from 2009 to 2015. The clinical presentation and MR images were variable and diagnosis was mainly made by the presence of eosinophilic pleocytosis of CSF. In general they carry good prognosis following immunosuppressive treatment, with 5 out of 8 cases (62.5%) in remission (off treatment) and 1 (12.5%) only needed AED due to persistent seizure.

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**CANNABINOID RECEPTOR TYPE 2 (CB2) EXPRESSION IN CANINE STEROID-RESPONSIVE MENINGITIS-ARTERITIS (SRMA) AND INTRASPINAL SPIROCERCOSIS. J. Freundt-Revilla1, F. Heinrich2, M.H. Shamir3, A. Oevermann4, W. Baumgärtner2, A. Tipold1.**

Increased levels of endocannabinoids were recently found in CSF of dogs suffering from Steroid-Responsive Meningitis-Arteritis (SRMA) and Intraspinal Spirocercosis (IS) (Abstract ECVN 2013). These endogenous ligands interact with two main types of cannabinoid receptors (CB1 and CB2). The CB2 receptor is highly expressed in inflammatory cells and is up-regulated in early phases of inflammation in cells of the CNS.

In the present study, CB2 receptor expression was evaluated in spinal cord lesions of dogs with SRMA (n=8) and IS (n=2) and compared to healthy control dogs (n=6). Therefore, a rabbit polyclonal anti-human CB2 antibody (LSBio®) was established on canine paraffin-embedded tissue samples using routine immunohistochemistry.

In cervical, thoracic, and lumbar spinal cord sections of dogs with SRMA and IS, CB2 was strongly expressed on the cellular surface of infiltrating leukocytes (i.e. neutrophils, eosinophils, lymphocytes, plasma cells, and macrophages). In SRMA, CB2-positive inflammatory cells were located within the adventitia of vessels, perivascular, subdural, subarachnoidal, and within white and grey matter. Moreover, moderate to strong CB2-positive endothelial cells and arachnoid mesothelial-like cells were present. In IS, CB2-expressing leukocytes were found adjacent to the parasite accompanied by severe necrosis and haemorrhage. Both diseases showed...
CB2-positive glial cells exhibiting a moderate to strong membranous signal. Likewise, scattered myelinophages and spheroids stained intensely positive with CB2. Dorsal and ventral neurons showed inhomogeneous slight to strong cytoplasmic immunoreactivity.

The present study demonstrates CB2 expression in inflammatory lesions of SRMA and IS and highlights the endocannabinoid system as a potential target for treatment of inflammatory CNS diseases.

INFLAMED INTRACRANIAL MENINGIOMA MIMICKING BRAIN ABSCESS IN A DOG. C. Tästensen¹, S. Hanemann¹, M.-K. Müller¹, M. Rosati¹, K. Matiasek¹, T. Fliegler¹. ¹Dept. of Small Animal Medicine, University of Leipzig, Germany; ²Clinical and Comparative Neuropathology, Centre for Clinical Veterinary Medicine, LMU Munich, Germany.

An 11-year-old mixed breed dog was presented with an acute onset of cluster seizures. At presentation, the dog showed a status epilepticus, which could be interrupted with anticonvulsive medication. Due to the stuporous state of the patient the following day, a thorough neurological examination could not be performed.

MRI of the head revealed an inhomogeneously contrast enhancing mass within the right frontal lobe adjacent to the cribiform plate and extending caudally to the rostral thalamus. CSF analysis showed a severe pleocytosis of 11540 cells/µl with 70% neutrophils and 30% monocytes and a protein of 2.63 g/l. Based on MRI findings and CSF analysis main differentials were intracranial abscesses versus neoplasia. Surgery was performed and a major part of the intracranial mass was removed through a bilateral transfrontal approach. Histological examination revealed a WHO grade I conforming meningothelial meningioma with multiple intratumoural microabscesses. Neither the CSF nor the mass itself showed bacterial growth. The dog recovered well over the following 7 days and was discharged for radiotherapy at which time the dog was neurological unremarkable.

This case report illustrates that even a severe neutrophilic pleocytosis in the CSF cannot rule out an intracranial neoplasia. To our knowledge this is the first report of a meningioma with sterile microabscesses in a dog.

CLINICAL AND EPIDURAL HISTOPATHOLOGICAL DIFFERENCES OBSERVED IN CERVICAL AND THORACOLUMBAR INTERVERTEBRAL DISC EXTRUSION IN DOGS. L. Züger¹,²,³, A. Fadda¹,²,³, A. Oevermann¹,⁴, F. Forterre²,³, D. Henke¹,²,³. ¹Division of Neurological Sciences, ²Division of Veterinary Surgery, ³Department of Clinical Veterinary Medicine, ⁴Department of Clinical Research and Veterinary Public Health, Vetsuisse Faculty, University of Bern, Switzerland.

Marked differences in clinical presentation and outcome between cervical and thoracolumbar disc extrusions have only been partially explained. We have recently shown that the inflammatory response in the epidural space has an impact on the outcome in thoracolumbar IVD extrusions.

The aims of the present study were to evaluate clinical data and histopathological parameters of epidural material from 55 dogs with cervical IVD extrusion, and to compare these data to those from 80 dogs with thoracolumbar IVD extrusion from a previous study.

Cervical epidural material was histologically examined, and associations between severity of inflammation and selected clinical and pathological parameters, impact of chondrodystrophic phenotype, and anatomic localization were evaluated statistically.

Dogs with a cervical IVD extrusion were significantly older (pathological parameters, impact of chondrodystrophic phenotype, and anatomic localization were evaluated statistically."

Somatosensory and Motor Evoked Potentials Under General Anesthesia in Dogs with Thoracolumbar Intervertebral Disc Extrusion. MCCM Inglez de Souza¹, RJR Ferreira², GCF. Patricio¹, JM Matera¹. ¹School of Veterinary Medicine - University of São Paulo, São Paulo, Brazil. ²Institute of Orthopaedics and Traumatology, University of São Paulo, São Paulo, Brazil.

Somatosensory evoked potentials (SEPs) and transcranial motor evoked potentials (TMEPs) provide information regarding sensory and motor pathways, and dogs are considered translational models for naturally-occurring spinal cord injury. Our aim was to describe SEPs and TMEPs technique in uninjured and in affected chondrodystrophic dogs (CD). Paraplegic CD (5 with pain perception, 5 with loss of pain perception) due to thoracolumbar disc extrusions confirmed by computed tomography; and 5 neurologic normal CD were anesthetized with Fentanyl and Propofol in a continuous infusion rate.

SEPs were recorded with electrodes positioned subcutaneously on scalp following median and tibial nerves stimulation. TMEPs were obtained by electrical stimulation applied transcranially and captured via electrodes inserted into extensor carpi radialis and cranial tibial muscles.

SEPs waves were identified in all dogs after median nerve stimulation, and 5 dogs had no SEPs recordings on pelvic limbs, and they were clinically without pain perception. TMEPs were recorded on thoracic limbs in all dogs, but were severe attenuated in 7 dogs and absent in 3 dogs. Even if no voluntary movement could be detected clinically, electrophysiological responses were present caudal to spinal cord lesion, i.e., these patients may be paraplegic from clinical assessment, but not concerning electrophysiological function. All neurologically normal CDs presented SEPs and TMEPs on pelvic limbs.

Combined SEPs and TMEPs techniques appear to be reliable for spinal cord lesion evaluation under general anesthesia. TMEPs could
be detected caudal to the lesion even in severely affected patients, possibly being a useful tool for spinal cord therapies evaluation.


Development of objective prognostic tools for paraplegic dogs suffering from spinal cord injury (SCI) is mandatory for novel treatment selection and implementation. The aim of the study was to compare fractional anisotropy (FA) values with intramedullary hyperintensity length (IMHL) in T2-weighted (T2W) MRI sequences and presence or absence of deep pain perception (DPP) as prognostic factors for motor function recovery (MFR).

Thirty-three paraplegic dogs with acute or subacute thoracolumbar SCI were prospectively recruited and tested for presence or absence of DPP. MRI including T2W and diffusion tensor sequences of the thoracolumbar spinal cord was performed using a 3T MRI scanner. IMHL was measured and compared to the length of L2 vertebral body; FA values were obtained from SCI epicentre and one vertebral body cranially and caudally of the lesion epicentre. After surgical decompression 19 dogs showed MFR, 14 dogs did not recover. Variance analysis and logistic regressions were calculated between dogs with and without MFR for IMHL and FA values. Sensitivity and specificity were calculated for DPP as dichotomous model.

Neither group differences nor prognostic value could be determined for IMHL. FA values measured caudally of the lesion were significantly different between dogs with and without MFR (p=0.0271). Negative outcome could be predicted using FA with a 62.5% sensitivity, 63.16% specificity, applying cut-off value set at FA > 0.714, whereas DPP revealed 62.5% sensitivity and 73.68% specificity.

In conclusion, pre-operative quantitative MRI displayed no advantage over DPP testing concerning MFR in paraplegic dogs.

**EX-VIVO EVALUATION OF THE THREE-COLUMN CONCEPT IN THORACOLUMBAR FRACTURES IN DOGS.** G.A.C. Diamante1, P.V.T. Marinho2, C.C. Zani1, M. V. Bahr Arias4, 1Department of Veterinary Clinics, Universidade Estadual de Londrina, Paraná, Brazil, 2Faculdade de Medicina Veterinária e Zootecnia, Universidade de São Paulo, São Paulo, Brazil

The three-column theory was developed in human medicine to assess the presence of vertebral instability by imaging and assist in the selection of treatment, with biomechanical studies that demonstrate its applicability in humans. Despite the anatomical and postural differences between humans and dogs, this theory has been applied in veterinary medicine for 26 years, without biomechanical studies in dogs.

The objective of this study was to evaluate the applicability of three-column theory in thoracolumbar fractures in dogs. Local ethical permission was obtained for this study. Eighteen intact thoracolumbar segments (T12-L2) were collected from dogs that had died for reasons unrelated to this study, and then T12 and L2 vertebrae were fixed in a resin base. After that, they were subjected to computed tomography (CT) scanning to detect any fractures or injuries that had not been diagnosed previously. The range of motion (ROM) parameters of flexion-extension and lateral bending was measured with a goniometer before trauma. Fractures were induced using a powered machine applying compressive loads; after the fracture induction, CT scanning was used to classify the test units according to fractures affecting one, two, or three columns. ROM parameters of all specimens were measured again, and statistically compared.

Results showed that specimens that had a fracture in only one column had no statistical difference in ROM in any of the axis, while the specimens that had fractures in two or three columns showed instability in both axis, concluding this way that the three-column concept can be applied to thoracolumbar segment fracture in dogs.

**REMOTE ISCHEMIC POSTCONDITIONING IN DOGS UNDERGOING ELECTIVE SPINAL CORD DECOMPRESSIVE SURGERY.** Mortera, V1; Rose J1, Harcourt-Brown T1, Granger N1. 1University of Bristol, The School of Veterinary Science, Bristol, United Kingdom

Ethical consent (VIN/15/034) obtained from the University of Bristol.

Ischemia-reperfusion injury is a common pathological mechanism in chronic compressive myelopathies. It contributes to neurological deterioration after spinal cord surgical decompression, which can be severe, resulting in prolonged hospitalisation, cost and complications.

Remote ischemic postconditioning (RIPC) consists of eliciting temporal ischemia-reperfusion in a chosen body part to protect distant organs against the consequences of an anticipated episode of ischemia-reperfusion injury. It is effective for spinal cord protection in laboratory animals. A primary concern for companion animals is to ensure safety of the technique.

We applied RIPC to one forelimb (three cycles of 5-minutes ischemia-reperfusion) in ten dogs with chronic cord compression (7 sub-arachnoid cysts, 3 intervertebral disc protrusion) during anaesthesia and before the start of elective decompressive surgery. Seven dogs deteriorated neurologically postoperatively. No adverse effects were observed during RIPC and for 48 hours after surgery. During RIPC, the heart rate increased up to a maximum of 15 heart beats per minutes and the mean arterial blood pressure increased up to a maximum of 20mmHg from pre-RICP baseline values. Serum potassium, lactate and blood gases remained within normal limits and we collected pre, intra and postoperative serum to measure S100B and neuron specific enolase as biomarkers of neuronal damage. Thromboelastography showed a reduction in maximal amplitude and G-value (clot strength) after RIPC, however no dog showed post-operative vascular complication.

RIPC was safe and easy to perform in the studied dogs. These preliminary results allow us to progress to a randomised trial looking at RIPC benefits for dogs with chronic cervical myelopathy.
Surgical Treatment of Chronic Spinal Cord Compression in Two Coatis. N. Meyerhoff1, M. Fehr1,2, J. Neßler1, A. Maiolini1, J. Tünsmeyer1, P. Dziallas1, V. Molnár1, C. Ludwig1, V. Stein1, A. Tipold1. 1Small Animal Clinic, University of Veterinary Medicine Hannover, Germany, 2Clinic for small mammals, reptiles and birds, University of Veterinary Medicine Hannover, Germany, 3Hannover Adventure Zoo, Germany, 4Allwetterzoo Münster, Germany.

Whereas intervertebral disc herniation (IVDH) is considered a frequently occurring diagnosis in dogs, clinical signs and outcome of chronic IVDH with spinal cord compression in coatis (Nasua nasua) are unknown.

The purpose of this case report is the description of successful surgical treatment of chronic IVDH despite challenging circumstances of postoperative care in zoo animals. Two male, middle-aged coatis were presented with mild chronic progressive paraparesis. MRI revealed moderate to severe ventral spinal cord compression due to herniated disc material between the first and second lumbar vertebrae, resp. the twelfth and thirteenth thoracic vertebrae. Treatment included mini-hemilaminectomy and partial corpectomy in one animal, in the other one dorsal laminectomy. The spinal cord was bluish, compressed and deviated. After surgery, both coatis were isolated from the group, objects for climbing were removed from the cage to grant restricted mobility. Follow-up was achieved via personal visits and video-observation. Both coatis were ambulatory the day after surgery and showed continuous slow improvement of neurological status. Both coatis are again presented to the public, one has a completely normal gait 6 months after surgery while the second shows low carriage of the tail. In conclusion, surgical treatment followed by restricted mobility seems to be a useful treatment in chronic IVDH in coatis.


Intervertebral disc disease is one of the most common neurologic disorders in chondrodystrophic breeds. Cervical Intervertebral Disc Herniation (IVDH) represents about 15% of all IVDH.

The objective of this retrospective study was to identify specific features of cervical IVDH in French Bulldogs.

Fifty French Bulldogs with surgically confirmed cervical IVDH, managed at our hospital from 2004 to 2016, were selected. Cervical IVDH were 26% of all IVDH (192) in this breed. Thirty-one dogs were males (62%). Mean age at presentation was 4.9 years, and mean weight was 13.1 kg. Patients were grouped according to the severity of neurological deficits: 28 dogs (56%) with neck pain as only clinical sign, 10 dogs (20%) with ambulatory tetraparesis, and 12 dogs (24%) with non-ambulatory tetraparesis. Mean duration of clinical signs before presentation was 9.9 days. Time from surgery to greatest neurological improvement after surgery (recovery time) was 18, 19.2 and 46.5 days for each group, respectively. The most commonly affected disc space was C3-C4 (31 dogs, 62%), followed by C2-C3 and C4-C5 (7 dogs each, 12%). Neck pain as sole clinical sign was the most frequent sign.

The results suggest that C3-C4 is the most commonly herniated cervical disc in French Bulldogs, and this differs from affected discs in others chondrodystrophic breeds such as Beagles or Dachshunds (C2-C3). French Bulldogs appear to develop IVDH at younger age (4.9 years old) than these other breeds, to have a higher male predisposition and longer recovery time, and cervical IVDH seems to have a higher prevalence in our study population than in others previously described.

The Effect of Kyphoscoliosis on Intervertebral Disc Extrusion in French Bulldogs. MCCM Inglez de Souza1,2, R. Ryan1, RMA Packer2, G. Ter Haar2, S. De Decker2, 1Depatment of Surgery, School of Veterinary Medicine - University of São Paulo, São Paulo, Brazil. 2Royal Veterinary College, University of London, Hatfield, United Kingdom

Although thoracic hemivertebra with kyphoscoliosis is often considered an incidental finding in brachycephalic breeds, it has been suggested to interfere with spinal biomechanics and intervertebral disc degeneration. Our aim was to evaluate if the occurrence of kyphoscoliosis was associated with a higher prevalence of cervical or thoracolumbar intervertebral disc extrusion (IVDE) in French Bulldogs (FB). FB that underwent computed tomography for reasons unrelated to spinal disease (n=70), FB with cervical IVDE (n=24), and FB with thoracolumbar IVDE (n=35) were included. Signalment, occurrence, number and anatomical location of hemivertebra, spinal kyphosis, scoliosis, and, if relevant, location of IVDE were recorded. Imaging studies were evaluated by two authors, after which a consensus opinion was reached.

There was no significant association between the presence of kyphosis, scoliosis, or hemivertebrae and the occurrence of thoracolumbar or cervical IVDE. There was no significant association between the occurrence of kyphosis, scoliosis, or hemivertebrae and the age of dogs with cervical or thoracolumbar IVDE. There was a significant association between the presence of kyphosis and the anatomical location of thoracolumbar IVDE (p=0.036). Dogs with kyphosis were more likely to have caudal lumbar IVDEs (L2-L6) compared to FB without kyphosis. There was no association between the presence of scoliosis and the location of the affected disc.

The results of this study do not support the hypothesis that vertebral malformations in French Bulldogs increase the risk of cervical or thoracolumbar IVDE. In agreement with previous findings, dogs with kyphosis are more likely to have a caudal lumbar IVDE.

Comparison of the Accuracy of Radiography and Conventional Computed Tomography for Detection of Congenital Thoracic Vertebral Malformations in Brachycephalic “Screw-Tailed” Dog Breeds. J. Brocal1, S. De Decker2, R. Jose-Lopez2, J. Guevar2, M. Ortega2, G. Ter Haar2, R. Gutierrez-Quintana2. 1College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, UK. 2Clinical Science and Services, The Royal Veterinary College, Hatfield, Hertfordshire, UK. 3Centro Clínico Veterinario Indautxu, Bilbao, Spain.
Congenital vertebral malformations (CVM) are relatively common in the thoracic vertebrae of brachycephalic dogs. They can lead to kyphosis of the vertebral column and secondary neurological deficits. The purpose of this retrospective study was to compare the accuracy of radiography and computed tomography (CT) for detection of CVM’s.

Brachycephalic dogs, which had both radiographs and CT of the thoracic vertebral column performed for a variety of reasons, were retrospectively reviewed by three observers, which classified each thoracic vertebra into normal or abnormal. This process was performed with lateral radiographs alone, with both lateral and ventro-dorsal views, and CT independently. One observer reviewed the images again two weeks later. The intra and inter-observer agreement was calculated.

A total of 630 vertebrae in 49 dogs were reviewed. All observers identified more affected vertebrae when evaluating lateral and ventro-dorsal radiographic views compared to lateral views alone (P<0.05); and more with CT when compared to lateral and ventro-dorsal radiographic (statistically significant in two observers). Intra-observer agreement in diagnosing absence/presence of malformations for all three techniques was very good (κ: 0.91). Inter-observer agreement varied from moderate (κ: 0.588) to good (κ: 0.755).

Approximately 60% of dogs had more than one affected vertebra and the number of dogs identified with no CVM’s was not significantly different between the two comparisons described above.

A hereditary component for the development of CVM’s has been suggested and CT seems to be an accurate imaging screening modality for selective breeding.

RESULTS OF NON-SURGICAL TREATMENT FOR CONGENITAL VERTEBRAL BODY MALFORMATIONS IN ELEVEN DOGS. S. Wyatt1, R. Gonçalves2, R. Gutierrez-Quintana3, S. De Decker1. 1Royal Veterinary College, Hatfield, UK, 2University of Liverpool, Neston, UK 3University of Glasgow, Glasgow, UK.

Although several surgical techniques have been reported, little is known regarding results of medical management for dogs with clinically relevant hemivertebra. The aim of this study was to evaluate the outcome of medical management for dogs with thoracolumbar hemivertebra.

An electronic medical database was searched for dogs with neurological signs caused by hemivertebra with or without spinal kyphosis. Diagnosis was confirmed by MRI in all cases. Dogs were excluded if records or imaging studies were incomplete or unavailable for review, or if dogs had concurrent disorders that could contribute to clinical signs. Medical management typically consisted of exercise modification in combination with anti-inflammatory or analgesic drugs. Follow-up data was obtained by information from re-examination visits and a standardized telephone questionnaire.

Eleven dogs of screw-tailed brachycephalic breeds with a median age of 6 months were included. All dogs presented with ambulatory paraparesis and ataxia and in one dog spinal hyperesthesia could be elicited. Medical/conservative management consisted of restricted exercise with (n=3 dogs) or without (n=3) physiotherapy in six dogs, physiotherapy without restricted exercise in three dogs, and no exercise modification in two dogs. Seven dogs received additional medication, which consisted of prednisolone in five dogs and gabapentin in two dogs. Of the eleven dogs included, four were ultimately euthanized due to progressive neurological deterioration, two underwent surgery due to progressive neurological deterioration, and the remaining five dogs were alive despite progressive neurological deterioration.

Medical management was not associated with a favourable outcome as all dogs demonstrated progression of clinical signs.

CASE SERIES: MRI FINDINGS AND FOLLOW-UP AFTER SURGICAL TREATMENT IN THREE FRENCH BULLDOGS WITH MENINGOMYELOCELE. L. Martin1, V. Cervera2, J. Cabré3, S. Ródenas1. 1 Service of Neurology and Neurosurgery of Valencia Sur Hospital, Silla (Valencia), Spain, 2 Service of Imaging Diagnosis of Valencia Sur Hospital, 3 Vetamic Veterinaris Hospital, Cambrils (Tarragona), Spain.

Spina bifida (SB) is a developmental defect characterized by incomplete fusion of the vertebral arches. Spina bifida can be accompanied by meningocele/meningomyelocele (protrusion of meninges/nervous tissue). Only one case of SB with meningocele/myelocele describing MRI findings and surgical treatment has been reported in dogs. The aim of this case series study is to report MRI findings, surgical treatment and follow up in three French bulldogs with SB and meningocele/myelocele.

Three French bulldogs were enrolled in this study: one 5 month old male and two 4 month old female littermates. Common clinical signs were fecal, urinary incontinence and dimpling of the skin. All cases showed hipoalgesia of the perineal area and absence of perineal reflex and tone. Only one dog presented mild paraparesis.

Lumbar MRI revealed an incomplete dorsal lamina of the L7 and sacrum in two dogs, and the same defect in L6-L7 in the other dog, with protrusion of the meningeal sac and nervous tissue in all cases.

Surgical treatment consisted in dissection of the abnormal skin attached to the meningeal structures.

Two cases remained incontinent and the other case was urinary continent after surgical treatment.

In this study one dog was successfully urinary continent after surgery. MRI was very useful in order to characterize the protrusion of the nervous tissue and meninges through the defect. Early surgical treatment as in humans is indicated in dogs with SB and meningocele/myelocele. Surgery of SB/meningocele/myelocele may be successful in some dogs in order to regain urinary continence.

SYRINGOMYELIA CLASSIFICATION ACCORDING TO ASSOCIATED MAGNETIC RESONANCE IMAGING FINDINGS IN FRENCH BULLDOGS: 64 CASES (2008-2016). A. Suñol Iniesta1, M. López-Font2, C. Morales1,3, J. Mascort1, M. Manera4, P. Montoliu1,2,3, S. De Decker1. 1Imagovet, Barcelona. 2Hospital Ars Veterinaria, Barcelona. 3Hospital Clínic de Barcelona. 4Hospital Clínic de Barcelona.

Syringomyelia is reported mainly associated to Chiari-Like Malformation syndrome (CLM). In dogs, it has infrequently been related to other causes, including other craniocervical malformations and spinal or brain neoplasia. In human medicine, syringomyelia
is classified according to suspected aetiology.

The objective of this retrospective study was to evaluate syringomyelia in French bulldogs according to suspected aetiology based on magnetic resonance imaging (MRI) findings. Medical records and MRI series of French bulldogs with diagnosis of syringomyelia were retrieved from two MRI centres (2008-2016). Signalment, indication for MRI, location of syringomyelia, primary diagnosis, other imaging findings, presence of CLM, and presence of ventricular enlargement were evaluated for each dog.

Sixty-four dogs met the inclusion criteria, 21(33%) females and 43(67%) males. Median age was 6 years. Clinical signs could be related to syringomyelia in 48(75%) dogs, whereas in 16(25%) dogs syringomyelia was considered an incidental finding. Only 6 dogs were referred for cervical hyperesthesia or phantom scratching. In addition to syringomyelia, a total of 115 lesions were identified; 46(72%) dogs had at least 2 abnormalities. Alterations apparently associated to the syringomyelia were classified into 5 categories: craniocervical malformations (CLM, atlantooccipital overlapping, dural band) in 19(30%) cases, intracranial space-occupying lesions (including hydrocephalus) in 22(34%), spinal compressive diseases (mainly disc herniation) in 13(20%), and non-compressive hemivertebral in 4(5%). In 6(11%) dogs no associated lesion was identified.

Results suggest that syringomyelia in French bulldogs is frequently unrelated to CLM. Males were overrepresented, and signs of neuropathic pain are uncommon or poorly recognized in this breed.

INTROOPERATIVE ULTRASOUND ELASTOGRAPHY OF THE CANINE SPINAL CORD. Prager, J1; Delaney A2, Rose J3, Harcourt-Brown T4, Chari D5, Granger N6, 1 University of Bristol, The School of Veterinary Science, Bristol, United Kingdom, 2 University of Keele, Institute for Science and Technology in Medicine, Keele, United Kingdom

This pilot study investigated the feasibility of using intraoperative ultrasound elastography to determine elasticity of the canine spinal cord. Establishing the mechanical characteristics of injured spinal cord may: (i) help predict recovery; and (ii) allow design of novel therapies such as implantable hydrogels with tissue-matched elasticity.

Dogs undergoing routine decompressive surgery following acute thoraco-lumbar intervertebral disc herniation were recruited. Measurement of shear wave velocity (m/s) of the spinal cord was obtained using Acoustic Radiation Force Impulse Elastography (Siemens Acuson S2000 ultrasound machine), with sterile saline used as contact medium. Shear wave velocity was recorded cranially, caudally and at the lesion site. Ultrasound elastography was also performed at the thoraco-lumbar junction on unfixed fresh normal canine spinal cord specimens within 8 hours of euthanasia. A CIRS Ultrasound Elastography QA Phantom (Model 049A) was used to provide known values of elasticity (kPa).

Measurements were obtained from 6 dogs intraoperatively taking <15 minutes each. The median cord elasticity was 13.3kPa (interquarte range: 10.3-63.9kPa) at the lesion epicentre, and 30.5kPa (interquarte range: 15.4-35.6kPa) and 26.7kPa (interquarte range: 16.7-56.3kPa) cranial and caudal to the lesion respectively, although this was not different from the epicentre values. Median cadaver spinal cord elasticity was 7.58kPa (interquarte range: 3.41-18.4kPa) and significantly different from intraoperative values (p=0.0081, Mann-Whitney U). Elasticity values calculated from ultrasound measurement of the phantom were within 30% of certified values.

We demonstrate that intraoperative ultrasound elastography of the canine spinal cord is feasible, and that post-mortem spinal cord elasticity is not representative of in vivo elasticity.

MAGNETIC RESONANCE IMAGING CHARACTERISTICS OF CAUDA EQUINA NERVE ROOTS IN 50 DOGS WITH DEGENERATIVE LUMBAROSACRAL STENOSIS. D. Alder1, S. Ohlert2, F. Steffen1, 1. 1Clinic for Small Animal Surgery and 2Section of Diagnostic Imaging, Vetsuisse Faculty, University of Zurich, Switzerland.

Nerve root position and morphology observed on MRI yield important diagnostic information in people with lumbar pain because they can be used to differentiate between non-specific back pain and compressive lesions. In dogs, demonstration of nerve root compression is the main imaging criteria for the diagnosis of DLSS. While histopathologic alterations in chronically compressed nerve roots have been described, MRI-abnormalities in nerve root morphology and signal behaviour have not been reported in dogs with DLSS. MR images of 50 dogs with and 17 dogs without clinical signs of DLSS were retrospectively evaluated for presence of abnormalities in size and signal behaviour of cauda equina nerve roots. Three evaluators used sagittal and transverse T2-weighted images to independently score the subjective increase in size and signal changes of L7- and S1- roots. The findings were correlated with the presence of foraminal and/or central stenosis. Interobserver agreement for nerve root changes was assessed with Cohen’s kappa (paired comparison).

A total of 268 nerve roots were examined: 20% were enlarged (L7: 69%; S1: 31%) and 16% were hyperintense (L7: 72%, S1: 28%). No enlarged nerve roots were found in control cases. Foraminal stenosis was present in 64/134 foramina, and central stenosis was found in 33/67 cases. Association between enlarged nerve roots and foraminal/central stenosis was significant. Interobserver agreement was fair (0.41 to 0.6) to good (0.61 to 0.8) for both criteria, increase in size and hyperintensity.

In conclusion, L7 and S1 nerve root changes occur frequently in dogs with DLSS and support the clinical diagnosis.

CLINICAL PRESENTATION AND MANAGEMENT OF GERMAN SHEPHERD DOGS WITH LUMBOSACRAL PAIN PRESENTED IN FIRST OPINION PRACTICE. G. Harris, D. O’Neill2, D. Brodbelt2, D. Church1, S. De Decker2. 1The Queens Veterinary School Hospital, Cambridge University, Madingley Road, Cambridge UK. 2The Royal Veterinary College, University of London, Hatfield, UK.

German Shepherd Dogs (GSDs) are predisposed for lumbosacral disease. Previous research, evaluating dogs presented at a referral
institution, suggested medical management of LS disease was associated with a fair prognosis. This study evaluates clinical management of LS pain in GSDs in first-opinion practice.

Data on GSDs with confirmed lumbosacral pain was extracted from the VetCompass database of primary-care veterinary clinical records in the UK. Of 85 GSD identified, 60.0% were female, and 68.5% were neutered. The median age at diagnosis was 8.3 years. Concurrent hip pain was shown in 57.7% of cases. Of the 44.7% of dogs that underwent neurological examination, 31.8% had proprioceptive deficits. Incontinence was recorded in 10.6% of dogs. 4.7% dogs were referred to a referral hospital. Radiographs were performed in 25.9% of cases. Analgesia was given to 95.3% of dogs. Non-steroidal-anti-inflammatory-drugs were given to 84.7% of dogs. The most used analgesic protocols were NSAIDS alone (50.6%), opioids and NSAIDS (17.7%) and glucocorticoids and NSAIDS (11.8%). Rest was advised in 23.5% of cases. The vet or owner noted improvement in 64.7% of cases.

During the study period, 44.7% of the dogs died with 34.2% of these deaths being ascribed to lumbosacral pain.

Although this study had limitations in diagnostic accuracy, it overcame selection biases from those dogs that are referred for their condition. This study shows very low numbers of dogs are referred, therefore allowing a different population of dogs with lumbosacral pain to be evaluated.

**MAGNETIC RESONANCE IMAGING FINDINGS OF SPINAL DYSRAPHISM IN A WEIMARANER DOG. F. Tirrito, F. Cozzi, M. Bonaldi, R. Lombardo.**

Spinal dysraphism (SD) is an abnormal condition characterized by a variety of structural and functional anomalies of the spinal cord, due to a defect in closure of neural tube and malformative lesions of spinal cord structures, mostly in lower thoracic and lumbosacral regions.

SD has been mostly described in Weimaraners and a hereditary basis has been identified.

Characteristic clinical signs are observed by 4-6 weeks of age and include postural abnormalities, simultaneous hind limb gait (bunny hopping), ataxia and paresis, bilateral synchronous withdrawal reflex in the hind limbs.

A 1.5 year old male Weimaraner was presented with a history of non progressive gait abnormalities. Neurological exam revealed hind limbs ataxia and mild paresis, bunny hopping and simultaneous bilateral flexor reflex of both hind limbs.

Spinal magnetic resonance (MR) showed a well defined T2-WI and STIR linear hyperintensity, iso-hypointense in T1-WI, extending on the dorsal spinal cord midline from T9 to L1. On transverse images, this midline T2-WI hyperintense area expanded from dorsal to central parts of the spinal cord, with supposed direct connection with the dorsal subarachnoid space. As a consequence of these alterations, the spinal cord appeared almost heart shaped. No abnormal gadolinium enhancement was observed.

These MR findings were considered suggestive of a neural tube defect such as partial duplication of the spinal cord (hemidydemia), diastematomyelia, spinal cord midline cavitations (siringomyelia) or other aberrations possibly associated with abnormal cerebrospinal fluid distribution.

To author’s knowledge MR findings of spinal dysraphism have not been previously described in dogs.

**LIPOMENINGOMYELOCELE ASSOCIATED WITH DIPLOMYELIA IN A DOG. S. Schulze, N. Ondreka, M. Kolecka, M.J. Schmidt.**

A two year-old male neutered mixed breed dog presented with a soft tanged subcutaneous mass dorsal to the spinous processes of T11/12, which was tender on palpation. Furthermore proprioceptive ataxia of the hind limbs was noted upon clinical workup. On magnetic resonance imaging (MRI) the spinous process of T11 presented a sagittal split intersected by epidural and epaxial soft tissue. A thin T2-hypointense band could be traced from the skin surface to the dura through the split spinous process of T11. The dural tube was focally lifted towards this T2-hypointense band. Level with the disc space T11/T12 severe dilation of the subarachnoid space was noted. At T12 the spinal cord was U-shaped with a dorsal split and then completely bipartite into two cords at T11. From T6 to T8 the central canal presented marked widening. The MRI findings were consistent with a spina bifida with a lipomeningomyelocele and diplomyelia. Surgery was performed to remove the lipomeningomyelocele via hemilaminectomy. On necropsy and patho-histology connective and fatty tissue with vessel sections were found.

The MRI findings as well as the patho-histological results in this report are compatible with a spina bifida with a lipomeningomyelocele and diplomyelia in the caudal thoracic spine. To the author’s knowledge this is the first case-report of a lipomeningomyelocele associated with diplomyelia in a dog.

**A CANINE BRAIN TEMPLATE FOR IMAGE PROCESSING OF CLINICAL MAGNETIC RESONANCE IMAGING DATA. S. Schulze, M.J. Schmidt, T. Flegel, E. Ludewig, M. Gounis, J. Boltze and B. Nitzsche.**

In humans, surgical treatment of drug resistant epilepsy (‘epilepsy surgery’) reduces the seizure frequency with a good prognostic outcome. Knowledge of epileptogenic zones, especially in focal cortical malformations are essential for the successful resection of an epileptogenic focus. Structural and functional magnetic resonance imaging (MRI) support the focus determination but, unfortunately, diagnostic capability is limited by missing brain references. Computational neuroscience may overcome the limitation with the help of population-averaged reference space (template). The techniques allow for comparison across individuals including quantification of anatomical features. Here we present an atlas of the canine brain that may be suited for this purpose.
T2-weighted MRI data (3 T Siemens and 1 T Gyroscan Intera Phillips) of 37 dogs without structural or cerebral-functional lesions were used. Statistical Parametric Mapping (SPM8, UK) and Matlab (Mathworks, UK) were used for the co-registration of canine neuroimages. This includes manual (by using F is ImageJ, FIJI, Germany) and automatic ‘unified’ segmentation procedure of SPM to retrieve grey (GM) and white (WM) matter as well as cerebrospinal fluid (CSF).

The established template showed detailed and precise defined GM, WM just as CSF. Cerebral gyri and sulci are highly contrasted and exactly described. Consequently, our framework provides an automatically neuroimage processing of clinical canine MRI data for brain tissue analysis. Further work will include more decided templates and a priori tissue information in respect to the morphologically variance of different breeds. This includes a spatial canine brain model with labelled areas to allow further analyses of cortical structures.

**APPLICATION OF A FUNCTIONAL BRAIN ATLAS TO INTERPRET HUMAN EPILEPTIC SEIZURE-RELATED fMRI MAPS AND CONSIDERATIONS FOR APPLICATION IN ANIMALS.** M. Charalambous1, L. A. van Graan1, A. Liston2, L. Lemieux3. 1Dept. of Clinical and Experimental Epilepsy, UCL Institute of Neurology, Faculty of Brain Sciences, 2Dept. of Medical Physics, University College London, UK

Contrary to veterinary patients, humans with drug-resistant epilepsy might be considered for epilepsy surgery. Advanced neuroimaging techniques such as magnetic resonance imaging (MRI) are routinely used to help localize the surgically resectable epileptogenic area successfully in some patients. However, this approach often fails and new methods need to be developed. Recently, functional MRI (fMRI) has been used alone or in combination with electroencephalography (EEG) to obtain maps of cerebral activity during ictal and interictal phases, thereby providing a possible avenue for improved localization of the brain areas directly responsible for epileptic seizures.

In our project, seven patients with drug-resistant epilepsy were studied. Simultaneous EEG-fMRI was performed to map the specific brain networks involved during seizures, which were divided into a series of phases: ictal onset, ictal established and late ictal. Statistical parametric mapping (SPM) was then used to generate haemodynamic maps which were analyzed using a new atlas to measure the levels of involvement of ten normal functional brain networks. Similarities in brain activation during seizures across patients were found, and the level of involvement of the networks varied across ictal phases.

In conclusion, we have measured the relationship between ictal activity and brain networks involved in normal brain activity, opening the way to a more quantitative approach to the study of ictal semiology. To consider this in veterinary medicine, similar neuroimaging methods should be recruited and developed. The increasing use of EEG in veterinary patients might be a stepping-stone for the introduction of further neuroimaging techniques, which could actually form the base of epilepsy surgery in animals.

**THE EDINBURGH COMPANION ANIMAL BRAIN BANK – A NEW RESOURCE FOR CROSS-TRANSLATIONAL NEUROLOGY.** N.M. Rzechorzek1,2, M. Flook3, C. Pennycook3, E. Jeffery1, S. Smith3,4, C. Smith2, K. Marioni-Henry1. 1Neurology/Neurosurgery Service, Hospital for Small Animals, Royal (Dick) School of Veterinary Studies and Roslin Institute, 2Centre for Clinical Brain Sciences, 3Easter Bush Pathology, Royal (Dick) School of Veterinary Studies, 4Centre for Comparative Pathology, University of Edinburgh, UK.

Access to high quality brain tissue is critical for understanding disease pathogenesis and to validate novel pre-mortem biomarkers for neurological disorders. An optimal resource would promote cross-translation between human and veterinary neurologists, through comparative clinical and molecular phenotyping. Successful human brain banks continue to expand, yet there is no equivalent archive for veterinary patients. We sought to establish the UK’s first Companion Animal Brain Bank.

Adapting protocols from the MRC Edinburgh Brain Bank, we have developed standardized methods for archiving brain tissue from animals euthanased on welfare grounds. Samples are collected with informed consent and approval of the R(D)SVS Veterinary Ethical Review Committee. Whole brains are evaluated grossly then bisected to provide fresh-frozen and formalin fixed tissue for matched molecular and histopathological readouts respectively. Fixed hemibrains are processed in transverse section and 31 specified brain regions are embedded.

To date, 30 brains have been banked. 11 of these are derived from animals with non-neurological conditions (designated control tissue). Mean canine fresh brain parameters ± standard error include brain length (rostral tip of the frontal cortex to the caudal tip of cerebellar vermis; 79.0 ± 1.5 mm), brain weight (91.8 ± 3.72 g) and post-mortem interval (28.2 ± 4.7 h). Brain length and weight correlate with $r^2 = 0.843$.

Our protocols optimise sample quality within the logistics of a referral setting and can be reproduced for multi-centre collaborations or for donation to a central bank. Our objective is to create an online searchable database to facilitate tissue requests for ethically-approved research.

**BRAINSTEM AUDITORY EVOKED POTENTIALS IN DOGS WITH IDIOPATHIC PERIPHERAL VESTIBULAR SYNDROME.** T.A. Shaw, F. Liebel, N. Granger, T.R. Harcourt-Brown. The School of Veterinary Sciences, University of Bristol, United Kingdom

Dogs with idiopathic vestibular syndrome can also have involvement of nearby cranial nerves (for instance the facial nerve in idiopathic facial neuropathy). The proximity of the sensory axons transmitting vestibular and auditory information within cranial nerve VIII means that concomitant vestibular and auditory dysfunction is plausible in these dogs, but remains to be investigated. The aim of this study was to evaluate dogs with idiopathic vestibular syndrome for hearing loss and cochlear nerve dysfunction.

In this retrospective study (over 6 years including 12 dogs), we reviewed BAEP traces of dogs diagnosed with idiopathic...
vestibular syndrome. Wave I-II and I-V interpeak latency (IPL) was compared between the affected side (ipsilateral to the vestibular localisation) and the unaffected contralateral side via a repeated measures t-test.

Nine dogs were diagnosed with idiopathic facial neuropathy and ipsilateral idiopathic vestibular syndrome and three dogs were diagnosed with idiopathic vestibular syndrome only. All dogs were considered to have morphologically normal I, II and V waveforms. Affected/unaffect ed I-II and I-V IPLs were 0.91 ±0.049 / 0.90 ±0.067 ms and 2.72 ±0.23 / 0.277 ±0.26 ms, respectively. The difference between the affected and unaffected side was not statistically significant (I-II IPL: mean difference 0.01583 ms; 95% confidence interval -0.00892, 0.0405; p=0.187; I-V IPL: mean difference -0.482 ms; 95% confidence interval -0.102, 0.00546; p=0.927).

The data do not support the hypothesis that dogs with idiopathic vestibular syndrome have cochlear nerve dysfunction, and suggest that all dogs were able to hear. This information could help further characterise canine idiopathic vestibular syndrome and idiopathic cranial polyneuropathies.

FACIAL NERVE PARALYSIS IN DOGS: A RETROSPECTIVE STUDY OF 69 CASES. C. Rico, L. Giraud, L. Cauzinille. Centre Hospitalier Vétérinaire Frégis, Arcueil France

Facial paralysis is readily recognised in small-animal veterinary practice because of its manifestation of facial asymmetry; the idiopathic form has been previously reported to be present in 75% of dogs. The purpose of this study in dogs was to classify and determine the origin of facial nerve dysfunction using enhanced diagnostic procedures, including magnetic resonance imaging (MRI).

The medical records of 69 dogs admitted for facial paralysis were reviewed. Neurological examination confirmed facial nerve abnormalities, which were all investigated with MRI.

Idiopathic facial paralysis was diagnosed in 48% of dogs. Vestibular signs were the most common additional clinical signs and were observed in 36% of dogs with idiopathic facial paralysis.

Peripheral nervous system disease was diagnosed in 19% of dogs, and central nervous system disease occurred in 30% of dogs. Two new predisposed breeds are added, the French bulldog and the Cavalier King Charles spaniel.

Improved diagnostic methods depend on the frequency of inflammatory/infectious diseases, which were absent in the central nervous system aetiologies of a previous similar study, and revealed metabolic (hypothyroidism), inflammatory and neoplastic aetiologies for peripheral nervous system disease.

COMPARISON OF THE INTEROBSERVER AGREEMENT IN THE EVALUATION OF THE PATELLAR TENDON- AND BICIPITAL REFLEX IN DOGS, F Giebels, B Kohn, L Pieper, S Loderstedt. Small Animal Clinic, Faculty of Veterinary Medicine, Freie Universität Berlin, Berlin, Germany.

The reliability of reflex-assessment differs between the authorship. Since the patellar tendon reflex (PTR) is accepted to be highly reliable, the biceps tendon reflex (BTR) is regarded to be of low reliability. Nevertheless, these statements base on subjective observations than on an empirical study. It has been postulated, that the expertise of the observer influences the interobserver agreement (IA). The goals of this study were: (1) quantification of the interobserver agreement of PTR and BTR and (2) evaluation of the influence of the observer’s level of expertise on the IA.

For PTR-assessment 56 forelimbs and for BTR-assessment 64 hindlimbs of neurological unremarkable dogs were examined in lateral recumbency by the same examiner and videotaped. Examination sequences were anonymised and evaluated blinded by 12 observers divided in 3 groups of 4 observers: veterinary-neurologists (group1), veterinary-surgeons (group2), last year veterinary-students (group3). Observers evaluated two categories: reflex-presence (0;1), reflex-briskness (0 (absent)-4 (clonic)). IA was evaluated with reliability analysis for BTR and PTR separately and compared to each other.

Reflex-presence IA was significantly highest for group1 in both reflexes. Reflex-briskness IA of BTR was significantly highest for group1, for PTR significantly lowest for group3. Reflex-briskness IA was higher for BTR compared to PTR in group1. In group2 and 3 reflex-briskness of PTR showed higher IA. Level of expertise showed a higher influence on reflex-briskness IA of BTR.

BTR can be assessed by neurologists more reliable than PTR and reflex assessment is highly dependent on observer’s level of expertise.

CANINE IDIOPATHIC EPILEPSY: REAL WORLD EFFECTIVENESS OF TREATMENT AND ITS EFFECT ON DOG AND OWNER QUALITY OF LIFE, L.A.J. Smith, P. Freeman, L. Alves. ‘Department of Veterinary Medicine, The University of Cambridge

A retrospective, questionnaire based study was carried out to: assess the effectiveness of treatment of idiopathic epilepsy (IE) in terms of the owners’ perceptions, to discover how caring for an epileptic dog affects owner’s quality of life (QOL), and to assess how IE and its treatment affects the QOL of dogs.

Cases of canine IE were found by searching the database of the Queen’s Veterinary School Hospital, Cambridge. An online questionnaire was designed based on previous studies and the QOL assessment questionnaire designed by Wessman et al. (2014), and sent to owners. 19 completed questionnaires were returned. 30% of owners described the seizure frequency of their dogs on treatment as not acceptable. There was no correlation between owners’ perception of acceptability of seizure frequency and seizure frequency. 89% of dogs showed adverse effects of anti-epileptic drugs (AEDs). Abnormal behaviours were present in 63% of dogs. AEDs improved some behaviours and made others worse. 68% of owners described their dog’s QOL as good, but QOL improved on treatment in only 42% of dogs. 95% of owners reported that caring for their dog was either not at all or only slightly bothersome.

Owners’ ideas of effective seizure control are variable. IE in dogs is linked with behavioural changes and treatment worsens some behaviours while improving others. Owners perceive that their dogs have a good QOL although this may not be improved by treatment,
OVERSHUNTING AND SUBDURAL HAEOMORRHAGE AFTER IMPLANTATION OF A LOW-PRESSURE VALVE VENTRICULOPERITONEAL SHUNT IN A DOG WITH HYDROCEPHALUS INTERNUS, QUADRIGEMINAL CYST AND HIGH INTRACRANIAL PRESSURE. S. Hanemann, I. Merseburger, V. Fromme, S. Piesnack, T. Flegel. Department of Small Animal Medicine, University of Leipzig, Germany.

A three-month-old mixed breed dog was presented with generalized ataxia, hypermetria, head tilt, intention tremor and absent menace response. MRI revealed hydrocephalus internus, quadrigeminal cyst and foramen magnum herniation. A ventriculoperitoneal shunt (VPS) with opening pressure of 5cm H₂O was placed in the right ventricle. Intraoperatively intracranial pressure (ICP) was 21cm H₂O.

One month later the dog was presented with acute onset of nausea, salivation and right-sided central blindness. MRI revealed a bilateral high grade subdural haemorrhage with collapse of underlying brain parenchyma and deterioration of the foramen magnum herniation. Trepanation with hematoma evacuation was performed and the VPS was ligated. After initial improvement, the dog showed acute vestibular signs again. A third MRI pictured a mild subdural hematoma and a high degree of foramen magnum herniation. Foramen magnum decompression and fenestration of quadrigeminal cyst was performed. Two months later, the dog presented without neurological deficits except of a mild hypermetria. Control MRI showed no recurrence of the quadrigeminal cyst, an organisation of the remnants of the subdural hematoma. There were no signs of increased ICP.

It can be speculated that the quadrigeminal cyst was communicating with the hydrocephalus internus. So foramen magnum decompression and fenestration of the cyst could have been enough to drain the hydrocephalus. Overshunting is one complication after VPS implantation. That’s why ICP measurement should be performed before VPS surgery and the opening pressure should be selected accordingly. However, if overshunting develops, it can be treated successfully by reducing CSF drainage and removal of subdural hematoma.

FRAMELESS STEREOTACTIC VOLUMETRIC MODULATED ARC RADIOTHERAPY OF BRACHIAL PLEXUS TUMORS IN DOGS: 10 CASES. M. Dolera1, L. Malfassi1, C. Bianchi1, N. Carrara1, L. Corbetta1, S. Finesso1, S. Marcarini1, G. Mazza1, S. Pavesi1, M. Sala1, G. Urso1,2. 1La Cittadina Fondazione Studi e Ricerche Veterinarie, Romanengo, Italy, 2Azienda Socio Sanitaria Territoriale di Lodi, Lodi, Italy.

Canine peripheral nerve sheath tumors (PNSTs) can involve the brachial plexus, its peripheral branches, proximal nerves, and roots. Prognosis after surgical resection is poor. The aim of this study was to evaluate the feasibility and the efficacy of stereotactic radiotherapy.

Dogs with clinical signs and MRI findings consistent with PNSTs of brachial plexus, branches and nerve roots were treated with LINAC based Volumetric Modulated Arc Radiotherapy (VMAT). Mean delivered dose was 35 Gy in 5 fractions. Clinical and MRI follow-up examinations were planned every two months. Neurological dysfunction, volumetric response and radiotoxicity were graded and recorded. Overall and progression-free survival time were estimated.

Ten dogs were enrolled. Progressive forelimb paresis, axillary pain and various degrees of tetraparesis were the most frequent presenting complaints. Tumors involved the plexus and proximal nerves in 3 dogs, the plexus, proximal nerves and nerve roots in 5 dogs, the nerve roots and proximal nerves in 2 dogs. Partial or complete reduction of neurological deficits were observed in all treated dogs. Partial responses were observed in 10/10 patients. Local recurrence was observed in 9/10 of treated dogs. Mean overall survival of 371 days and mean progression-free survival of 240 days are comparable to surgical literature data regarding the plexus and proximal nerves localization but are superior in comparison to nerve roots localization. No radiotoxic effects occurred.

VMAT RT can be a safe and viable alternative to surgery in case of canine brachial plexus PNSTs involving the proximal nerves and roots.

FRAMELESS STEREOTACTIC RADIOTHERAPY ALONE AND COMBINED WITH TEMOZOLOMIDE FOR CANINE GLIOMAS. M. Dolera1, L. Malfassi1, C. Bianchi1, N. Carrara1, L. Corbetta1, S. Finesso1, S. Marcarini1, G. Mazza1, S. Pavesi1, M. Sala1, G. Urso1,2. 1La Cittadina Fondazione Studi e Ricerche Veterinarie, Romanengo, Italy, 2Azienda Socio Sanitaria Territoriale di Lodi, Lodi, Italy.

The aims of this work were to evaluate curative intent volume modulated arc hypo fractionated radiotherapy (VMAT RT) for canine gliomas alone and in combination with temozolomide.

A prospective trial was performed in dogs with brain gliomas. The cohort was divided into three arms: palliation, radiotherapy alone (RT), RT + temozolomide (RT+TMZ). The RT schedule was ranged between 33 Gy/5 fx and 42 Gy/10 fx. Temozolomide was administered during and after the treatment. Serial clinical and MRI examinations were planned 2, 4, 6, 12, 18, 24 months after irradiation. Overall and disease specific survival time was estimated.

30 dogs were palliated, 22 dogs were treated with RT and 20 with RT+TMZ. Complete and partial responses were observed on the whole in 63.2% and 90.9% of alive patients in RT and RT+TMZ arm at one year. Median survival in palliation arm was 94 days. Median survival of RT arm (383 days) and RT+TMZ arm (420 days) were not significantly different (p=0.61). The progression free survival in RT arm (255 days) and RT+TMZ arm (345 days) were significantly different (p=0.027). The grade of the tumor was not correlated with the survival. The ratio between tumor and brain volume <5% and the clinical presentation with normal mental status were positively correlated with the survival.
VMAT hypo fractionated RT is feasible and effective for canine brain gliomas. The combination with TMZ ameliorate the progression-free survival. A further escalation of TMZ dose trial could be advisable.

MENINGEAL CARCINOMATOSIS AND SPINAL CORD INFILTRATION CAUSED BY A LOCALLY INVASIVE PULMONARY ADENOCARCINOMA IN A CAT. C. Posporis1, L. Grau-Roma1, M. Bertal2, M. Oliveira2, L. Polledo1, A. Wessmann2.

1School of Veterinary Medicine and Science, University of Nottingham, UK, 2Department of Neurology and Neurosurgery, Pride Veterinary Centre, Derby, UK

A 12-year-old domestic cat presented with acute non-painful hind limb ataxia localising to T3-L3 spinal cord segments. MRI revealed no significant findings other than paravertebral muscular hyperintensity on T2WI at the level of T7-T8 vertebrae. The cat improved on conservative management but returned 3 months later with acute deterioration. Repeated MRI showed meningeal enhancement at the level of T7-T8 vertebrae and STIR hyperintensity of the paravertebral musculature extending to the right thoracic wall and pleural space. CT of the thorax showed mineralised consolidated lesions of the right lung, restricted pleural effusion, and peristitis of multiple ribs. The cat had been treated for a pyothorax five years earlier but showed no current respiratory signs. Cerebrospinal fluid examination showed lymphocytic pleocytosis but no neoplastic cells. Biopsy of the affected muscles and cytology of the lung and pleural fluid suggested a malignant epithelial cell tumour. Post-mortem examination confirmed an invasive pulmonary adenocarcinoma locally infiltrating the thoracic musculature, T7 and T8 vertebrae and the spinal cord white matter. Meningeal carcinomatosis was detected with neoplastic cells found within the ventral median fissure of the spinal cord. No metastases were observed in any other organs indicating that neoplastic cells reached the spinal cord by direct extension.

Given the location of the neoplasia and the history of pyothorax, a potential influence of the thoracocentesis and/or the chronic inflammation in the tumour development is speculated. To the authors’ knowledge, neither local infiltration nor meningeal carcinomatosis by extension affecting the spinal cord has been described in dogs or cats.

CLINICAL OUTCOME OF A NEW SURGICAL TECHNIQUE FOR STABILIZING THORACIC KYPHOSIS IN FOUR PUGS WITH SECONDARY MYELOPATHY AND COMPARISON TO CONSERVATIVE MANAGEMENT. R. Cappello, B. de la Puerta, C. Behrens Mathiesen, A. Groth, S. Rutherford. North Downs Specialist Referrals, Bletchingley RH1 4QP, UK

This retrospective case series investigated the clinical outcome of a novel surgical technique for stabilising thoracic kyphosis in four pugs with secondary myelopathy. Neurological score pre- and post surgery as well as an owner questionnaire were evaluated.

The surgical cases were pugs with a history of chronic progressive hind limb ataxia and ambulatory paraparesis with a mean age of 6 months (5-7 months). They were diagnosed with thoracic kyphosis using MRI. A CT scan was performed for three-dimensional printing of the kyphotic vertebral segment to aid surgical planning and precontouring of the SOP plate. A bilateral double thoracotomy was performed and locking (SOP) plates were placed bilaterally on the kyphotic thoracic vertebral bodies. No decompression was performed. No intra-operatively complications occurred. The conservatively managed cases did not receive any treatment.

No post-surgery complications were observed and the neurological score improved in all four dogs. All owners reported improvement of the neurological status post-surgery, and all rated the quality of life of their dogs “excellent”.

Of the seven dogs (5 pugs, 2 French bulldogs) that were managed conservatively, six responded to the questionnaire. Two dogs were euthanized few days after presentation, and the owners of the remaining four dogs reported deterioration of the neurological status in three of the four dogs since initial presentation.

Bilateral SOP placement through bilateral thoracotomy is a promising alternative for stabilisation of thoracic kyphosis in dogs with secondary myelopathy. Improvement of the neurological score suggests instability to be the cause of the myelopathy. Conservative management is a suboptimal solution to thoracic kyphosis causing secondary myelopathy.

SOMASTATIN RECEPTOR (SSTR2) IN CANINE MENINGIOMA: PRELIMINARY RESULTS OF IMMUNOHISTOCHEMICAL AND QRT-PCR INVESTIGATIONS. G. Foiani, G. Guelfi, C. Trivelli, C. Boccanera, M.T. Mandara. Dept. of Veterinary Medicine, University of Perugia, Italy.

The neuropeptide somatostatin (SST) plays an important regulatory role in the proliferation of both normal and neoplastic cells. Five subtypes of somatostatin receptors (SSTRs) have been identified in several human tumours, including meningioma. The receptor most commonly identified is the SSTR2a subtype. Long half-life somatostatin analogues (i.e. octreotide) are today included in chemotherapy schedules for unresectable or radiation-refractory recurrent human meningiomas.

The aim of this study is to test the expression of SSTR2a in canine meningioma by immunohistochemistry and qRT-PCR analyses. Twenty-one FFPE meningiomas were used for IHC investigations performed with rabbit anti-human SSTR2 antibody (1:500, Alomone Labs, Jerusalem, Israel) and avidin-biotin-peroxidase complex method. For each tumour, area of labeling was assessed in five grades, ranging from (+) = absent to (++++) = > 75% of tumour.

Twenty-five meningiomas were also submitted to qRT-PCR investigations performed with Taqman probe (Life Technologies). Total RNA was extracted from 3 µm sections of FFPE tissue with FFPE-RNA Purification Kit (Norgen), and mRNA was reverse-transcribed with iScript cDNA synthesis (Bio-rad). At IHC, SSTR2a was expressed in 17/21 cases (81%) showing a diffuse cytoplasmic immunoreaction. The most common histotypes, including meningothelial, fibroblastic, and transitional meningiomas as well as the papillary meningiomas were positive, ranging from (+) to (+++). Grade I, grade II and grade III expressed SSTR2 in 86%, 91%, and 33%, respectively. The PCR-amplification tests gave positive results in the majority of the canine meningiomas. These preliminary results encourage continuing this study aimed to find new chemotherapeutic protocols for dogs.
INFLAMMATORY MYOFIBROBLASTIC TUMOUR AFFECTING THE SPINAL CORD IN THREE DOGS. M.T. Mandara¹, G. Foiani¹, S. Felici¹, A. Sidoni², F. Gernone³, N. Gasparinetti⁴, M. Baroni⁵. ¹Dept. Veterinary Medicine, University of Perugia, Italy, ²Dept. Experimental Medicine, University of Perugia, Italy, ³“Pingry” Veterinary Hospital, Bari (Italy), ⁴“Diagnostica Piccoli Animali”, Vicenza, Italy, ⁵“Valdinievole” Veterinary Clinic, Monsummano Terme, Italy.

Inflammatory Myofibroblastic Tumour (IMT) has long been described as an Inflammatory Pseudotumour (IP) lesion. Today, it is recognized as a neoplastic lesion in human medicine, more clearly distinguished from IP. Albeit IMT generally shows a benign behaviour, an aggressive behaviour has been recognized in humans.

In this study three cases of canine neurological IMT affecting the spinal cord are described. They occurred as extradural masses, at T6-T7, T9-T10 and T4, respectively. In all cases, the mass was removed with hemilaminectomy. It extended to a maximum of 2.5 cm. For the diagnosis, histological examination of the removed masses showed in all three cases a spindle cell proliferation associated with a mixed inflammatory infiltration mainly of lymphocytes and plasma cells. Based on the prevalence of spindle cells on the inflammatory cells, a fibrohistiocytic histotype was recognized. At immunohistochemistry study, spindle cells were positive for vimentin and smooth muscle actin (SMA) in all three cases, and positive for desmin in two cases. Spindle cells were positive for anaplastic lymphoma kinase-1 (ALK-1) in all cases. A mild mitotic index was observed at Ki67-immunoreaction. At the time of writing (32, 15 and 9 months, respectively) the dogs do not show recurrent neurological signs. Compared to ALK-1 negative IMT, for ALK-1 positive IMT a complete resection is strongly recommended.

GENE EXPRESSION OF MMP-2 AND MMP-9 AND CORRELATED RATIO WITH SPECIFIC INHIBITORS (TIMP-1 AND TIMP-2) IN CANINE MENINGIOMA. M.T. Mandara, A. Reginato, G. Guelfi, G. Foiani. Dept. of Veterinary Medicine, University of Perugia, Italy.

In the recent years, metalloproteinase activity of neoplastic cells has been studying as a possible independent prognostic marker and target for therapeutic options. Degradation of extracellular matrix is associated with tumour invasion and metastasis, and matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) are the key mediators of this process. In this study the expression of MMP-9 and MMP-2, known as type IV collagenases, and their inhibitors TIMP-1 and TIMP-2 was investigated in canine meningioma. Forty-three cases of both intracranial and spinal tumours were selected for the study. RNA was obtained from FFPE tissue, converted to cDNA and submitted to quantitative PCR. Statistical analysis was performed to assess the variation of the expression of these molecules and their relative ratio among the three histological grades of meningioma.

MMP-9 expression was undetectable in all the investigated meningiomas, while TIMP-1 expression increased significantly from grade I to grade II (p<0.001) and in papillary meningiomas (p<0.5), and it decreased in grade III tumours with no significant difference between benign and anaplastic meningiomas. All the tumours expressed MMP-2 though without any significant differences in the three histological grades. MMP-2/TIMP-2 ratio didn’t differ in benign, atypical and anaplastic meningiomas. Significantly higher (p<0.001) was the expression of MMP-2 in the papillary meningiomas that showed MMP-2/TIMP-2 ratio strongly skewed in favour of metalloproteinase. This finding suggests MMP-2/TIMP-2 imbalance as one of the molecular bases of the aggressive biological behaviour that seems to characterize this histologic subtype also in dogs.