ESVN European Society of Veterinary Neurology

ECVN European College of Veterinary Neurology

33rd ESVN - ECVN Symposium

Online, 16-18 September 2021

PAIN

Agenda

Dear friends and colleagues,

On behalf of the European College and the European Society of Veterinary Neurology, we are proud to welcome you to the 33rd ESVN-ECVN annual Symposium, virtually held on 17th and 18th September 2021.

The main topic of the Symposium is “Pain”, chosen because not yet officially discussed in our meetings and increasingly common in our daily practice. Your incredibly positive response, leading to a record of participants, is the best confirmation that the choice was good!

The program of the keynote lectures was designed to include human and veterinary keynote speakers to provide a comparative view and new insights on the management of chronic pain. Some issues of great interest to the veterinary neurologist, such as pain in Chiari-like malformation and degenerative lumbosacral stenosis, will also be addressed.

“Neuroanaesthesia” is the topic of the Residents’ day, offered on Thursday 16th September 2021. Also for this pre-symposium event, the number of participants is very high, confirming the perception that the topic is considered of great importance among our community.

We are proud to announce that your scientific contribution to the Symposium has been extremely relevant. Among all the submitted abstracts, the Scientific Committee of the Symposium has chosen 25 oral research presentations, 25 flash presentations, and 77 poster presentations! Indeed, a big success for an online event and the best response of our community to these challenging times.

As you already know, given the persisting emergency across Europe related to the COVID-19 outbreak, the Organizing Committee and the ECVN Executive Committee have unanimously decided to hold the Symposium online. Nevertheless, we feel sure that the online symposium represents an opportunity for the community of veterinary neurologists to meet after a long time, and your high participation is the best confirmation that the neurology community has taken the chance.

Finally, we would like to reassure all those who feel discouraged about losing the chance to meet in the wonderful setting of Venice. Given its specificity, we have decided to retain the Venice location for the 2023 ECVN Symposium!

It is great pleasure and honor for the local organizing committee to welcome you all to the 33rd ECVN-ESVN Annual Symposium!

Gualtiero Gandini
DVM, PhD, Dipl ECVN

Massimo Baroni
DVM, Dipl ECVN

Cristian Falzone
DVM, Dipl ECVN

Programme Overview

RESIDENTS' DAY I THURSDAY 16th September 2021

Neuroanaesthesia

Residents' Day

08:45	Welcome	Gualtiero Gandini (Chair)
09:00	Effects of general anaesthesia on CNS and mechanism of action of anaesthetics	**Dr. Federico Corletto**
10:00	Anaesthesia and analgesia for intracranial surgery	**Dr. Federico Corletto**
11:00	**COFFEE BREAK**	
	Chairperson: Federica Balducci	
11:30	Anaesthesia and analgesia for spinal surgery	**Dr. Francesco Aprea**
12:20	Anaesthesia considerations for neuroimaging	**Dr. Francesco Aprea**
13:10	**LUNCH BREAK**	
	Chairperson: Federica Balducci	
14:30	Perianaesthetic complications in neurosurgery	**Dr. Francesco Aprea**
15:30	**COFFEE BREAK**	
	Chairperson: Gualtiero Gandini	
15:50	First interactive session: management of a case undergoing intracranial surgery	**Dr. Francesco Aprea** **Dr. Federico Corletto**
17:00	Second interactive session: management of a case undergoing spinal surgery	**Dr. Francesco Aprea** **Dr. Federico Corletto**
18:00	Discussion & final remarks	
18:30	End of the day	

Symposium Day 1 - FRIDAY 17th September 2021

08:30		Opening ceremony & Welcome	Veronika Stein (President ECVN) and Gualtiero Gandini (Chair)
08:45		**Keynote - Pathophysiology of pain: a short review**	**Dr. Federico Corletto**
09:30		**Keynote - The "classic" management of chronic pain in veterinary medicine** Boehringer Ingelheim	**Dr. Louise Clark**
10:15		**COFFEE BREAK – EXHIBITION AND POSTER AREA**	
		Chairperson: Angela Fadda	
11:00		**Research Presentations**	
	O1	INCREASED RESTING STATE CONNECTIVITY IN THE ANTERIOR DEFAULT MODE NETWORK OF IDIOPATHIC EPILEPTIC DOGS	K. M. Beckmann
	O2	miR-134: A NEW THERAPEUTIC TARGET FOR DRUG-RESISTANT IDIOPATHIC EPILEPSY IN DOGS?	R. Gutierrez-Quintana
	O3	RISK FACTORS ASSOCIATED WITH SHORT-TERM MORTALITY AND RECURRENCE OF STATUS EPILEPTICUS IN DOGS	R. Fentem
	O4	THE PHARMACOKINETICS OF SINGLE ORAL DOSE EXTENDED-RELEASE TOPIRAMATE AND ADVERSE EFFECTS AFTER MULTI-DOSE ADMINISTRATION IN HEALTHY CATS	L.T. Graham
	O5	SOUNDS OF SEIZURES – ACOUSTIC INFORMATION ENABLES IMMEDIATE RECOGNITION AND DETECTION OF GENERALIZED TONIC-CLONIC SEIZURES IN DOGS	S. Meller
	O6	COMPARISON OF BRAIN METABOLITES BETWEEN IDIOPATHIC EPILEPTIC DOGS AND HEALTHY CONTROL DOGS WITH SINGLE VOXEL PROTON MAGNETIC RESONANCE SPECTROSCOPY OF THE THALAMUS	N. Mauri
	O7	SURFACE ELECTROENCEPHALOGRAPHY ALLOWS TO RECORD EVENT RELATED POTENTIALS DURING QUANTITATIVE SENSORY TESTING IN AWAKE CATS	A. Castel
12:15		**Keynote - A riddle wrapped in a mystery inside an enigma: lumbosacral neuropathic and discogenic pain**	**Dr. Frank Steffen**
13:00		**LUNCH BREAK – EXHIBITION AND POSTER AREA**	
		Chairperson: Luisa De Risio	
14:30		**Keynote - Pain and Chiari-like malformation: pathophysiological mechanisms and treatment options**	**Dr. Clare Rusbridge**
15:15		**Flash Presentations**	
	FP1	AN EPISODIC MOVEMENT DISORDER IN JUVENILE WEIMARANERS	M. Green
	FP2	ORTHOSTATIC TREMOR IN DOGS: 60 CASES (2003-2020)	T. Liatis
	FP3	A CASE SERIES OF THREE DOGS PRESENTING WITH NEUROLOGICAL DEFICITS DUE TO SUSPECTED NUTRITIONAL SECONDARY HYPERPARATHYROIDISM AFTER BEING FED AN EXCLUSIVE DIET OF BARF (BIOLOGICALLY APPROPRIATE RAW FOOD) DIET	L. Nowak
	FP4	THE EFFECTS OF EXERCISE RESTRICTION ON DOGS AND THEIR OWNERS: A PILOT STUDY	G. Walmsley
	FP5	VERTEBRAL AND ENDPLATE CHANGES IN DOGS WITH SUSPECTED FIBROCARTILAGENOUS EMBOLIC MYELOPATHY	C. Llanos
	FP6	USEFULNESS OF FOLLOW UP MRI IN DOGS WITH DISCOSPONDYLITIS: A RETROSPECTIVE EVALUATION	M.I. de Freitas
	FP7	A NEW FORM OF HEREDITARY ATAXIA IN AUSTRALIAN SHEPERD. FPHENOTYPIC AND GENETIC CHARACTERIZATION	C. Escriou
15:45		**SHORT BREAK**	
		Chairperson: Alejandro Luján Feliu-Pascual	
16:00		**Flash Presentations**	
	FP8	HEAD TURN: A STUDY OF NEUROLOCALISATION	A. Nagendran
	FP9	URINARY NEUROTRANSMITTER PATTERNS ARE ALTERED IN CANINE EPILEPSY	T. Schmidt
	FP10	THE REIBERGRAM IN NEUROLOGICAL DISEASES OF DOGS	M. Püschel
	FP11	EVALUATION OF THE EFFECT OF PHENOBARBITAL ADMINISTRATION ON BIOCHEMISTRY PROFILE WITH FOCUS ON SERUM LIVER CONCENTRATIONS IN CATS WITH EPILEPSY: A MULTI-CENTER STUDY	M. Hermans
	FP12	FELINE TEMPORAL LOBE EPILEPSY: SEVEN CASES OF HIPPOCAMPAL AND PIRIFORM LOBE NECROSIS IN ENGLAND AND LITERATURE REVIEW	B. Scalia
	FP13	CONCENTRATION OF C REACTIVE PROTEIN IN SERUM AND CEREBROSPINAL FLUID IN DOGS WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN OR STEROID RESPONSIVE MENINGITIS ARTERITIS	R. Cavalerie
	FP14	COMPARISON OF SERUM CK AND AST LEVELS IN CANINE PROTOZOAL MENINGOENCEPHALITIS AND NON-INFECTIOUS MENINGOENCEPHALITIS	B.S. Jones
	FP15	APPLICATION OF MACHINE LEARNING TO GUIDE THE CLINICAL REASONING IN DOGS PRESENTING WITH SEIZURES AND A NORMAL INTER-ICTAL NEUROLOGICAL EXAMINATION	C. Smith
16:35		**COFFEE BREAK – EXHIBITION AND POSTER AREA**	
17:00		**Annual General Meeting**	Veronika Stein *President ECVN*
18:45		End of the first day	

Symposium Day 2 - SATURDAY 18th September 2021

		Chairperson: Veronika Stein	
08:30		**Research Presentations**	
	O8	A NOVEL LATERAL APPROACH TO THE C7 AND C8 SPINAL NERVES AND NERVE ROOTS FOR RESECTION OF MALIGNANT PERIPHERAL NERVE SHEATH NEOPLASIA IN TWO DOGS	O. Marsh
	O9	SPINAL ARACHNOID DIVERTICULA CONFORMATIONAL VARIATIONS IN DOGS	J.M. Frias
	O10	SPINAL SUBARACHNOID WEBS - ARE THEY A VARIANT OF SUBARACHNOID DYVERTICULA IN DOGS?	E. Bersan
	O11	TRAUMATIC AND IATROGENIC SCIATIC NERVE INJURY IN THIRTY-NINE DOGS AND TEN CATS: CLINICAL AND ELECTRODIAGNOSTIC FINDINGS	D. Dell'Apa
09:15		**Keynote - Cannabinoids: just fashion or real opportunity?** PURINA	**Dr. Renato Vellucci**
10:00		**COFFEE BREAK – EXHIBITION AND POSTER AREA**	
		Chairperson: Rita Goncalves	
10:30		**Keynote - Future perspectives in the management of chronic pain in human medicine**	**Dr. Renato Vellucci**
11:15		**Research Presentations**	
	O12	VALVELESS VENTRICULOPERITONEAL SHUNT IN DOGS AND CATS - CLINICAL EXPERIENCE AFTER 20 YEARS	R. F. Schamall
	O13	COMPARISON OF NEUROTRANSMITTERS CONCENTRATION IN CANINE CEREBROSPINAL FLUID, BLOOD, AND URINE SAMPLES MEASURED VIA HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY	S. Meller
	O14	APPLICATION AND ACCURACY OF A MAGNETIC RESONANCE IMAGING-GUIDED NEURONAVIGATION SYSTEM FOR BRAIN BIOPSY IN SMALL ANIMALS	C.C. Yang
	O15	OPTIMISATION OF CEREBROSPINAL FLUID METABOLOMICS	F. Verdoodt
	O16	OLIGOCLONAL BANDS IN DOGS WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN (MUO)	J. K. Prümmer
12:10		**Flash Presentations**	
	FP16	USE OF 3D-PRINTING TECHNOLOGY TO CREATE A SIMULATOR FOR CEREBROSPINAL FLUID SAMPLING AT THE LUMBAR SUBARACHNOID SPACE	M. Madden
	FP17	UTILITY OF A FLEXED NECK SAGITTAL MRI SEQUENCE PRIOR TO CSF SAMPLING FROM THE CEREBELLOMEDULLARY CISTERN IN DOGS	D. Sivolapenko
	FP18	NONINVASIVE MONITORING OF INTRACRANIAL PRESSURE WAVES USING BCMM 2000 BRAIN4CARE MONITOR IN DOGS WITH MYELOPATHIES UNDERGOING MYELOGRAPHY	M. V. Bahr Arias
	FP19	DO HASTE MRI SEQUENCE FINDINGS CORRELATE WITH CLINICAL SIGNS IN DOGS WITH THORACOLUMBAR DISC EXTRUSIONS?	S.H. Khan
	FP20	LONG TERM OUTCOME IN DOGS WITH COMPLETE SENSORY AND MOTOR LOSS FOLLOWING THORACOLUMBAR INTERVERTEBRAL DISC HERNIATION	A. Barriere
	FP21	SAFETY OF EARLY POSTOPERATIVE HYDROTHERAPY IN DOGS UNDERGOING THORACOLUMBAR HEMILAMINECTOMY	A. Mojarradi
	FP22	LONG-TERM FOLLOW-UP OF THE SPINAL SEGMENTAL STABILISATION TECHNIQUE FOR THE SURGICAL TREATMENT OF DORSAL HEMIVERTEBRAE ASSOCIATED WITH KYPHOSIS	D.E. Mavrides
	FP23	EVALUATION OF THE EFFECT OF EXTRADURAL ADMINISTRATION OF MORPHINE FOR POSTOPERATIVE ANALGESIA FOLLOWING VENTRAL SLOT SURGERY IN DOGS WITH CERVICAL DISK HERNIATION	F. Tirrito
	FP24	THE NOCICEPTIVE WITHDRAWAL REFLEX FOR THE EVALUATION OF ANALGESIA IN PIGS UNDERGOING EXTRACORPOREAL MEMBRANE OXYGENATION: A PILOT STUDY	M. Petrucci
	FP25	TONGUE ATROPHY AS A NEUROLOGICAL SIGN IN HEREDITARY POLYNEUROPATHY IN ALASKAN MALAMUTES	J. Hultman
13:00		**LUNCH BREAK – EXHIBITION AND POSTER AREA**	
		Chairperson: Cristian Falzone	
14:30		**Keynote - Future perspectives in the management of chronic pain in veterinary medicine**	**Dr. Louise Clark**
15:15		**Research Presentations**	
	O17	IS CEREBROSPINAL FLUID ANALYSIS USEFUL IN SUSPECTED INTRACRANIAL DISEASE WITH NORMAL MAGNETIC RESONANCE IMAGING?	S. Monteiro
	O18	TBA	
	O19	CLINICAL OUTCOME OF SUBCLINICAL BACTERIURIA IN DOGS FOLLOWING SURGICAL DECOMPRESSION OF HANSEN TYPE I THORACOLUMBAR INTERVERTEBRAL DISC HERNIATION	H. Rylander
	O20	ALTERATION OF Th17 AND Treg CELLS IN DOGS IN THE ACUTE PHASE OF PAINFUL INTERVERTEBRAL DISC HERNIATION	P. Can
16:00		**COFFEE BREAK – EXHIBITION AND POSTER AREA**	
		Chairperson: Cristian Falzone	
16:30		**Research Presentations**	
	O21	PAEDIATRIC NEUROLOGICAL DISORDERS IN DOGS AND CATS: A RETROSPECTIVE MULTICENTRIC STUDY OF 888 CASES (2003-2019)	A. Cloquell
	O22	DIFFUSION TENSOR IMAGING IN SYRINGOMYELIA SECONDARY TO CHIARI MALFORMATION IN CAVALIER KING CHARLES SPANIEL. PRELIMINARY STUDY	K. Owsińska-Schmidt
	O23	FORAMEN MAGNUM DECOMPRESSION AND MODIFIED CRANIOPLASTY USING TITANIUM MESH PLATE IN SMALL DOGS WITH CAUDAL OCCIPITAL MALFORMATION SYNDROME AND SYRINGOMYELIA	Y. Nakano
	O24	EVALUATING THE BENEFIT OF CONTRAST MAGNETIC RESONANCE (MR) IMAGES IN DETECTING SPINAL CORD PATHOLOGY: A RETROSPECTIVE STUDY	E. Robinson
	O25	JUVENILE-ONSET MOTOR POLYNEUROPATHY IN 15 CATS	N. Van Caenegem
	O26	MECHANICAL NOCICEPTIVE THRESHOLDS AND ASSESSMENT OF DESCENDING INHIBITORY CONTROLS IN HEALTHY CATS AND THOSE WITH DIABETES MELLITUS	H.L.M. Ruel
17:30		**Awards & Closing Remarks**	**Veronika Stein, Gualtiero Gandini, Massimo Baroni, Cristian Falzone**
18:00		End of the Symposium	

FRANCESCO APREA

DVM, CertVA, Dipl. ECVAA, MRCVS

EBVS and RCVS Specialist in Veterinary Anaesthesia and Analgesia

Francesco graduated with honors from the University of Bari in 2005; since then he has focused his professional interest on anaesthesia and analgesia. After a rotating internship Francesco moved to the UK in 2006 to complete an internship in veterinary anaesthesia at the Queen Veterinary School Hospital (University of Cambridge). After a short period in general practice, Francesco joined one of the biggest private vet hospitals, Dick White Referrals (UK) where he completed his ECVAA residency. In 2008 he obtained the Certificate in Veterinary Anaesthesia (CertVA), issued by the Royal College of Veterinary Surgeons, and in 2012, the EBVS Diploma becoming a European specialist. In 2011 Francesco moved to Majorca (Spain) where he currently runs the anaesthesia and analgesia service of the Hospital Canis, one of the biggest private veterinary hospital in Spain.

Francesco is author of several papers and regularly he runs CPDs in Spain and in Italy and he is member of the education committee of the ECVAA. The control of pain is Francesco main clinical interest and out of work he enjoys outdoor sports and being with his family, pets and friends.

LOUISE CLARK

BVMS, MRCVS, CertVA, Dipl ECVAA, MSc, FRCVS

EBVS European Specialist in Veterinary Anaesthesia and Analgesia

Louise is a European and Royal College of Veterinary Surgeons recognised Specialist in Veterinary Anaesthesia and Analgesia. She was awarded her Diploma in Veterinary Anaesthesia and Analgesia in 2003 following a residency at the University of Edinburgh R(D)SVS. She was then part of a large Anaesthesia/critical care team at the Animal Health Trust in Newmarket before moving to Davies Veterinary Specialists in Hertfordshire to Head the Anaesthesia team in 2007. In 2014 Louise was awarded an MSc (Distinction) in the Clinical Management of Pain from Edinburgh University. She is Past President of the Pain Medicine Section Council at the Royal Society of Medicine and has been an invited examiner on the European Diploma examination and a Treasurer of the Association of Veterinary Anaesthetists.

She is involved with charitable work in the developing world to improve the welfare and management of dogs undergoing anaesthesia in resource poor settings, "an opportunity to make a lot of difference to a large number of animals".

FEDERICO CORLETTO

PhD, CertVA, Dipl ECVAA, FRCVS

EBVS specialist

Federico Corletto graduated with honours from Padova in 1997. After a residency in Veterinary Anaesthesia and Analgesia at the Animal Health Trust (Newmarket, UK), he obtained the RCVS Certificate in Veterinary Anaesthesia in 2002 and the European Diploma in Veterinary Anaesthesia and Analgesia in 2003. In 2011 he has been awarded a PhD by Cambridge University for his research project on Traumatic Brain Injury, funded by the Wellcome Trust and based at Addenbrooke's Hospital (Cambridge, UK). He has worked as Assistant Professor in Padova University, Clinical Anaesthetist at the Animal Health Trust, Clinical Research Fellow at Addenbrooke's Hospital and since 2008 he leads the anaesthesia service at Dick White Referrals (Six Mile Bottom, UK). In 2020 he became Professor of Veterinary Anaesthesia and Analgesia at Nottingham University (part time position). He has served as officer for the ECVAA for 12 years, including the role of President.

CLARE RUSBRIDGE

BVMS, PhD, Dipl ECVN, FRCVS, RCVS and European Specialist in Veterinary

Clare graduated from University of Glasgow in 1991 and following an internship at University of Pennsylvania and general practice in Cambridgeshire, she completed a BSAVA/Petsavers residency and was staff clinician in Neurology at the Royal Veterinary College. She became an ECVN Diplomate in 1996, a RCVS Specialist in 1999 and RCVS Fellow in 2016. She has researched Chiari-like malformation and syringomyelia (CMSM) for over 20 years. In 2007 she was awarded a PhD from Utrecht University for her thesis on CMSM and in 2011 she received the J. A. Wright Memorial Award by The Blue Cross Animal Welfare Charity. Clare joined Fitzpatrick Referrals and the University of Surrey in 2013; for 16 years prior she operated a neurology and neurosurgery service in Wimbledon. She has authored or co-authored over 140 scientific articles (over 50 on CMSM) in addition to several book chapters and co-edited a human medical textbook on syringomyelia. Her other professional interests include neuropathic pain, neurological diseases related to conformation, epilepsy, the interplay between neurology and behaviour, polymyositis and rehabilitation following spinal injury.

FRANK STEFFEN

Prof.Dr.med.vet., Dipl ECVN

Frank Steffen is head of the section of neurology/ neurosurgery at the Vetsuisse faculty of the University of Zurich, Switzerland.
Frank graduated at the University of Bern in 1991, followed by a residency in neurology at the Institute for Animal Neurology, University of Bern. After receiving the diploma of the European College of Veterinary Neurology in 1995, he worked as consultant for neurology/neurosurgery in referral centers in Switzerland until he returned to academia. As a faculty member of the Vetsuisse faculty, Frank is responsible for teaching students and training of ECVN residents.
Frank's research interests include diseases of the spine and spinal cord, neurosurgical procedures and regenerative strategies for degenerative disc disease. His publication list entails > 80 peer-reviewed articles and book chapters on all fields of veterinary neurology.

RENATO VELLUCCI

Senior Consultant at the Complex Departmental Organizational Structure of Palliative Care and Pain Therapy

Dr. Vellucci is a contract professor employed at the Department of Anesthesia of the University Hospital of Careggi Firenze (Italy) where, since 2002, he is Senior Consultant at "PALLIATIVE CARE AND TREATMENT OF PAIN". He graduated from the Faculty of Medicine of Perugia and Postgraduate Diploma in Anesthesia and Intensive Care. In 2009, he achieved Inter-University Master Degree in E-Medicine Training in the analysis, design and management of telemedicine (telemedicine), the distance learning (e-learning) and medical informatics. Member of the Committee of the Ministry of Health for the implementation of the principles of law "provisions to ensure access palliative care and pain therapy" from May 13, 2010 to 15 April 2015.
In 2015 was elected as Coordinator of the Study Group "Acute and Chronic Pain" of the Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care -SIAARTI da ottobre 2015 al 2018. Teacher in more than 200 International and National courses and invited speaker in approximately 80 International and National congresses.
He is an author/co-author of more than scientific publications, 34 in peer reviewed international journals.

Residents' day Abstracts

Analgesia and anaesthesia for spinal surgery

Francesco Aprea,
DVM, CertVA, Dipl. ECVAA, MRCVS

- **Subject related factors**
- Toy breeds (mitral valve disease, tracheal collapse, difficult monitoring), giant breeds (cardiomyopathies, AF, OA, difficult management), French bulldogs (BOAS, malformations), pugs (meningitis, BOAS, vertebral malformation), dachshund (increased vagal tone, difficult IV access), Dobermann (Von Willebrand factor deficiency)
- Some subjects might be aggressive or immobile due to anticipation of pain
    - Cortico-limbic (emotional) response
- Geriatric subject
    - Consider lack of reserves and comorbidities

- **Disease related changes**
- ++ Degenerative MSK disease (IVDD)
    - Trauma, neoplasia, malformations
- Presence of paralysis, paresis (ambulatory and no ambulatory), ataxia, stiffness has to be taken into consideration due to related comorbidities
    - Venus stasis, blood hyperviscosity, decreased pulmonary circulation
    - Renal/metabolic changes
        - Preanaesthetic stabilization could be crucial
        - Base line values (Hct, TP, glycaemia)
        - Rule in/rule out approach
    - Increased sympathetic tone
- Reflex paraspinal muscle spasms (leading to chronic back pain)
    - Nociceptive pain radiates to limbs
    - Rigidity, weakness (worst with time)

- **Pain related changes**
- Anatomical features
    - Meninges and perineurium are widely innervated by sensory fibres
    - ++ Mechanical and inflammatory stimuli
    - Intervertebral disk (++ annulus), longitudinal ligaments, facet joints have dense sensory and autonomic supply
    - Extruded nucleus pulposus causes chemical inflammation of meninges and perineurium around spinal roots and nerves
- **Primary sensitization** (paraesthesia, hyperalgesia, allodynia-see below)
- Increased sympathetic tone (energy wastage and increased O2 demands, amplification of pain)
- Peripheral neuropathic pain affects motor, sensory, autonomic fibres leading to aberrant somato-sensory processing (pain in the hypo-aesthetic area)
- Decreased thoracic expansion (decreased O2 intake, decreased vital capacity, increased secretions and decreased cough)
- Decreased intestinal transit, bladder hypokinesia
- Decreased per os intakes (dehydration and negative nitrogen balance)
- Behavioural changes
- **Preoperative pain facilitates intra operative pain which facilitates post-operative pain** (becoming increasing more difficult to control)

- **ASA classification**
- Exclude systemic conditions
- Owners expectations (CEPSAF: ASA I 0.05% VS ASA III 1 % fatalities)

- Examination of peripheral nerves (peri-operatively)
    1 Allodynia (pain elicited by a stimulus that does not provoke pain)
    2 Hyperpathia (abnormally painful reaction to a repeated stimulus)
    3 Hypoaesthesia (decreased sensitivity to a stimulus)
    4 Hyperaesthesia (increased sensitivity to a stimulus)
    5 Hyperalgesia (increased pain in response to a normally painful stimulus)
    6 Paraesthesia (unpleasant abnormal sensation, spontaneous of provoked)

- In order to better treat pain, identify its components:
- **Pain caused by the herniated disk**
- Inflammatory (neuroinflammatory)
    - Peripheral and central sensitization
- Somatic
    - Superficial (skin, muscle) deep (joints, bones)
- Autonomic (sympathically driven and visceral)
    - Systemic signs
- Neuropathic
    - Spontaneous or evoked , with or without sensitive deficit
    - Lack of response from first line analgesic treatment
    - Allodynia, hyperalgesia
- MSK
    - **Spinal segmental response:** increased muscle tone, vasoconstriction, ischemia, hyperalgesia of local area

- Acute VS chronic
  - Different management, pharmacological history

- **Pain caused by the surgery**
- Inflammatory (Neuroinflammatory response)
- Somatic
- Neuropathic
  - Damage to the nerve
    - Axonotmesis (structural axonal discontinuation, possible re-growth)
      - Interrupted transport and membrane remodelling
      - Ectopic hyperexcitation
      - Wind-up
      - Increased sympathetic response
      - Silent nociceptors activation (Ab fibres)
    - **Neurotmesis** (complete axonal discontinuation, no re-growth)
- Benefit provided by (comprehensive) decompression

- **Synaptic plasticity can lead to a normal, suppressed or facilitated sensitivity process (reversible) or not**
- **Preventive analgesia**

- Anaesthetic technique
- **First do not harm**
- Sedatives/Analgesics:
  - **Improve the autonomic balance (towards parasympathetic activity)**
  - Dexmedetomidine (0.001-0.002/kg IV up to 0.004-0.01 mg/kg IM)
    - Not in combination with opioids for doses higher than 0.005 mg/kg (especially IV)
  - Methadone 0.2-0.3 mg/kg IV or IM
    - NMDA antagonist activity
- NSAIDs
  - COX-2 preferential or selective
  - First line in absence of contraindications
  - Once recovered? (**normothermic and normovolemic subject**)
  - No evidence about contraindications in the perioperative period in the veterinary neuro subject
  - Meloxicam strongest evidence of efficacy (more studies available)
- **Gabapentionids**
  - Perioperative use of gabapentin and pregabalin reduce post-operative pain in humans undergoing spinal surgery

- Paracetamol
  - Useful in dogs when a NSAIDs cannot be administered (concurrent steroids therapy)
    10 mg/kg q 8 hr (IV, P/os)
    - NOT IN FELINE

- **General anaesthesia**
- Pre oxygenation might be useful if the subject tolerates it
- Gentle induction, tracheal intubation, positioning and movements (use trolley and stretchers)
  - Muscle relaxation may facilitate spinal movements and worsen spinal cord compression and lesion
  - In human spinal surgery most complications are related with prone position on the surgical operating table
  - Propofol (1- 10 mg/kg) or alfaxan (1-5 mg/kg)IV to effect
  - In not sedated (and not bradycardic) subjects, fentanyl (0.003-0.005 mg/kg) can be used as co-inductor (given 5 minutes before induction)
  - Care especially when intubating the trachea of subject with cervical lesions
  - An armoured ET tube can be used to prevent kinking
  - Be sure the ET tube is well fixed and connected to avoid accidental dislodgment
- Inhalational anaesthesia
  - Low flow in an AIR:O2 mixture
  - Do not exceed MAC (deeper the anaesthesia deeper is the depression of protective reflexes)
    - ISO 1.2-1.5%
    - Sevo 2.2.-2.4 %
  - Use a multimodal approach in order to maintain your values under MAC
- TIVA
  - Propofol 0.1-0.5 mg/kg/min
  - Alfaxan 1-5 mg/kg/hr
    - Frequent shivering during recovery

- PIVA
  - Volatile agent associated to a CRI (providing sparing effect)
  - CRI Lidocaine, ketamine, ultra-short acting opioids, dexmedetomidine (0.001-0.002 mg/kg/hr IV)
- Both SSEPs and MEPs (see below) are depressed by general anaesthetics
  - Propofol based techniques depress neurofunction less than volatile anaesthetics thus are preferred when neurophysiological monitoring is employed (++ human)

- **Control of nociception**
- Lidocaine CRI (1-2 mg/kg loading does, 2 mg/kg/hr CRI)
  - Dogs
  - No evidence in humans
  - Contraindicated in cats
- Ketamine CRI (0.2 mg/kg LD, 0.005-0.01 mg/kg/min CRI)
  - Dogs and cats
  - Some evidence in humans
- Ultra-short acting opioids
  - Fentanyl (0.002-0.005 loading dose, 0.001-0.05 mg/kg/hr CRI)
  - Target controlled infusion (TCI) possible in dog
  - Alfentanil
  - Remifentanil
    - First choice for evoked potential monitoring
    - No loading dose required

- Regional anaesthesia
  - **Erector spinae block**
    - Fascial block, US guided
    - Cadaveric studies available in dogs
    - Drugs used: bupivacaine, levobupivacaine, ropivacaine 0.25-0.5 % VOLUME: 0.4-0.6 ml/kg
    - Bilateral (need for dilution) or unilateral
    - Differentiate the transverse (closer to the target) and the articular (mammillary) processes of the vertebras
    - Thoracic or Lumbar approach
      - Between iliocostalis and longissimus dorsi muscle
- Local infiltration of the area

- Other techniques
  - Morphine (preservative free) local instillation (0.1 mg/kg diluted to a convenient volume and splashed extra durally prior to surgical closure)
  - Neuraxial anaesthesia (extra and intradural local anaesthetic administration)
    - In human continuous epidural analgesia (patient controlled) is commonly used although this technique might affect neurophysiological monitoring
  - Dexmedetomidine CRI
    - Improves recovery quality and reduces fatigue in humans

- **Monitoring**
- Essential: ECG, SpO2, temperature, NIBP, EtCO2
  - Basic spirometry monitoring is essential for IPPV
    - Tidal volume, peak and plateau pressure, PEEP
- Highly recommended
  - Invasive (direct) arterial blood pressure
    - Useful to detect and treat hypotension and hemorrhages
  - Anaesthetic gas monitor (EtAA)
    - Essential to prevent too deep anaesthetic plane
    - Useful to assess the sparing effect obtained by associated techniques
- Neurophysiological monitoring
  - **Multimodal intraoperative neuromonitoring** (human)
    - Somatosensory evoked potentials (SSEPs)
      - Assess posterior somatosensory column
      - To detect sensory and motor injury
      - Amplitude and latency
      - Stimulation of a peripheral nerve
    - Motor evoked potentials (MEPs)
      - Assess anterior motor columns
      - Presence or absence
      - Electrodes on the scalp
    - Electromyography (EMG)
      - Monitor nerve root injuries
    - **Wake up** test is considered the gold standard in humans
- Monitoring CNS and ANS
  - Cortical activity monitors : BIS, entropy etc.
  - Parasympathetic activity/nociception-antinociception monitors): PTA, QNox, pupillometry etc.
  - Useful to differentiate between lack of intraoperative anaesthesia or lack of analgesia
    - Associated with MEPs and SSEPs

- Recovery

- **Perform an Air Test prior to recovery to assess pulmonary gas exchange (if not contraindicated)**
- Providing that an oxygen analyser is available, increase the fraction of AIR (until FiO is about 30%) and assess SpO_2 (be sure the baseline value is real, should be > 98% when the subject is receiving an higher fraction of O_2) if a drop in SpO_2 is observed the subject might suffer of clinically significant lung atelectasis due to intrapulmonary shunting (mixing of not oxygenated blood with arterial one)
- Perform an alveolar recruitment and re-assess SpO_2, and treat systemic hypotension if present if there are not underlying pathologies SpO_2 should increase up to normal values and the subject can recovery
- In case of persistently low SpO_2, increase the FiO_2 slowly until SpO_2> 97% (for recovery we will need the least O_2 supplementation required using nasal or naso-tracheal tubes or O_2 cages)
- Keep the animal calm and provide oxygen supplementation in hypothermic subject
  - Shivering increases O_2 consumption 20 times
  - Subject with good analgesic control usually have a smooth recovery, in case of violent recovery dexmedetomidine (0.001 mg/kg IV) can be administered in a single dose or by CRI
- REMEMBER **CEPSAF** study showed that 60% of perioperative fatalities occur during the recovery period
- **Empty the urinary bladder** (if not catheterised)
- **Keep instrumental monitoring in critical subject**
- Trazadone can be used orally for longer term anxiolysis

- Post-operative care

- **REMEMBER: Hand over from theatre to kennel is a critical point and clear, written communication is advocated**
- Fill in all the appropriate forms/sheets
  - Catheters, regional analgesia, possible complications, plan

- **Pain assement**
- SF-GCPS
- Sensory testing (dynamometer)
- Analgesic tests
- Exclude complications

- **Comfort assessment**
- Temperature
- Urinary management
- Ins and Outs
- TLC, good bedding, change in recumbency, eye and mouth care, fisio-rehab.

Complications in spinal surgery

Francesco Aprea,
DVM, CertVA, Dipl. ECVAA, MRCVS

- In humans undergoing thoracic and lumbar surgical procedures (1223 subjects) most common complications detected were:
  - Respiratory complications (7%)
  - Pulmonary embolism (0.8%)
  - Cerebral vascular accident (0.25%)
  - Death (0.33%)
- In 224 dogs undergoing TL hemilaminectomy for disc extrusion complications observed were (Bruniges & Rioja 2019):
  - Hypothermia 63.8%
    - Favoured by MRI, hypotension
    - Reduced by BW, alfa2 and mechanical ventilation (MV)
  - (MV implementation 63.4 %)
  - Hypotension 33.9 %
    - Favoured by hypothermia and PIHR (use of antimuscarinic to increase HR)
    - Reduced by BW
  - PIHR (24.&%)
    - Favoured by MV, hypothermia
    - Reduced by BW
  - Hyperthermia (20.5%)
    - Favoured by alfa2 and duration
  - Regurgitation (4.9%)
- Another published paper, reported morbidity and mortality in 157 dogs undergoing cervical and TL surgery (Posner et al. 2014)
  - 4/57 (7.6%) subjects undergoing cervical surgery did not survive
    - Two suffer of cardiac arrest during surgery for AA stabilization
    - Two were euthanised due to aspiration pneumonia developed post ventral slot surgery
  - Bradycardia was recorded (and treated) in 94/164 subjects (65%)
    - Six did not respond to glycopyrrolate but did to atropine
    - II-degree AV block were observed in 34/164 (21%)

- Intraoperative bleeding

- In human major spinal surgery is associated with risk of haemorrhage
  - ++ vertebral sinus
- Increased central venous pressure has a bigger impact on bleeding than high arterial pressure
  - -Increased intrabdominal pressure can promote bleeding
  - -Care when positioning subjects
- COX 2 preferential and selective NSAIDs preferred
- Monitoring and management
  - Canine : estimated blood volume 85-90 ml/kg
  - Feline : 65 ml/kg
  - Calculate 10 and 20 % of the total blood volume
  - Estimate the blood losses by
    - Content of suction jar (ml)– saline instilled in the surgical field (ml) = blood in the suction jar (ml)
    - Blood soaked swabs (g) – dry swabs (g)= blood in swabs (g, were 1g=1ml)
    - Blood in suction (ml) + blood in swabs= total estimated blood losses
  - When estimated blood losses > 20 % of total blood volume haemoglobin restoration is needed on top of volume expansion thus blood transfusion has to be considered
- Haemoglobin measurement of suction content can also be used to estimate blood loss in dog
- Visual estimation has been proved to be inaccurate
- Phrenic nerve damage

- Especially following ventral slot surgery (C5-C7)
- It has to be bilaterally damaged
- Clinically respiratory ***fatigue*** can be detected, respiration becomes heavy and discordant abdominal movements can be observed
- Blood gas analysis helps assessing metabolic and ventilatory status to act before irreversible worsening of the condition
- When diaphragmatic function is compromised assisted ventilation is required
- Long term IPPV is challenging and knowledge of basic respiratory physiology and ventilators functioning is required

- Technical skills, AW monitoring and intensive nursing care required
- Weaving the ventilator with assisted modes by gradually increasing negative pressure (spontaneous effort-diaphragmatic movement) required to trigger ventilation

• Hypoventilation can develop 6-12 hours post operatively (oedema formation) and 12-24 hr of IPPV might enough to resolve oedema
- Repeat imaging if needed
- Methylprednisolone 30 mg/kg, then 15 mg/kg, mannitol

- Aspiration pneumonia following spinal surgery (Posner et al. 2014)

• Damage to the recurrent laryngeal nerve

- Post-surgical, neuropathic and MSK pain

• In humans up to 10 % incidence of post op neuropathic pain following mayor surgery

• For pain management is essential to frequently and dynamically assess the impact of the treatment with most objective methods available (pain scale, sensory testing, drug trials)

• Pharmacological strategies
- NSAIDs (++COX2)
- Gabapentionoids
- Paracetamol
- Lidocaine CRI (or oral Mexiletine)
- Methadone
- Dexmedetomidine

• Non pharmacological
- Acupuncture (and electric AP)
- TENS
- Radiofrequency
- Manual therapies

• Interventional analgesia
- Neuraxial and perineural infiltrations performed under fluoroscopy or US guidance
- GA or deep sedation needed

- Other reported complications in spinal surgery

• Air or solid emboli
- Can be caused by a suctioning effect of circulation at big vessel level
- Make sure that the heart is at the same height with the rest of the body to reduce the chances of “suctioning”
- 5-10 ml/kg of air in the circulation are lethal

• Vagal stimulation
- ++ ventral slot
- Atropine 0.02-0.04 mg/kg IV
- Glycopyrrolate 0.02 mg/kg IV
- If extreme bradycardia is detected, cardiac compression will be necessary and large amount of fluid should be given to facilitate drug distribution and tissue perfusion

• **Et tube dislodgment/accidental extubation/disconnection**
- Very frequent during positioning in theatre of the subject undergoing ventral slot surgery due to neck hyperextension
- All of a sudden, the capnograph disappear
- Deflation, repositioning and reinflation of the pilot balloon are needed
- Perform a leak test

• Bezold Jarisch reflex
- Reflex hypotension might occur in response to intraoperative changes in recumbency of large breed dogs

More rehabilitation and pain clinic will be available in the next years to treat (non-surgical) neurological cases and to speed up recovery of surgical ones.
Following specialist diagnosis, interventional analgesia could be implemented in the treatment prior to surgery in selected cases.
Use of epidural and cervical steroids injection for lumbo-sacral stenosis, coccygeal and cervical pain has been reported in dog as an alternative to surgery and owners should be aware of this (less invasive) options.

Anaesthesia for neuroimaging

Francesco Aprea,
DVM, CertVA, Dipl. ECVAA, MRCVS

- General considerations

• What is the neurological status of the subject ?
- Poor mental status is associated with greater complications rate, subject with depressed mental status can suffer of profound sedation even with low doses of sedatives
- Is the animal in pain ?
  ◦ When pain is suspected, or an increase sympathetic activity is detected a sedative or hypoalgesic drug has to be implemented
    - Dexmedetomidine (0.005- 0.01 mg/kg) IM
    - Methadone (0.2 mg/kg) IM
    - Dexmedetomidine (0.002-0.005 mg/kg) + methadone (0.2 mg/kg) IM
    - Butorphanol (0.1-0.3 mg/kg) IM or IV is not a good analgesic for a subject with spinal disease especially if surgery is planned
    - NSAIDs and gabapentinoids should be considered
  ◦ Aggressive/nervous subject can be sedated with IM combination of dexmedetomidine (0.005-0.01 mg/kg) with methadone or butorphanol (both at 0.2-0.3 mg/kg)
    - In this case the dose of general anaesthetic will be reduced up to 60%
    - Place an IV catheter as soon as feasible and later use it to deeper sedation if needed
- Does the animal need assisted ventilation ?
  ◦ If an increase in ICP is suspected, assisted ventilation must be provided in order to maintain normocapnia (35-45 mmHg EtCO2) throughout general anaesthesia

Anaesthesia for MRI scan

• Avoid fatalities
- Remember you are in close proximity to a huge magnet
  ◦ Do not use any ferric material
  ◦ Apply the rules critically on a daily basis (do not get relaxed about it)
- MRI scan is related to an increased risk of perioperative hypothermia in subject undergoing TL surgery (Burgies & Rioja 2019)
  ◦ Low temperature in the scan
  ◦ Long scans
  ◦ No possible to use active warming devices (use bubble drape or blanket)
  ◦ In case a hypothermic subject has to proceed to theatre for surgery make sure you have a plan to avoid further hypothermia and potential fatalities (active warmer devices, fluid warmer, HMEs, low fresh gas flow , appropriate anaesthetic plane)

• Monitoring during MRI
- Capnography (EtCO2)
  ◦ Provides information about both the respiratory and cardiovascular system
  ◦ Essential to guide IPPV
  ◦ Key in subject suffering of increased ICP
  ◦ Sampling cable can be easily passed within the MRI cage
- Anaesthetic gas monitor (EtAA)
  ◦ Helpful to maintain an adequate anaesthetic level, lack of movement is an essential requirement to compare sequences and it is not practical to frequently assess the depth of anaesthesia
  ◦ High fresh gas flow, long hoses, ventilator, distance from the subject can “dilute” the anaesthetic within the system
- Oscillometric NIBP monitoring
  ◦ Normotension is always the goal in anaesthesia to prevent organs hypoperfusion
  ◦ MAP> 60 mmHg is the standard target , higher values in hypertensive and subjects with SOLs might required
    - CPP=MAP-(ICP+CVP)
  ◦ All plastic material and the long cable can be easily introduced within the MRI cage and attached to the appropriate size pressure cuff

• Oesophageal stethoscope
- Cheap and safe
- Relaxing

• MRI compatible monitors
- Considered in busy hospital
- Burns reported with ECG
- Operator within the MRI cage

- Loss of attention (boring procedure)
  - Human error is the most common cause of fatalities
  - Use monitoring sheet, checklist and SOPs
- Gadolinium IV administration
  - Adverse reactions are not common but reported (Girard 2010, Scarabelli 2016)
    - Immediate support treatment is required to treat hypotension and bronchoconstriction
  - Careful and continuous observation of monitored vital variables following administration is essential
    - Anaesthetic depth often becomes more superficial
- CSF tap
  - When cisterna magna is used for sampling, flexion of the neck causes an increase in ICP not helpful for the subject (optimize time)
  - Maximal immobility needed, irreversible complication for accidental movement
    - Be sure the anaesthetic plane is adequate prior to the puncture (absence of palpebral reflex, poor jaw tone)

Anaesthesia (or sedation) CT scan

- Rapid procedure but do not overlook the status of the subject
  - Geriatric
  - Medically compromised
  - Metastatic or OA pain
- Sedation or anaesthesia ?
  - Sedation can be an option for young, strong orthopaedic subjects (dexmedetomidine + opioids)
    - If the needed sedation is not achieved after the IM administration, place an IV catheter so the sedation can be titrated with small incremental doses (0.001 mg/kg dexmedetomidine) or with careful use of propofol (< 1 mg/kg) monitoring for apnoea
    - Does not allow full monitoring as in anaesthetised subjects
    - A deep sedation is often more detrimental than GA in subjects with poor organic reserve (geriatric or medically compromised)
  - General anaesthesia can be induced with IV propofol following the most appropriate anaesthetic premedication depending on the subject needs, trachea is intubated and most often anaesthesia is maintained with a volatile agent but TIVA with propofol CRI can be an alternative
  - General anaesthesia and control of the airways is essential when apnoea has to be induced
    - Fentanyl (0.050-0.01) mg/kg IV used as co-inductor prior to propofol will increase chances of post induction apnoea
    - Transient hyperventilation (increasing the minute volume so $EtCO_2$ lower to 25-28 mmHg) will cause a reflex apnoea by inhibiting the central ventilatory centre
    - Application of PEEP prevent lungs atelectasis and improve imaging
      - Optimal positive pressure during breath hold (++ metastatic checks) is between 10-12 cmH_2O
      - If ventilator with PEEP is not available, Peep valves (12.5 cmH_2O dog, 7.5 cmH_2O cat) can be included in the breathing circuit (at APL valve)
      - Use of higher fresh gas flow
- Contrast media IV administration
  - Can induce or worsen renal failure (not common but reported)
  - Pre anaesthetic fluid therapy and normotension might decrease the chances of renal damage
- Myelo-CT/ Myelography
  - Possible reaction to contrast media (Scarabelli 2016)
  - Possible increase in ICP and seizures
    - Inverse Trendelenburg position
- Monitoring
  - SpO_2, $EtCO_2$, NIBP (and ECG readily available) are recommended

SUGGESTED READINGS AND REFERENCES AVAILABES ON REQUEST f.aprea@canismallorca.es

Effects of general anaesthetics on CNS and mechanism of action of anaesthetics

Federico Corletto,
PhD, CertVA, Dipl ECVAA, FRCVS

The understanding of mechanisms of action of anaesthetic has dramatically evolved in the past 10-15 years. Theories suggesting a generalised effect of anaesthetics on the brain were adequate to partially explain the action of inhalation all anaesthetics, but cannot explain differences in onset, effect, and offset of modern anaesthetics. General anaesthesia is a reversible drug induced state characterised by unconsciousness, amnesia, analgesia, immobility, and (hopefully...) stability of cardiovascular, respiratory, and autonomic systems. With very few exceptions, a single drug is unlikely to cause all these effects.
Specific molecular targets have been identified for most anaesthetic agents, allowing to explain in detail how they affect membrane potential at cellular level and to try to develop new molecules with better pharmacokinetic or pharmacodynamic profile.
Much more interesting are the recent advances in understanding the mechanisms underpinning decreased states of consciousness, including sleep, sedation, anaesthesia and coma. Results from electroencephalografic and functional brain imaging studies, their correlation with the distribution of receptors in different nuclei and the clinical manifestations have allowed to develop detailed explanations of the effects of most anaesthetics, their peculiarities and their differences.
This presentation will focus on this specific aspect of anaesthesiology: relating the specific molecular target of anaesthetic to specific neural circuits, and their clinical correlates.

Before discussing in detail the neural mechanisms of anaesthesia, it is necessary to briefly mention control of arousal at different levels and introduce the basics to understand how an “anaesthetic signature” is recognised on a processed EEG.

The vast majority of nuclei controlling arousal are located in subcortical structures. Loss of consciousness is induced by anaesthetics interfering with the function of structures in the cerebral cortex, thalamus and brainstem, affecting the way they communicate.

Some nuclei play a key role in modulating the state of consciousness, because of their multiple connections:

- Locus coeruleus (LC): noradrenergic nucleus, implicated in maintaining arousal via inhibitory projections to the Ventrolateral Preoptic Nucleus, and excitatory projections to the Intralaminar nucleus of the thalamus, basal forebrain and cortex.
- Ventrolaeral Preoptic Nucleus (VPN): GABAergic and galaninergic nucleus, implicated in promoting unconsciousness, sends inhibitory projections to the Tuberomammillary nucleus, the ventral Periacqueductal grey, laterodorsal tegmental area, peduncolopontine tegmental area, dorsal raphe nuclei

The nuclei involved in maintain arousal with projections to cortical structures are:

- Ventral Periacqueductal Grey (vPAG), sending dopaminergic excitatory projections to the cortex
- The Dorsal raphe nuclei (DR), dopaminergic, sending excitatory projections to the cortex
- Tuberomammillary nucleus (TMN), with excitatory histaminerigic projections to the cortex
- Laterodorsal (LDT) and Peduncolopontine tegmental areas (PPT), sending excitatory cholinergic projections to the cortex
- Lateral Hypothalamus (LH), whose orexinergic neurons send excitatory projections to the cortex
- Basal Forebrain nuclei, sending cholinergic excitatory projections to the cortex
- Central thalamus: here ascending pathways from the basal forebrain and brainstem converge with pathways from the frontal cortex, maintaining organised behaviour and arousal. Selective stimulation of the central thalamus in rats lightly anaesthetised with isoflurane temporarily and completely reverses the effects of the anaesthetic, with rapid return to normal function, but this effect ceases immediately upon stopping the electrical stimulation. Similarly, electrical stimulation of the central thalamus in minimally conscious patients can temporarily increase the level of consciousness. The Central thalamus receive excitatory projections from the striatum, and inhibitory ones from the globus pallidus. Corticostriatal projections have an inhibitory activity on the inhibitory activity of the pallidus, promoting and maintaining arousal.

The activity of a large number of pyramidal neurons in the cortex is controlled and coordinated by the GABAergic inhibitory activity of a small number of inhibitory cortical interneurons, with cortical activity depending on this inhibitory mechanism and on excitatory projections from ascending arousal centres.

In this complex framework, decreased consciousness can be achieved either by direct inhibition of structures controlling arousal, or by stimulation of structures inhibiting nuclei controlling arousal, resulting in indirect inhibition of arousal.

All anaesthetics, with the notable exception of ketamine, will produce slowing of the EEG, but with characteristic effect on the power spectrum of the different waves.
EEG waves are classified according to their frequency, and the normal EEG is composed of multiple wave patterns

occurring at the same time, resulting in the raw signal recorded. The spectrum decompose the raw EEG into its frequency components, allowing to identify the relative contribution (measured as power, generally on a logarithmic scale) of different waves to producing it. The spectrum can be plotted against time, resulting in Compressed Spectral Arrays (3dimensional) and Spectogram (density spectral array, or spectrogram, with colour coded power).

The EEG waves are generally classified, according to their frequency, in:
Slow: < 1 Hz
δ: 1-4 Hz
θ: 5-8 Hz
α: 9-12 Hz
β: 13-25 Hz
γ: 26-80 Hz

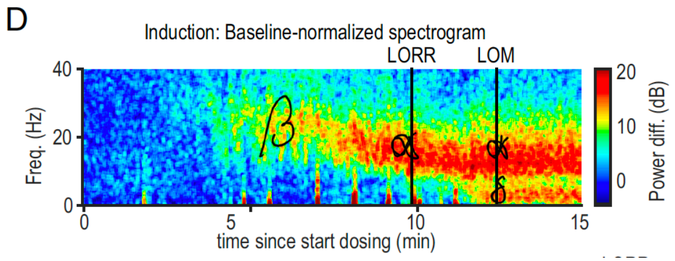
At this point it is necessary to specify that the description of the typical EEG changes induced by anaesthesia refers to recordings from the prefrontal and frontal cortex (FP1, FP2, F7, F8) in humans, with probably the canine equivalent being F3, F4 or F7, F8, as normally leads are not placed to investigate the activity in the prefrontal cortex, which is less developed than in humans.

The normal awake EEG is composed prevalently of β and γ oscillations. If a full EEG is performed, and the patient asked to close the eye and relax, coherent oscillations will appear and become prominent at the level of the occipital cortex. These oscillations are defined "coherent" as they are synced even in non adjacent locations. Just to understand the idea of coherence, imagine a group of people singing the same song. Singing at the same time, but not perfectly synced corresponds to an incoherent EEG signal- if we take each singer individually, they sing the same tune (ie the EEG recording in different parts look morphological identical), but if we listen to them at the same time, they are all slightly out of sync. Singing following the instructions of a director and all perfectly in sync correspond to a coherent EEG signal. As you can probably already suspect, coherent EEG oscillations suggest presence of a "director" somewhere, which is coordinating the singing, they are not just caused by random firing or propagation.
With progressing decreased consciousness, the EEG becomes slower and more regular. Sedation will show mostly α and β oscillations, while under moderate anaesthesia the EEG is characterised by slow waves and α oscillations. These oscillations are localised prevalently in the frontal cortex, and are coherent. This phenomenon is named "anteriorisation" of the EEG, and is characteristic of anaesthesia (the slow oscillations move from the back to the front). With further deepening of anaesthesia, the EEG will show burst suppression (periods of α and β activity alternating with isoelectric EEG) and eventually an isoelectric EEG.
The spectrogram allows to rapidly assess how the EEG frequency components change in time. Each anaesthetic presents a peculiar EEG time domain signature easily appreciated on the spectrogram, which is related to the anaesthetic agent, to the amount used, and to certain patient characteristics (for example age). The EEG signature of anaesthetics is remarkably similar in rodents, primates and humans, and can be explained by the specific way each anaesthetic interferes with awareness.
Some clinical monitors use EEG raw data to produce a semi-quantitative indicator of anaesthetic depth (for example Bispectral index, Entrophy), but they do not take into account the effect of the different anaesthetic agents on the EEG, so they may be inaccurate in certain age bands, or for certain anaesthetic agents (ketamine above all).

In clinical terms, the "switching off" of the brain progresses in a rostrocaudal direction for most anaesthetics, with loss of cortical function (loss of cognitive function and consciousness) followed by loss of function of subcortical structures (loss of coordinated movement) and finally of the brainstem (loss of cranial nerve reflexes, apnea, cardiovascular depression). The "switching on" process follows the reverse order, with ventilation and control of cardiovascular function returning first, then cranial nerve function (palpebral reflex, swallowing), ability to move and finally consciousness and cognitive function. This specific sequence can be explained by the mechanism of action of anaesthetics on neural connectivity.

Propofol, barbiturates, alfaxalone, etomidate, and inhalational anaesthetics (at least in part) are all $GABA_A$ receptor agonists, although at different sites of the receptor. Regardless of the mode, activation of the receptor induces hyperpolarisation of neurons, mediated by inward movement of Chloride ions.
The effect of **propofol** on neuronal connectivity will be described in detail as it is the one better characterised due to its widespread use. Propofol is mostly a $GABA_A$ agonist, but it also has agonist activity at the glycinergic receptor, and is a mild antagonist of the Ach, AMPA and NMDA receptors as well.
At cortical level, $GABA_A$ mediated inhibition of pyramidal neutrons increases the effect of cortical interneurons inhibition, literally starting "switching off" the cortex. Remember that each cortical interneuron controls the firing and synchronisation of many pyramidal neurons, making the latter very sensitive to any direct drug induced inhibition. This explains how very small doses of propofol are sufficient to cause sedation.
Slightly increasing the dose will result in inhibition of the activity of the globus pallidus, due to the large number of GABA receptors present in this nucleus. The inhibition of the pallidus activity is also caused by decreased excitatory stimulation by the striatum, which is under control of cortical inputs (remember that cortical pyramidal cells have already been "switched off" by smaller doses of propofol). As previously mentioned, the pallidus sends tonic inhibitory projections to the central thalamus, therefore its inhibition will result in increased thalamic activity, shown on the EEG as an increase of β oscillations. Clinically this may be evident as paradoxical and non coordinated movements, as typically observed when basal ganglia function is compromised.
Further increasing the anaesthetic depth will result in disappearance of the β oscillations, with anteriorisation, prevalence of slow waves and appearance of a strong coherent wave oscillation. The coherence of the oscillations suggests that another structure is involved in their generation. Electrophysiological studies in laboratory animals have demonstrated coherence between the α oscillations in the cortex and those in the thalamus. This thalamocortical loop mechanism is a characteristic feature of propofol anaesthesia. The neural mechanism for these changes is the inhibitory effect of propofol on neurons in the vPAG, DR, LC and TMN, the structures involved

in maintaining arousal. Once these structures are inhibited, the "wiring" of the arousal network is compromised to such an extent that the subject becomes unconscious. The GABAergic inhibition of the brainstem nuclei controlling ventilation (dorsal and ventral respiratory groups), antigravity muscles (pontine and medullary antigravity nuclei), cranial nerves, and spinal motoneurons explains the other effects of propofol: ventilators depression, muscle relaxation/immobility, loss of palpebral and gag reflexes and change of eye position.



The above spectrogram (from Flores et al, 2017) shows the typical propofol signature in a rat anaesthetised with propofol. The first change in the spectrogram is the appearance of β oscillations, transitioning to α oscillations when the animal loses the Righting reflex (LORR); once loss of movement occurs (LOM), slow oscillations appear as well. Direct thalamic recordings in the same experiment have demonstrated coherence between the thalamic oscillations and the cortical and oscillations, confirming that it is a thalamocortical loop that causes this specific EEG signature.

When the anaesthetic plan is further deepened, there are periods of isoelectric activity (blue colour in the spectrogram) alternated with period of α and δ oscillations (burst suppression), with the duration of isoelectric EEG intervals becoming longer the deeper the anaesthesia, until an isolectric EEG state is achieved.

In the recovery phase, a gradual shift to higher frequencies and decrease of power are observed, with appearance of β and γ oscillations and disappearance of the oscillations. The pattern observed on the spectrogram resemble a "zipper opening". The loss of coherent α oscillations is associated with reversal of anteriorisation and return of normal thalamocortical and brainstem activity.

The neural mechanism described so far also explain three interesting facts:

- Reversal of effect by methylphenidate (better known as Ritalin); methylphenidate interferes with dopaminergic (increased dopamine in the mesocortical pathway, at level of frontal cortex, amygdala and hippocampus), and NAdr circuits. This probably explain why intravenous administration of methylphenidate to rats hastens recovery from anaesthesia after administration of a propofol bolus.
- Hastened recovery from propofol anaesthesia by physostigmine; physostigmine increases cholinergic activity in the brain, increasing the activity of cholinergic nuclei involved in arousal mechanism. This is not observed with the commonly administered neostigmine because, differently from physostigmine, it does not cross the blood brain barrier. Physostigmine has also been used clinically to treat emergence delirium from anaesthesia.
- Reversal of propofol anaesthesia by electrical stimulation of the central thalamus, demonstrated in rodents and in non-human primates.

The anaesthetic effect of propofol has also been investigated in humans *in vivo* using fMRI, looking at the changes of cerebral blood flow (CBF) caused by propofol in specific brain areas. This has demonstrated reduction of CBF in the posterior cingular cortex, thalamus and basal forebrain, which somehow makes sense with propofol postulated mechanism of action, but does not bring any extra information about its effect on neural mechanism of action.

Much more interesting are the studies investigating propofol sedation and anaesthesia using resting state fMRI, a powerful tool to identify functional correlation between specific brain areas using BOLD signal in absence of stimuli or tasks (resting state). This technique allows to acquire dynamic time series with moderate spatial resolution. After correction for respiratory and cardiac artefacts, which can affect BOLD signal, it is possible to investigate functional connectivity of specific areas of the brain, where functional connectivity is defined as the "temporal dependence of neuronal activation patterns of anatomically separated brain regions"- in very simplistic terms we assume that if two areas of the brain "switch on" at the same time, they are functionally connected. This interesting methodology has allowed to demonstrate decreased functional connectivity between the frontal cortices, and between the thalamus and the cortex under propofol anaesthesia. Further, maintenance of anaesthesia with propofol is associated with reduced functional connectivity between the thalamus and the Default Mode Network (DMN, including Posterior Cingular Cortex, Precuneus, Medial prefrontal cortex, inferior parietal cortex), and within the component of the DMN, which is one the resting state networks involved in maintaining arousal and is active when an individual is "restfully awake".

Inhalational anaesthetics show a spectrogram signature very similar to propofol, with and slow oscillations, when administered at concentrations below their MAC. When the concentration is increased, a θ component becomes very evident, filling the gap between the slow δ and α oscillations, essentially creating a nearly solid red band occupying the bottom half of the spectrogram. Presence of θ oscillations has been interpreted as an indication or a more profound unconsciousness and immobility. When the anaesthetic concentration is reduced in the recovery phase, the component θ disappears, and eventually the spectrogram shows the same "opening zipper" appearance observed with propofol, with decreased power and shift to higher frequencies, transitioning to the normal β and γ oscillations characteristic of the awake status. The different spectrogram is thought to be caused by the slightly different mechanism of action of inhalational anaesthetics. While propofol behaves essentially like a pure $GABA_A$ agonist, inhalational anaesthetics have significant effect also on other molecular structure, for example the facilitation of the activity of two-pore potassium channels (essential in regulating neuronal resting membrane potential and excitability), and antagonism of NMDA receptor. This theory would also explain why at lower concentration (prevalent $GABA_A$ agonism) the EEG signature of inhalational agents is indistinguishable from the one of propofol, while at higher concentration, when the effect on other targets may become more significant, the signature changes. This "dirty" mechanism of action may also explain why recording of spinal cord motor-evoked potential is more difficult in subjects anaesthetised with inhalational anaesthetics compared to propofol.

Two other anaesthetic agents for which the EEG signature has been well characterised are ketamine and dexmedetomidine. The former is interesting because it generates a dissociative state, while the latter is of

particular interest, due to the extremely specific mechanism of action, the $_2$ adrenergic agonism.

Ketamine's prevalent mechanism of action is antagonism at the level of NMDA receptors. Analgesia is mediated by its activity in the spinal cord, and in this abstract we will focus only on the supraspinal mechanism of action.
NMDA antagonism is more effective when the channel is open, therefore at low dose ketamine acts mostly on cortical inhibitory interneurons, which are more likely to be active as they continuously modulate the activity of pyramidal neurons. Inhibition of this inhibitory mechanism results in increased excitatory activity of pyramidal neurons, producing high frequency γ oscillations, which are typically observed after administration of a low dose of ketamine, and are accompanied by increased cerebral metabolic consumption of both oxygen ($CMRO_2$) and glucose (CMRGlu). The oscillations induced by ketamine are coherent, and different from those observed in awake individuals, because they are constrained to specific frequencies and have different spatial and temporal characteristics. This suggests disruption of the normal cortical spatial and temporal processing, in particular cortico-cortical coupling, which is probably the cause of the dissociative state induced by ketamine. In animal models, this state has been associated with a prevalent cholinergic tone in the brain, which suggests an active arousal system in face of reduced consciousness. Inhibitions of inhibitory neurons in the thalamus, hippocampus and limbic system probably explains this concurrent activation of the arousal system.
While at subanaesthetic doses ketamine produce these typical γ oscillations in bursts (periods of γ oscillation alternating with slow δ oscillations), anaesthetic doses of ketamine result in a stable β/γ rhythm. Coherent θ oscillations have also observed in subjects receiving ketamine, particularly when administered at very low analgesic doses.
Ketamine is less effective in patients receiving lamotrigine, probably because of the reduced glutamate release (caused by inhibition of presynaptic sodium channels) interferes with ketamine mechanism of action on the NMDA receptor. There is one case report in which IV administration of 250 mg of ketamine failed to sedate a 80 kg subject who overdosed on lamotrigine. It is, however, necessary to point out that the subject was also chronically receiving carbamazepine and fluoxetine, due to a psychiatric disorder. Propofol eventually managed to induce anaesthesia.

Last, but not least, it is worth discussing the EEG signature and neural mechanism of action of **Dexmedetomidine**. Dexmedetomidine is of particular interest not only because of its very specific mechanism of action, but also because it is capable of inducing a state of decreased consciousness very similar to sleep, included the possibility of rapid and complete arousal.
The main mechanism of action of Dexmedetomidine is binding to the $_2$ receptor in the locus ceruleus, hyporpolarising its neurons and decreasing their NAdr inhibitory activity on the Ventrolateral Preoptic Nucleus of the hypothalamus, and their excitatory activity on the basal forebrain, thalamus and cortex. As explained at the beginning of this abstract, this VPN sends inhibitory projections to the major arousal centres in the midbrain, pons and hypothalamus. This dual mechanism of action triggered by inhibition of Nadrenergic neurons in the locus ceruleus is similar to the mechanism that triggers naturally occurring sleep, in which the adenosine accumulated from degradation of ATP during prolonged wakefulness binds to adenosine A2 receptors in the VPM, increasing its activity and therefore the inhibition of arousal centres. Incidentally, caffeine is an adenosine inhibitor.

The EEG pattern induced by dexmedetomidine administration is very similar to the one observed in non REM sleep. Anteriorisation, characteristic of propofol and inhalational anaesthesia is not observed with dexmedetomidine.
Low dose dexmedetomidine induces a state of sedation in which the subject is able to respond to auditory or tactile stimuli, with EEG signature characterised by slow oscillations in the 0-4 Hz range and spindles (intermittent short lasting 9-15 Hz oscillations, with less power than the oscillations observed with propofol). Similar spindles are seen also in non REM sleep. If the dose of dexmedetomidine is increased, the spindles disappear and the δ oscillations power increases, but is still less than the one observed in propofol induced δ oscillations. This pattern is similar to stage III non REM sleep. A study in healthy volunteers investigated the effect of dexmedetomidine on cerebral blood flow and metabolism, as well as functional connectivity using PET and resting state MRI at the same time. It demonstrated reduction of regional CBF and CMRGlu in specific brain areas involved with awareness (DMN, frontoparietal network, thalamus), with preserved cerebral flow-metabolism coupling. When looking at functional connectivity, a reduction of connectivity was observed between the thalamus and DMN, but not between the cortical regions of the default mode network and frontoparietal network. The connectivity between the cortex and the cerebellum was also impaired, and since we know that the thalamus is mediating cortico-cerebellar connections, these information altogether support a central role for the thalamus in dexmedetomidine induced unconsciousness, while cortico-cortical connectivity appear to be maintained. Another very interesting finding of this study was that despite functional connectivity being rapidly restored upon discontinuation of dexmedetomidine sedation, at the same time point rCBF of DMN and thalamus remained similar to those of the unconscious state. The authors hypothesised that at this stage subjects had recovered consciousness and were responsive to external stimuli, but still sedated.
The changes in connectivity observed for dexmedetomidine (preservation of cortical-cortical connectivity, decreased thalamocortical connectivity) mirror those observed in naturally occurring non REM sleep, while they are different from those induced by propofol anaesthesia, in which both thalamocortical and cortico-cortical connectivity are disrupted. Connectivity between the thalamus and the brainstem is also better maintained with dexmedetomidine compared to propofol, and this alongside the preserved cortical-cortical connectivity probably explains why both natural sleep and dexmedetomidine sedation can be easily interrupted by external stimuli, which would result in ascending pathways restoring thalamic function to a cortex "ready to operate normally". In propofol anaesthesia, on the other hand, the impaired cortico-cortical and thalamic-brainstem functional connectivity affects the ability to recover consciousness in response to ascending stimulation. Direct thalamic stimulation, on the other hand, is able to reverse propofol anaesthesia by addressing the crucial role of the thalamus in maintaining unconsciousness.

References available on request

Anaesthesia and analgesia in animals undergoing intracranial surgery

Federico Corletto,
PhD, CertVA, Dipl ECVAA, FRCVS

Management of anaesthesia in animals undergoing intracranial surgery is mainly based on publications related to human medicine. Despite this, the vast majority of physiology and effect of pharmacological interventions have been characterised in laboratory animals prior than being applied in human medicine.
There is not such a thing as an "anaesthetic protocol" for intracranial surgery, as this term includes different procedures in animals with different level of compromise of the central nervous system (consider elective removal of a small frontal lobe meningioma vs removal of a large cerebellopontine one, with brain herniation). It is important to consider the goals we want to achieve, and understand how different drugs affect their achievement, adapting our approach to each patient, condition and procedure. Finally, the anaesthetic protocol should be the final result of considerations of the anaetshesiologist and discussion with the neurosurgeon, who is in the best position to tell what will happen, what are the best conditions that could be achieved to operate and what could go wrong.
Some general principles used in clinical anesthesia in animals undergoing intracranial surgery are founded on well established evidence, while other interventions are still subject of controversy.
The presentation will discuss the basic principles related to anaesthetic management of animals undergoing intracranial surgery focusing on the following areas: physiological goals and "neuroprotective" interventions, inhalational versus total intravenous anaesthesia (TIVA), use of mannitol vs hypertonic saline to control intracranial pressure (ICP), use of α_2 agonists, management of early anaesthetic recovery, use of ketamine.

Physiological goals and problems

When anaesthetising animals for intracranial procedures, the three most common settings are: treatment of intracranial neoplasia, treatment of traumatic brain injury (TBI) and anaesthesia in experimental animals to cause brain injury (ischaemic or traumatic) or implant recording devices. Despite the great differences related to the specific setting, some common principles of management exist.
Three main problems affect anaesthetic management of animals with intracranial disease: the rigid skull enclosing the brain does not accommodate changes in its content, resulting in increased pressure in presence of space occupying lesions or oedema; the brain is a highly vascular structure, therefore surgery is often problematic and postoperative bleeding a possible complication; the brain is very susceptible to ischaemic and hypoxic damage.
The main physiological goals of anaesthesia for intracranial procedures are therefore maintaining adequate perfusion and oxygenation of the brain, decreasing metabolic requirements, and providing favourable conditions for the surgeon to operate (i.e. "brain relaxation"). Maintenance of cerebrovascular reactivity in response to changes in arterial blood pressure and partial pressure of carbon dioxide is desirable to ensure that the physiological interventions aimed at protecting the brain are effective.
While maintenance of adequate cerebral perfusion pressure (CPP) is considered fundamental in neuroanaesthesia, this parameter is not representative of local events that may affect outcome during and after surgery. CPP depends on mean arterial blood pressure (MAP), ICP, and central venous pressure (CPV):

CPP = MAP - ICP (or CVP, whichever is higher)

It can easily be appreciated why this equation adequately describes only global perfusion, while is not representative of local perfusion and oxygenation. ICP is not homogenous within the brain, and areas of greater pressure may develop next to expanding masses and in proximity of bony structures, or at the level of interface between structures with different density, resulting in focal ischaemic injury. Local disruption of the blood brain barrier associated to perineoplastic oedema, brain inflammation, physical injury further affect susceptibility of the brain tissue to damage.
The suggested target for CPP is 70 mmHg. When targeting CPP in a setting where ICP cannot be measured, it should be considered that clinical signs (depression, neurological deficits) become evident when ICP approaches 20 mmHg, and that a decompressive craniotomy/craniectomy will result in a considerable decrease of ICP.
ICP can also be controlled reducing cerebral blood volume (CBV), and this can be achieved elevating the head (10-15 degrees) to promote venous drainage, controlling blood pressure to reduce vasodilation in response to hypotension, administering osmotic agents, optimising autoregulation of blood flow by inducing controlled hypocapnia (Warner 2002).
When planning the anaesthetic protocol for an animal undergoing intracranial surgery, it is indicated to work with the neurologist to ensure that an accurate baseline neurological evaluation is performed, an that the procedure and relative imaging (i.e. MRI and CT) are reviewed to anticipate problems.
Surgery of the caudal fossa presents specific concerns related to its small volume (and therefore reduced capacity to accommodate oedema and haemorrhage), to the possible catastrophic effect of brainstem oedema and manipulation on haemodynamic stability, respiratory and cranial nerve function. Loss of gag reflex and impaired swallowing may result in occult aspiration of food or gastric content, leading to pneumonia, hypoxaemia and eventually death. Surgery involving structures in the cranial fossa and in particular frontal lobes may result in transient postoperative delirium/agitation, with risk of hypertension and possibly postoperative bleeding.

TIVA versus inhalational anaesthesia

While a propofol based TIVA has been considered for decades the golden standard for maintaining anaesthesia in patients undergoing intracranial surgery, a constantly growing body of literature has questioned the belief that use of inhalational anaesthetic agents always leads to loss of cerebrovascular reactivity and increase in intracranial pressure.

The different effects of sevoflurane and isoflurane on cerebrovascular reactivity have been characterised at concentrations inferior and similar to their MAC and after different challenges. Hypocapnic vasoconstriction at 0.6-0.7 MAC multiples was greater with isoflurane than sevoflurane in an experimental setting in which the change of cerebral blood flow (CBF) in the middle cerebral artery (MCA) was investigated in response to step-wise changes of $PaCO_2$ from 20 to 50 mmHg (Nishiyama et al. 1999). While the finding of this study seem to suggest that control of CBV induced by modification of the $PaCO_2$ may be easier using isoflurane, the majority of published research points to a different direction, suggesting that cerebral autoregulation is better preserved during sevoflurane anaesthesia. At 1.5 MAC equivalents, recovery of CBF velocity in the MCA (V_{MCA}) after inducing a sudden 20 mmHg decrease of mean arterial blood pressure was considerably faster in healthy human volunteers anaesthetised with sevoflurane compared to isoflurane, suggesting a better preservation of dynamic cerebral autoregulation (Summors et al. 1999). Preservation of cerebrovascular reactivity was demonstrated after investigating the changes of V_{MCA} after a sudden transient increase of blood pressure induced by administration of phenylephrine in volunteers anaesthetised with sevoflurane (0.5 and 1.5 MAC) (Gupta et al. 1997). The effect of graded haemorrhage on CBF autoregulation in rats confirmed that autoregulation is maintained in animals anaesthetised with sevoflurane (1 MAC), until the anaesthetic agent concentration is increased to 2 MAC (Lu et al. 1998).

The cerebral vasodilatory effects of isoflurane and sevoflurane have been characterised both ensuring exposure to the same MAC equivalent (Matta et al. 1999), and identical degree of suppression of auditory evoked potential (Holmström & Åkeson 2004), suggesting that sevoflurane causes less vasodilation than isoflurane at similar depth of anaesthesia.

The experimental and clinical evidence suggests that the effect of inhalational agents on ICP and CBF is complex and related not only to the agent used, but more importantly to the amount of anaesthetic used: while at low concentrations the prevalent effect observed is a decrease of CBF related to metabolic suppression with preserved flow-metabolism coupling, at higher concentrations vasodilation is predominant, resulting in an increase of CBV and, potentially, ICP, despite decreased cerebral metabolism, suggesting uncoupling. (Gunduz et al. 2009).

Propofol, on the other hand, has been demonstrated to consistently reduce CBV and metabolism, resulting in a decrease of ICP. Administration of sevoflurane or propofol and remifentanil titrated to reduce Bispectral Index (BIS) to 35 resulted in uncoupling of flow and metabolism when sevoflurane was used (Conti et al. 2006). It must be pointed out, however, that a high concentration of sevoflurane (up to 4%, therefore outside the normal therapeutic range) was used in the study to achieve the desired level of BIS suppression.

The clinical implication of choosing sevoflurane over propofol have been investigated in humans undergoing elective intracranial surgery. Subjects were randomly allocated to receive either sevoflurane and remifentanil or propofol and remifentanil to maintain anaesthesia. Interestingly hypotensive episodes were more frequent during anaesthesia in patients allocated to receive sevoflurane, and hypertensive episodes were more frequent at emergence of anaesthesia in the same group. Despite these findings, both protocols were judged adequate in this setting (Sneyd et al. 2005).

Based on the current evidence available in human trials, some authors have suggested that while sevoflurane does not increase ICP, propofol remains the agent of choice when lowering ICP is desired. Studies comparing the two protocols are lacking in veterinary medicine, as in one of the two published study investigating an anaesthetic protocol in animals undergoing intracranial surgery, only TIVA is used (Raisis et al. 2007) and in the other one, only sevoflurane is used (Marquez-Grados et al, 2020).

The peculiar pharmacokinetic of propofol in cats negates some of the desirable effects of propofol (i.e. rapid and predictable recovery), therefore in this species sevoflurane is still frequently used in combination with opioids to maintain anaesthesia. The pharmacokinetic profile of alfaxalone is more amenable to administration in infusion in cats compared to propofol and although a cyclodextrin formulation is available for veterinary use, the effect of this drug on cerebral autoregulation, CBV, and ICP have not yet been well characterised. Some studies performed in the 70s and 80s in cats anaesthetised with alfaxalone/aldadolone suggest that neurosteroids may have a neuroprotective effect, decreasing CBF and CBF. More recently, a MR-spectroscopy study in dogs suggested that alfaxalone and propofol have similar effect on brain metabolism (Sobbeler et al, 2018) and a case report suggested that an alfaxalone based propocol can be safely used in dogs undergoing intracranial surgery (Warne LN et al, 2014).

Mannitol versus hypertonic saline

Osmotherapy is a cornerstone of management of raised ICP. Mannitol has traditionally been used to control ICP, however use of hypertonic saline (HS) solutions has been investigated both in experimental and clinical settings. The major advantage of using hypertonic solutions is related to their effect of cardiovascular performance: while mannitol may decrease circulating volume and blood pressure, administration of hypertonic saline is likely to improve haemodynamics, especially in traumatised patients.

When mannitol and HS were used to control ICP in a rodent model of TBI, a greater reduction of ICP (54% vs 35%) and a longer lasting effect (500 min vs 120 min) were observed after HS administration (Mirski et al. 1999). HS (23.4% and 3%) was demonstrated to be more effective in reducing ICP compared to mannitol (1 g/kg) also in dogs in which intracerebral haemorrhage was induced experimentally. Interestingly, 3% HS was the most effective treatment in this study, and the only one still effective after 120 min (Qureshi & Suarez 2000). Two recent meta-analyses, however, have found no significant advantages in using one over the other in terms of outcome (Miyoshi et al, 2020; Shwimmenback et al, 2019).

The relative efficacy of mannitol and HS has also been compared in humans undergoing intracranial surgery. In a randomised clinical trial, a combination of HS and hydroxyethylic starch was more effective in reducing ICP compared to mannitol (Harutjunyan et al. 2005). HS proved to be effective in reducing ICP also in elective supratentorial intracranial surgery (Gemma et al. 1996) and in treating refractory elevated post-traumatic ICP (Vialet et al. 2002). A recent metanalysis suggest that it is difficult to establish whether HS is generally superior to mannitol or not, however, HS is more effective in treating refractory hypertension (Gu et al, 2018).

Vascular expansion leading to increased brain perfusion and reflex vasoconstriction, improvement of blood rheology, reduction of CSF production and reduction of cerebral cell volume have all been proposed as possible mechanisms of action of HS. The most common undesired effect of HS administration is hypernatremia, which is of great concern in the event of repeated administrations, due to its potential neurological effect.
The pharmacokinetic of mannitol in dogs and humans is similar, with a very rapid distribution half-life (a couple of minutes) and an elimination half-life of approximately 80 minutes (Cloyd et al. 1986). The effect peaks immediately after end of administration and although osmolarity increases after mannitol administration, this is not as marked as with HS.
Furosemide is often used to potentiate the effect of mannitol. Furosemide is administered to promote diuresis and to decrease CSF production. Interestingly, while common sense and clinical practice suggest that administration prior to mannitol should have greater effect on ICP, an experimental study in dogs, using an inflatable balloon to simulate the increase of ICP, suggested that the greatest reduction of ICP was achieved when furosemide was administered 15 minutes after mannitol, with one of the possible reasons being preferential renal elimination of water over mannitol after furosemide administration (Alex Roberts et al. 1987). On the other hand, in rats subjected to cortical fluid percussion injury, the addition of furosemide to mannitol did not result in a further decrease of cerebral water content (Tod et al, 2006).
Provision of perioperative analgesia has also to be discussed. Although the animal should be kept as comfortable as possible, for ethical reasons and to avoid the detrimental sympathetic stimulation induced by pain, liberal use of opioids should be avoided, as they may cause ventilatory depression and promote regurgitation and altered behaviour. Intraoperative analgesia can be easily managed either with opioids or with Dexmedetomidine infusion and postoperatively a combination of paracetamol (in the dog) and opioids as needed is generally adequate to provide analgesia with minimal sedation and side effects. If the animal is kept sedated with a Dexmedetomidine infusion, it is plausible that this drug is also providing adequate analgesia and particular attention should be used if adding opioids, due to the synergistic effect in causing sedation- in this case use small doses to effect, rather than “normal” doses.

Use of dexmedetomidine

Dexmedetomidine is of particular interest for neuroanaesthesia, as it allows to achieve haemodynamic stability, has some analgesic effect, and does not depress ventilation. Dexmedetomidine is known to induce cerebral venous vasoconstriction, reducing CBV, it decreases neuronal driven increase of CBF, triggering the natural sleep inducing neural mechanism, potentially improving cerebrovascular autoregulation. Administration of 10 µg/kg dexmedetomidine to dogs anaesthetised with isoflurane resulted in a marked decreases of CBF, but not accompanied by a significant decrease of cerebral metabolic rate ($CMRO_2$), suggesting that, differently from propofol, the reduction of CBF is driven by a direct vasoconstrictive effect, rather than being a response to decreased metabolic rate. Interestingly, no evidence of ischaemia was found, and it was suggested that the discrepancy observed may have been caused by a localised effect of dexmedetomidine in areas of the brain with greater density of α_2 receptors, which fits perfectly with current knowledge on its mechanism of action (Zornow et al. 1990). Administration of dexmedetomidine doses closer to the clinical dose-range (0.5-2 µg/kg) attenuates cerebral vasodilation induced by isoflurane and sevoflurane (0.5-1.5 MAC), in a dose-independent way (Ohata et al. 1999). Dexmedetomidine effect on CBF in dogs anaesthetised with isoflurane was evident both during normocapnia and hypercapnia (90 mmHg) (Fale et al. 1994).
The greatest concern related to use of dexmedetomidine in subjects undergoing intracranial procedures relates to the decrease of CBF not accompanied by a parallel decrease of $CMRO_2$, as this situation may lead to ischaemia of the brain tissue adjacent to the lesion and not yet committed to death. A more recent study (Laaksonen al, 2018), investigated in detail the effect of dexmedetomidine and other injectable agents on global and local CMR-Glu, and their finding suggest that the reduction of blood flow induced by dexmedetomidine is accompanied by a reduction of metabolic rate, therefore does not increase the risk of ischaemia. Interestingly, the metabolic suppressant effect of dexmedetomidine in this setting was superior to that of propofol and sevoflurane, and this is probably confirmed but its typical EEG signature, characterised by presence of only low power slow oscillations.
Use of dexmedetomidine infusion as part of the anaesthetic protocol has also been investigated in patients undergoing intracranial surgery (supratentorial tumours) and with neurovascular injuries. Drummond et al demonstrated that a detrimental role of dexmedetomidine on brain oxygenation could not be supported, and that in the patients investigated -anaesthetised with sevoflurane and sufentanil- dexmedetomidine did not induce a detrimental level of vasoconstriction and improved mean arterial pressure and brain tissue oxygenation (Drummond & Sturaitis 2010).
A similar study has been performed in dogs undergoing elective cranial fossa surgery (Marquez-Grados et al, 2020), comparing a sevoflurane-dexmedetomidine to a sevoflurane-opioid protocol. The only two significant differences reported were a higher mean arterial blood pressure in animals receiving dexmedetomidine, and a longer extubation time in the same group, with the latter probably explained by a bias in case management, as dexmedetomidine infusion was started only at the end of surgery in the opioid group, probably allowing extubation to occur before the plasma concentration was sufficiently high to delay it. Unfortunately, due to the retrospective nature of the study, it was not possible to determine whether in animals receiving dexmedetomidine instead of a short acting opioid presented spontaneous ventilations returned sooner or not.
The effect of dexmedetomidine on perioperative haemodynamics has been investigated in patients undergoing intracranial surgery to resect supratentorial tumours, demonstrating superior haemodynamic control and less respiratory depression compared to use of fentanyl (Tanskanen et al. 2006).
Unfortunately, use of perioperative dexmedetomidine infusion in animals anaesthetised for intracranial surgery has not yet been fully characterised, despite the availability of the drug and its use in other settings. A possible limitation of this drug, at least in dogs, is the exquisite sensitivity of this species to the peripheral vasoconstrictive effects of dexmedetomidine, resulting in bradycardia and increase of blood pressure even after administration of low doses.

Management of early anaesthetic recovery

Emergence from anaesthesia after intracranial surgery is probably one of the most challenging moments for the veterinary anaesthetist. Hypertension and disorientation are commonly observed and it may be difficult to rule out complications. The only study reporting postoperative complications after elective intracranial surgery in

dogs documented bradycardia in 66% of the cases, and hypertension and agitation in 52% and 57% of the half of the cases, similarly to what has been reported in humans (Marquez-Grados et al, 2020).
Hypertension is commonly observed after brain surgery in humans, even in absence of raised ICP, and the exact causes of this phenomenon have not been characterised yet. Although a direct link between transient postoperative hypertension and bleeding has not been demonstrated, most patients that present postoperative bleeding have experienced hypertension after emergence from anaesthesia (Warner 2002). Confusion/disorientation is not commonly reported in humans, but seems to be a significant problem in animals undergoing cranial fossa surgery if they are recovered rapidly after the procedure. It should be pointed out that rapid recovery is not a paradigm in human intracranial surgery, unless the procedure has been performed in an awake patient. Disorientation and stress cause catecholamine release and increase the risk of hypertension. It is important to establish whether the changes observed in recovery (altered mentation, hypertension) are transient and related to the procedure performed or are indicative of ensuing complications. Frequent neurological evaluation and a team approach (neurologist and anaesthetist) are paramount to characterise and manage these episodes.
Administration of sedation (i.e. dexmedetomidine) prior to recovering the animal from anaesthesia smoothes recovery without causing respiratory depression, and may control haemodynamics. Administration of analgesic is warranted to rule out pain as the cause of the behavioural and haemodynamic changes observed, although this has to be balanced with ventilatory depression, especially if using opioids and administering them prior to recover the animal from anaesthesia. In selected cases, antihypertensive treatment (labetalol) may be indicated to control blood pressure. Preoperative anti-epileptic therapy may be helpful to smooth recovery and should be instituted whenever operating on the brain, to reduce the risk of postoperative seizures.

Ketamine and intracranial procedures

Inclusion of ketamine in the anaesthetic protocols for intracranial surgery is still controversial The evidence supporting the potential neuroprotective role of ketamine is significant in laboratory animals, but inconclusive in clinical settings. The main mechanism of ketamine-induced neuroprotection is antagonism of the NMDA receptor, protecting from the effects of excitatory neurotransmitters. Administration of ketamine prior to cerebral ischaemia and after TBI has been demonstrated to improve outcome in experimental animals, without negatively affecting haemodynamics. The possible concerns related to ketamine administration are the typical increase of $CMRO_2$ and CBF, with potential effect on ICP. These have been demonstrated to be negligible if ketamine is combined to other sedatives/anaesthetics, and if the subjects are ventilated. Despite the fact hat ketamine would be never used alone and in non ventilated patients, concerns related to possible neurotoxicity and to the lack of efficacy in clinical trials in humans has hindered its use in a clinical setting for many years (Himmelseher & Durieux 2005). A recent meta-analysis investigated 11 studies for a total of 342 patients in which ketamine was used in bolus or infusion (up to 100 µg/kg/min!) concluded that there was no evidence of harm, and hopefully this will give ketamine a new chance in intracranial surgery (Gregers et al, 2020). Recents reports about successful use of ketamine to control refractory status epilepticus in dogs showed no arm (though in one case the seizures worsened), but the protocol reported are extremely different: in one case 5 mg/kg IV boluses, in the other case 1 mg/kg bolus followed by an infusion of 1 mg/kg/h associated to a low dose dexmedetomidine infusion (Gioeni et al, 2020, Reynard et al, 2021), suggesting that further work is needed to characterise the use of ketamine in dogs wit seizures and intracranial disease.

References

Cloyd, J.C. et al., 1986. Mannitol pharmacokinetics and serum osmolality in dogs and humans. The journal of Pharmacology and experimental Therapeutics, 236(2), pp.301-306.

Conti, A. et al., 2006. Cerebral haemodynamic changes during propofol–remifentanil or sevoflurane anaesthesia: transcranial Doppler study under bispectral index monitoring. British journal of Anaesthesia, 97(3), pp.333-339.

Drummond, J.C. & Sturaitis, M.K., 2010. Brain Tissue Oxygenation During Dexmedetomidine Administration in Surgical Patients With Neurovascular Injuries. Journal of neurosurgical anesthesiology, 22(4), pp.336–341.

Fale, A., Kirsch, J.R. & McPherson, R.W., 1994. α2Adrenergic Agonist Effects on Normocapnic and Hypercapnic Cerebral Blood Flow in the Dog Are Anesthetic Dependent. Anesthesia and analgesia, 79, pp.892-898.

Gemma, M. et al., 1996. 7.5% hypertonic saline versus 20% mannitol during elective neurosurgical supratentorial procedures. Journal of neurosurgical anestehsiology, 9(4), pp.329-334.

Gioeni, D. Et al, (2020). Ketamine-dexmedetomidine combination and controlled mild hypothermia for the treatment of long-lasting and super-refractory status epilepticus in 3 dogs suffering from idiopathic epilepsy. J Vet Emerg Crit Care, 30(4): 455-460.

Gregers, M.C., et al, 2020. Ketamine as an Anesthetic for patients with acute brain injury: as systematic review. Neurocritical Care, 33:273-282.

Gu, J et al. Hypertonic saline or mannitol for treating elevated intracranial pressure in traumatic brain injury: a meta-analysis of randomized controlled trials. Neurosurgical Review (2018), doi 10.1007/s10143-018-0991-8.

Gunduz, M. et al., 2009. Comparison of Dexmedetomidine or Remifentanil Infusion Combined With Sevoflurane Anesthesia in Craniotomy: Hemodynamic Variables and Recovery. Neurosurgery Quarterly, 19(2), pp.116–119.

Gupta, S., Heath, K. & Matta, B.F., 1997. Effect of incremental doses of sevoflurane on cerebral pressure autoregulation in humans. British Journal Of Anaesthesia, 79, pp.469-472.

Harutjunyan, L. et al., 2005. Efficiency of 7.2% hypertonic saline hydroxyethyl starch 200/0.5 versus mannitol 15% in the treatment of increased intracranial pressure in neurosurgical patients–a randomized clinical trial. Critical Care, 9(5), pp.530-540.

Himmelseher, S. & Durieux, M.E., 2005. Revising a dogma: ketamine for patients with neurological injury? Anesthesia and analgesia, 101, pp.524-534.

Holmström, A. & Åkeson, J., 2004. Sevoflurane induces less cerebral vasodilation than isoflurane at the same A-line® autoregressive index level. Acta anaesthesiologica scandinavica, 48, pp.400-404.

Laaksonen, L. et al. 2018. Comparative effects of dexmedetomidine, propofol, sevoflurane and S-Ketamine on regional cerebral glucose metabolism in humans: a positron emission tomography study. BJA 121 (1): 281e290

Lu, H. et al., 1998. The effects of sevoflurane on cerebral blood flow autoregulation in rats. Anesthesia and analgesia, 8, pp.854-858.

Marquez-Grados F., Vettorato E., Corletto F., 2020 Sevoflurane with opioid or dexmedetomidine infusion in dogs undergoing intracranial surgery: a retrospective observational study. J Vet Sci, 21(1):e8

Matta, B.F. et al., 1999. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology, 91, pp.677-680.

Mirski, M.A. et al., 1999. Comparison between hypertonic saline and mannitol in the reduction of elevated intracranial pressure in a rodent model of acute cerebral injury. Journal of neurosurgical anesthesiology, 12(4), pp.334-344.

Miyoshi, Y., et al, 2020. Effects of hypertonic saline versus mannitol in patients with traumatic brain injury in prehospital emergency department, and intensive care unit settings: a systematic review and meta-analysis. Journal of Intensive Care, 8(61)

Nishiyama, T. et al., 1999. Cerebrovascular carbon dioxide reactivity during general anesthesia: a comparison between sevoflurane and isoflurane. Anesthesia and analgesia, 89, pp.1437-1441.

Ohata, H. et al., 1999. Intravenous dexmedetomidine inhibits cerebrovascular dilation induced by isoflurane and sevoflurane in dogs. Anesthesia and analgesia, 89, pp.370-377.

Qureshi, A.I. & Suarez, J.I., 2000. Use of hypertonic saline solutions in treatment of cerebral edema and intracranial hypertension. Critical care medicine, 28(9), pp.3301–3313.

Raisis, A.L. et al., 2007. Evaluation of an anaesthetic technique used in dogs undergoing craniectomy for tumour resection. Veterinary anaesthesia and analgesia, 34(3), pp.171–180.

Roberts P.A. et al., 1987. Effect on intracranial pressure of furosemide combined with varying doses and administration rates of mannitol. Journal of neurosurgery, 66(3), pp.440-446.

Reynard, P., Bilderback, A., Wells Dewey, C. (2021). Intravenous ketamine bolus(es) for the treatment of status epilepticus, refractory status epilepticus, and cluster seizures: a retrospective study of 15 dogs. Front Vet Sci, 10.3389/fvets.2021.547279.

Sneyd, J.R., Andrews, C. & al, E., 2005. Comparison of propofol/remifentanil and sevoflurane/remifentanil for maintenance of anaesthesia for elective intracranial surgery. British journal of anaesthesia, 94(6), pp.778-783.

Schwimmbeck F. Et al, 2019. Hypertonic saline vs mannitol for traumatic brain injury: a systematic review and meta-analysis with trial sequential analysis. J Neurosurg Anesthesiology 10.1097/ANA.0000000000000644.

Sobbeler FJ, Carrera I, Paslosle K, Ranasinghe MG, Kirchner P, Kastner RBS, 2018. Effects of isoflurane, sevoflurane, propofol and alfaxalone on brain metabolism in dogs assessed by proton magnetic resonance spectroscopy (1H MRS). BMC Veterinary Research (2018) 14:69.

Summors, A.C., Gupta, A.K. & Matta, B.F., 1999. Dynamic cerebral autoregulation during sevoflurane anesthesia: a comparison with isoflurane. Anesthesia and analgesia, 88, pp.341-345.

Tanskanen, P.E. et al., 2006. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: a double-blind, randomized and placebo-controlled study. British journal of anaesthesia, 97(5), pp.658-665.

Todd, MM, Cutkomp J., Brian, J.E., 2006. Influence of mannitol and furosemide, alone and in combination, on brain water content after fluid percussion injury. Anesthesiology, 105, 1176-1181.

Vialet, R. et al., 2002. Isovolume hypertonic solutes (sodium chloride or mannitol) in the treatment of refractory posttraumatic intracranial hypertension: 2 mL/kg 7.5% saline is more effective than 2 mL/kg 20% mannitol. Critical Care, 31, pp.1683-1687.

Warne LN., Beths T, Fogal S., Bauquier S.H. 2014. The use of alfaxalone and remifentanil total intravenous anaesthesia in a dog undergoing a cranio to my for tumour resection.Can Vet J, 55(11); 1083-1088.

Warner, D.S., 2002. Anesthesia for craniotomy. Canadian Journal of Anesthesia, 49(1), pp/R16-R23.

Zornow, M.H. et al., 1990. Dexmedetomidine, an α2Adrenergic Agonist, Decreases Cerebral Blood Flow in the Isoflurane-Anesthetized Dog. Anesthesia & Analgesia, 70, pp.624-630.

Main Symposium Abstracts

The “classic” management of chronic pain in veterinary medicine

Louise Clark, BVMS, MRCVS, CertVA, Dipl ECVAA, MSc, FRCVS

EBVS European Specialist in Veterinary Anaesthesia and Analgesia

Management of chronic pain in Veterinary Medicine has largely followed the trajectory of pain management in human medicine but with some distinct caveats. The “gold standard” for pain reporting in people remains that “pain is what the patient says that it is”, and whilst this approach has its own limitations, it exemplifies how challenging it is to assess chronic pain in non-verbal species.

For many years their failure to verbalise meant that many of our patients were probably denied effective analgesia, if it was available, and even now assessment of chronic pain remains challenging at best and often fraught with difficulty. Whilst not the subject of this presentation per se, it is imperative that everyone understands that chronic pain assessment differs substantively from acute pain assessment and that appropriate and validated tools are available to help assess the efficacy of your pain management. I would suggest that the following review is a good starting point to enable the reader to understand the assessment of chronic pain in dogs:

- Belshaw Z & Yeates J (2018) Assessment of quality of life and chronic pain in dogs. Vet Journal. 239, 59-64.

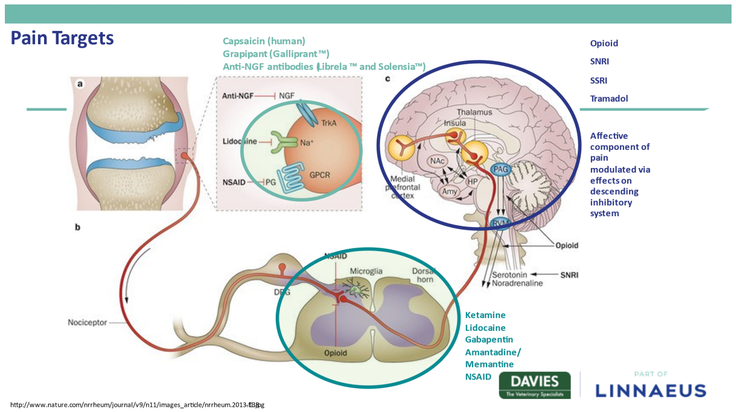
Cats have received less attention, and there is a smaller body of literature devoted to chronic pain, but this is good overview of the contemporary position.

- Monteiro BP & Steagall PV (2019) Chronic pain in cats: Recent advances in clinical assessment J Feline Med Surg 21,7,601-614.

A simple but powerful statement that exemplifies the impact of chronic pain on an individual is “….it is not how it feels but **how it makes me feel**”, a quote from a participant in a chronic pain trial. These are the motivational – affective components of chronic pain, the disturbances in the feeling of well-being that are an almost inevitable part of living with chronic pain. In people, chronic pain is intimately associated with anxiety and depression and recent data from dogs suggests that it may manifest similarly with many behavioural referrals having their roots in chronic pain. Thus, a more holistic and nuanced approach to treatment may be more rewarding, combining non-pharmacological aspects and targeted techniques with a lower risk of systemic side-effects. This however has only recently been accepted, and the “classic” management of chronic pain relies substantially on complex and often multimodal pharmacology, sometimes with a limited or non-existent evidence base.

An awareness of the multiple mechanisms that contribute to chronic pain is key to understanding the likely benefit of any pharmacological approach. With ongoing chronic pain, it is unusual for a single medication to result in satisfactory pain relief in a unimodal, stand-alone fashion. Therefore, combination pharmacologic treatment is an important aspect of multimodal chronic pain management. A key component of treating pain with medications is finding the balance between effective treatment and acceptable side effects. “Effective treatment” is difficult to define because it will almost never mean a complete remission of pain. An analysis from several human chronic pain trials suggests that a reduction of pain by 30% is clinically meaningful, because it is at this this level that patient ratings demonstrate “much improved” pain. This returns us as Veterinary Surgeons to the complex issue of pain assessment.

A rational approach is to consider the previously discussed mechanisms and assess potential targets that might respond to available analgesics; in the periphery, at the level of the spinal cord and within the brain/descending inhibitory pathways.



http://www.nature.com/nrrheum/journal/v9/n11/images_article/nrrheum.2013.43.jpg

It is also important to appreciate what “type” of pain you are treating.

A typical approach for pain management in human practice (IASP)

Nociceptive Pain	Neuropathic Pain	*Nociplastic Pain
NSAIDS	Amitriptyline	Amitriptyline
Paracetamol	SNRI	SNRI
Opioids	Gabapentinoids	Gabapentinoids
Local anaesthetic	Tramadol	Tramadol

*Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain. Essentially due to an alteration in central processing with increased excitability and decreased inhibition. Examples include fibromyalgia and non-specific lover back pain.

Pharmacological management of chronic pain, currently used options:

- The following information provides quick clinical reference for the use of common systemic pharmacological options for use in CANINE chronic pain
- It assumes that the other important non-pharmacological approaches to chronic pain management have been undertaken, these will be discussed further in the second presentation.

It also assumes that first line medication has been prescribed where this is mechanistically appropriate, not contra-indicated and is tolerated.

IMPORTANT POINTS:

- Note that NSAIDS are not considered in this lecture in any detail, because they are usual first line options for nociceptive pain and their mechanism of action limitation and contra-indications are widely understood. Readers are directed to the following resources:
  - KuKanich B, Bidgood T & Knesl O (2012) Clinical pharmacology of nonsteroidal anti-inflammatory drugs in dogs Vet Anaesth. Analg. 39, 1, 69-90. https://pubmed.ncbi.nlm.nih.gov/22151877/
  - Monteiro-Steagall BP, Steagall PVM & Lascelles BDX (2013). Systematic review of nonsteroidal anti-inflammatory drug-induced adverse effects in dogs J Vet Intern Med. 27, 5, 1011-9 https://pubmed.ncbi.nlm.nih.gov/23782347/
  - Hunt JR et al. (2015) An analysis of the relative frequencies of reported adverse events associated with NSAID administration in dogs and cats in the United Kingdom Vet J. 206, 2, 183-90. https://pubmed.ncbi.nlm.nih.gov/26361747/
- Grapiprant (Galliprant™) is another first line option in nociceptive pain with a specific licence for osteoarthritis. It will be considered further in the next presentation
- Many of these drugs are not licensed or do not have a market authorisation for use in this condition.
- Doses specified are often based on anecdotal use because the evidence base for some of these drugs is limited. Other sources may give variable information in this respect.
- The complete evidence base is NOT detailed in these notes. There are recommended readings and some interesting references noted. It does not serve as a complete review on the subject
- Attention must be paid to the appropriate legislation and informed consent for use of these medications should be obtained.
- Appropriate patient monitoring should always be undertaken. For older animals receiving polypharmacy, six monthly biochemical evaluations are generally recommended.
  - Some of the NSAID datasheets, advise routine blood sampling, and most animals are receiving NSAIDS as a first line analgesic.

Gabapentin and Pregabalin

Drug type:
• Gabapentinoids. • Anti-convulsant (anti-epileptic) and analgesic. • Gabapentin is a structural analogue of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), which explains its name but not its mechanism of action. • Pregabalin is structurally like gabapentin but has higher oral bioavailability and a longer half-life.
Mechanism of action:
• Selective inhibitory effect on voltage-gated calcium channels (in the CNS) containing the $\alpha_2\delta$-1 subunit - state dependent mechanism. • Prevents neurotransmitter release. • Little appreciable effect on the $GABA_A$ receptor complex. • Multiple other contributory mechanisms including Na+ channel blockade. • Only minor effects on normal nociceptive pathways, unlikely to be of benefit as sole agents where there is nociceptive and neuropathic pain.
Indications:
○ In people, first line agent for the treatment of neuropathic pain arising from numerous causes (NICE guidance in the UK). ○ Gabapentin provides good pain relief in approx. 1 in 3 of people who take it for neuropathic pain. ○ Primary indication is for assumed neuropathic pain in domestic animals.

Clinical use comments:

- Gabapentin: Limited pharmacokinetic data – suggests 8 hourly dosing due to shorter half-life in dogs compared to people.
- Gabapentin elimination half-life is 5-7 hours in man compared to terminal half-life of about 3.3 hours in dogs (Kukanich & Cohen 2011).
- It is rapidly absorbed and eliminated in dogs and frequent dosing is needed to maintain minimum targeted plasma concentrations.
- Gabapentin efficacy in humans is associated with 2 mcg/ml plasma concentrations, but the effective concentrations are unknown in the dog. Data suggest 10–20 mg/kg every 8 hours would maintain 2 mcg/ml plasma concentrations in dogs.
- Gabapentin should not be administered within two hours of oral antacids, or the antacids will hinder absorption of the gabapentin, making it less effective.
- Pregabalin: 4 mg/kg q12 hours produced plasma drug concentrations within the predicted therapeutic range extrapolated from the human literature.
- Plasma levels at typical therapeutic doses of pregabalin in the treatment of neuropathic pain are in the range of 2.0–8.0 mcg/mL
- Gabapentin been assessed versus topiramate, as an add-on treatment to carprofen, on quality of life (QoL) of dogs experiencing signs of neuropathic pain due to CM/SM. No significant difference was observed between VAS after gabapentin or topiramate at 2 weeks. However, an improvement in QoL was observed when gabapentin was compared with baseline, but not for topiramate.
- Pregabalin use in CM/SM has been reported.
- Perioperative pregabalin (4mg/kg PO 1 hour before surgery) has been assessed in dogs after intervertebral disc surgery. Pregabalin was given orally (4 mg/kg followed by postoperative treatment three times per day (4 mg/kg) for 5 days.) The outcome measures were the treatment-group differences in peri-incisional mechanical sensitivity and Glasgow Composite Measure Pain Scale (CMPS-SF) assessed during the first 5 postoperative days. Pregabalin serum concentrations were measured after 24, 72, and 120 hours.

  Pregabalin reduced pain levels in the treatment group by a mean of 2.5 CMPS-SF units compared with the control group. Pregabalin increased the mechanical nociceptive threshold. Mean levels of serum pregabalin were 5.1, 4.71, and 3.68 μg/mL at 24, 72, and 120 hours postoperatively, respectively. Postoperative signs of pain after surgical treatment of intervertebral disc herniation (IVDH) were reduced when dogs received perioperative pregabalin rather than opioids alone. Perioperative pregabalin reduces postoperative pain after surgical treatment of IVDH.
- Gabapentin (20mg/kg) PO 2 hours before anesthesia in dogs maintained with isoflurane had a MAC-sparing effect (~20%) with no effect on hemodynamic variables or vital parameters of dogs.
- Gabapentin may modulate DNIC in dogs with altered descending inhibition and a facilitatory pain profile, creating a more “normal” inhibitory profile.

Clinical side effects:

- Side effects of gabapentin in people include dizziness, fatigue, drowsiness, weight gain and peripheral oedema.
- Accumulation in renal and hepatic failure is possible because the drug is renally excreted and hepatically metabolized.
- A similar side effect profile is anecdotally reported in dogs and cats with sedation and ataxia being relatively commonly reported.
- Sedation is more common in patients receiving other sedating drugs (e.g. tramadol).

Potential dosing:

- Gabapentin: Data suggest 10–20 mg/kg every 8 hours would maintain 2 mcg/ml plasma concentrations in dogs.
- Warn owners of the potential for somnolence.
- Consider upwards titration of the dose to improve tolerability of side effects.
- Start administration at <10mg/kg twice daily and titrate upwards.
- Occasionally some dogs remain “sedated” on gabapentin without good clinical efficacy. Anecdotally, pregabalin may have a better side effect profile.
- Abrupt discontinuation of these drugs has resulted in seizures in people.

Costs and other considerations:

- Potential for abuse!
- In the UK: Controlled drug - Schedule 3.
- Prescribing restricted to 30 days` worth of drug and prescription validity 28 days.
- Gabapentin is cheap, pregabalin is relatively expensive in the UK.
- Veterinary Specials manufacturers provide a variety of gabapentin products.
- Avoid any liquid containing xylitol.

Interesting references and further reading including for clients:

- Guy S et al. (2014) Anticonvulsant medication use for the management of pain following spinal cord injury: systematic review and effectiveness analysis. Spinal Cord. 52, 89–96.
- Johnson BA et al. (2019) Effect of oral administration of gabapentin on the minimum alveolar concentration of isoflurane in dogs Am J Vet Res. 80,11,1007-1009.
- Moore SA (2016) Managing Neuropathic Pain in Dogs. Front Vet Sci. 22, 3, 12.
- Plessas IN et al. (2015). Comparison of gabapentin versus topiramate on clinically affected dogs with Chiari-like malformation and syringomyelia. Vet Rec. 17, 288.
- Ruel HLM et al. (2020) Pain burden, sensory profile, and inflammatory cytokines of dogs with naturally occurring neuropathic pain treated with gabapentin alone or with meloxicam PLoS One. 30,15,11
- Schmierer PA et al. (2020) Randomized controlled trial of pregabalin for analgesia after surgical treatment of intervertebral disc disease in dogs Vet Surg. 49,5,905-913
- https://todaysveterinarypractice.com/gabapentin-and-amantadine-for-chronic-pain/

Amantadine and Memantine

Drug type:

- Originally an anti- viral (influenza) and anti-parkinsonian drug.

Mechanism of action:

- Amantadine works by increasing the rate of channel closure following activation of the NMDA complex.
- It is a weak dopamine agonist and glutamate antagonist.

Indications:

- Amantadine should be considered as part of the initial multimodal therapy for any patient that has moderate to severe chronic osteoarthritis pain and as an add-on drug for patients that have worsening chronic pain despite previously adequate pain control and no worsening of the inciting disease.
- Because amantadine's contribution to pain relief is not really analgesia (it is technically an anti-hyperalgesic), the drug must be used as part of a multi-modal approach alongside analgesic drugs such as NSAIDs/grapiprant.

Clinical use comments:

- To decrease the central sensitization component of chronic pain, treatment duration probably needs to be long; thus, the current minimum recommended duration is 21 days.
- Long duration therapy may be necessary, and many patients may need amantadine for life.

Clinical side effects:

- Adverse effects or drug interactions in dogs or cats receiving amantadine are relatively uncommon.
- Some dogs may develop agitation, vomiting, flatulence, or diarrhoea (which may be watery), particularly in the early days of amantadine therapy.
- If the patient vomits after receiving the medication on an empty stomach, try giving it with a small meal or treat.
- Amantadine can be stopped without a withdrawal period.
- The following medications should be used with caution when given with amantadine: anticholinergic drugs, CNS stimulants (includes selegiline), trimethoprim/sulphonamide, thiazide diuretics, triamterene, or urinary acidifiers.

Potential dosing:

- The dosage for dogs and cats is 3 to 5 mg/kg orally once to twice daily, with twice daily being preferable.
- Data from recent studies indicate that twice daily dosing is probably more effective in dogs and cats.
- In cats (Siao et al., 2011). Half-life of approx. 5hrs following 4mg/kg PO (does suggest that BID dosing may be more suitable in cats).
- In greyhounds 2.8mg/kg PO produced a Cmax at 2.6 hours with a terminal half-life of 4.96hrs suggesting dosing should be more frequent than SID. (Norkus et al. 2014)
- Note: Edition 10 of the BSAVA Formulary recommends once daily dosing.

Costs and other considerations:

- Moderately expensive, liquid, capsules, and tablets available.
- Avoid any product containing xylitol.
- Amantadine hydrochloride 50mg/5mL oral solution: licensed in humans, available from AAH Pharmaceuticals; Alliance Healthcare (Distribution); Teva UK.
- Amantadine hydrochloride 10mg, 25mg, 50mg, 75mg tablets: Veterinary Specials available from Summit Veterinary Pharmaceuticals. 100mg available from multiple suppliers.

Useful links and further reading including for clients:

- https://todaysveterinarypractice.com/gabapentin-and-amantadine-for-chronic-pain/
- https://vetspecialists.co.uk/fact-sheets-post/our-guide-to-amantadine/
- https://www.zeropainphilosophy.com/post/amantadine-for-chronic-pain

Memantine:

- Similar mechanism of action to amantadine
- Much cheaper
- Less data, information and dosing extrapolated from behavioural medicine
- Use in chronic pain remains anecdotal with no clinical trials to support its use.
- Lower incidence of vomiting.
- Dosing 0.3-0.8mg/kg once (or twice) daily.
- https://www.zeropainphilosophy.com/post/memantine-or-amantadine

Tramadol

Drug type

- Tramadol is a weak opioid and has serotoninergic effects.

Mechanism of action

- Weak OP3 (μ) receptor agonist.
- Inhibits reuptake of noradrenaline and 5-HT.

Indications

- Licensed in chewable tablet form for chronic soft tissue pain.

Clinical Use Comments

- Some individuals do not produce significant quantities of the active metabolite O-desmethyl tramadol – tramadol itself is a pro-drug.
- Dosing is somewhat empirical due to lack of good PK/PD studies.
- Effects can be variable – inconsistent results!
- In chronic pain it is presumed that it is the effects on the descending inhibitory pathways that may be beneficial and the opioid like effects may promote sedation, hyperalgesia and dysphoria.
- The SPC for Tralieve® chewable tablets states that "the analgesic effects of tramadol hydrochloride may be variable and is thought to be due to individual differences in the metabolism of the drug to the primary active metabolite O-desmethyltramadol"……."in some dogs (non-responders) this may result in the product failing to provide analgesia; for chronic pain, multimodal analgesia should be considered; dogs should be monitored regularly by a vet to ensure adequate pain relief and in case of recurrence of pain or insufficient analgesia the analgesic protocol may need to be reconsidered" .

Clinical side effects

- Sedation and dysphoria are relatively common.
- Behavioural change without analgesic benefit can occur.
- Careful assessment and discussion with the owner is necessary.

Potential dosing

- 2-5mg/kg PO every 8 hours.

Costs and other considerations:

- UK Controlled drug - Schedule 3.
- RCVS advises storage in a locked cupboard (though strictly legally exempt).
- Tramadol chewable tablets for dogs (brand name Tralieve) are available as 20mg and 80mg tablets that can be broken into 2 or 4 parts.
- Subject of a recent systematic review and meta-analysis that concluded: "The overall CoE of the analgesic efficacy of tramadol for postoperative pain management in dogs was low or very low, and the main reasons for downgrading the evidence were risk of bias and imprecision".

Useful links and further reading:

- Donati LT et al. (2021) Efficacy of tramadol for postoperative pain management in dogs: systematic review and meta-analysis. Review Vet Anaesth Analg. May;48(3):283-296. Efficacy of tramadol for postoperative pain management in dogs: systematic review and meta-analysis - PubMed (nih.gov)
- https://www.youtube.com/watch?reload=9&v=oeSgd07xGbI CAM interview with Kenneth Joubert
- https://www.zeropainphilosophy.com/tramadol (pay to view webinar)

Paracetamol

Drug type

- Simple analgesic

Mechanism of action

- Paracetamol has multiple effects
  - Weak anti-inflammatory effect.
  - Antagonizes COX-3 centrally, inhibiting CNS prostaglandins.
  - Serotonin agonist working via the descending inhibitory mechanisms.
  - Intact cannabinoid receptors are required for paracetamol's actions.
- Justification for using paracetamol alongside NSAIDs.

Indications

- Useful as an alternative to NSAIDs in dogs that will not tolerate an NSAID or as an adjunct to NSAIDs in chronic pain.
- *Paracetamol should never be used in cats.*

Clinical Use Comments

- The antinociceptive plasma concentration of paracetamol in dogs has not been established. The short half-life suggests that plasma concentrations may only remain high enough to provide antinociception for short periods of time. However, it is not clear how the half-life relates to clinical effect with chronic use.
- Evidence for use in acute pain is growing. No evidence for the use of paracetamol long term beyond anecdote.
- Paracetamol is being used as an analgesic for chronic pain with efficacy documented based on owner assessment.
- Given that we have a huge body of evidence regarding safety and efficacy with NSAIDs in dogs, NSAIDs are always our first line option for chronic pain.
- Justification for moving from the licensed product.
  - Potential adverse events from Pardale-V.
  - Behavioural alterations attributable to the low level of codeine in Pardale-V (although at 4% bioavailability this has little clinical analgesic effect), may give us justification for using generic paracetamol.
  - There is a potential starting dose range from 10-33mg/kg every 8-12 hours and therefore some flexibility in finding a dose that suits your patient.

Clinical side effects

- Toxicity due to accidental ingestion (dogs have some ability to eat significant quantities of paracetamol despite its disgusting taste)
- Metabolism of paracetamol in all species is via glucuronide and sulphate conjugation pathways, and to a minor extent, cytochrome P450 (CYP450)-mediated oxidation pathways. The glucuronidation and sulphation pathways produce non-toxic metabolites which are excreted in bile and urine. At higher doses of paracetamol, the glucuronidation and sulphation pathways become saturated causing the oxidation pathway to be more significant leading to the production of toxic metabolites.
- In dogs, concomitant metoclopramide (which promotes gastric emptying) has been reported to increase and prolong plasma concentrations of paracetamol.
- In contrast, drugs that delay gastric emptying (e.g. codeine) may delay or reduce paracetamol's absorption. Paracetamol has been reported to lower the absorption and protein binding of oral cefalexin.

Potential dosing

- Paracetamol is licensed in dogs as Pardale V for 5 days.
- Dose in Pardale V works out at 33mg/kg q 8 hours.
- The listed dose in most formularies is 10mg/kg BID-TID, although the origins of this recommendation are unclear.
- This discrepancy does lead to some uncertainty and confusion about how we should be dosing paracetamol for long term use in chronic pain.
- A sensible approach is to assess efficacy at reduced dose of 10-25mg/kg q 8 hours, but realistically 10 mg/kg is likely too low.
- If you do reduce the dose and the owner considers comfort levels to have decreased then consider increasing.
- There is no evidence that this dose long term is detrimental.
- Remember paracetamol is hepatically metabolized (like all our options for chronic pain) but this does not mean that it causes hepatic damage.
- Paracetamol tablets and oral suspension are available. In the UK there is a veterinary special (200mg) from Bova.

Costs and other considerations:

- Extremely cheap

Useful links and further reading:

- •://www.zeropainphilosophy.com/post/paracetamol-for-long-term-use

Amitriptyline

Drug type

- Tricyclic Antidepressants

Mechanism of action

- The effects of neuromodulatory drugs such as TCA in managing neuropathic pain are distinct from their antidepressant effects.
- Inhibiting reuptake of serotonin and norepinephrine, antagonism of voltage-gaited sodium channels, and antagonism of NMDA receptors.

Indications

- There are no clinical trials, or experimental studies evaluating the use of TCAs for neuropathic pain in dogs,
- Case can be made based on the human literature.

Clinical Use Comments

  - Case series: management of neuropathic pain in three dogs with mixed results using amitriptyline alone or in conjunction with other analgesics.

Clinical side effects

- Sedation
- Urinary retention
- Tachycardia and ventricular arrhythmia
- Potentiating seizures
- KCS

Potential dosing

- Pharmacokinetic study of amitriptyline in dogs suggests that dosing at 3–4 mg/kg every 12 h will reach target drug concentrations extrapolated from people.

Costs and other considerations:

- Not stocked in our hospital

Useful links and further reading:

- Little available robust information regarding pain management

Future perspectives in the management of chronic pain in veterinary medicine

Louise Clark, BVMS, MRCVS, CertVA, Dipl ECVAA, MSc, FRCVS
EBVS European Specialist in Veterinary Anaesthesia and Analgesia

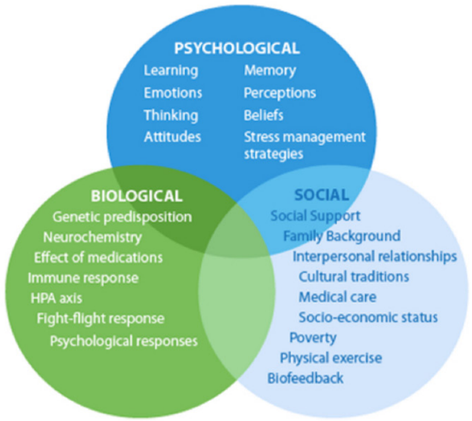
A Biopsychosocial Approach to Animal Pain: A new way of thinking about pain? Beyond the biological…

Currently Veterinary pain research focused on:

- Sensory modalities
- Neurological transmissions identified solely on a biological level
- New "drugs" are important but are not the sole approach to contemporary pain management

What is a Biopsychosocial model?

- A broad view that attributes disease outcome to the intricate, variable interaction of:
- Biological factors (genetic, biochemical, etc.)
- Psychological factors (mood, personality, behaviour, etc.)
- Social factors (cultural, familial, socioeconomic, etc.)



Biopsychosocial model of pain
Championed by Butler and Moseley and others. 2000

<u>Treating the ill individual</u>

- Biopsychosocial model of pain views "the pain experience" from a systematic perspective.
- As the biological condition worsens, psychological and social factors follow, which also need to be managed
- Treat the individual involved, in their "environment" not just the pain
- Emphasis on the unique interactions among biological, psychological, and social factors
- Treating the "whole" person is far more important than focusing merely on a disease
- "Holistic approach to patient management"

Benefits in human pain management: "The biopsychosocial model has led to the development of the most therapeutic and cost-effective interdisciplinary pain management program and makes it far more likely for the chronic pain patient to regain function and experience vast improvements in quality of life"

- Patients with the same diagnosis can respond differently to a standard treatment protocol
- The goal in the biopsychosocial approach to assessment and management is to:
- tailor the treatment to the specific needs of the individual

Is there ANY relevance to our cases?

- Pain component that mediates the suffering associated with pain
- When pain persists or becomes chronic, the affective-motivational component of the pain experience becomes more significant in evaluation and treatment
- Lasting pain affects virtually every aspect of day-to-day life, from sleep patterns to ability to concentrate, to social and personal relationships
- Animal Behaviourists often dealing with pain…
- Do dogs get depressed?
- Stress response to inability to perform simple movements, to pain when interact with owner…….

Impact of canine chronic pain on dog/owner relationship

- Dogs have owners….
- Dog owner interactions
- Does having an ill dog affect the owner?
- Does the dog perceive this effect?
    - *Belshaw Z, Dean R & Asher L (2020) "Slower, shorter, sadder: a qualitative study exploring how dog walks change when the canine participant develops osteoarthritis" BMC Veterinary Research 16, 85*

How does this affect our clinical approach?

- A biopsychosocial approach is more nuanced when assessing dogs and cats with chronic pain
- It is important to avoid a reductionist view
- At the very least consider emotional impact of pain……
- Assessment of emotional impact?
- Relevance of relationship with owner?
- A bio-behavioural approach?

<u>Getting back to the biological:</u>

Future methods of pain assessment?

- "Evaluation of the response to externally applied physical stimuli, such as pressure, heat, or cold is termed quantitative sensory testing (QST).
- QST may be used to identify and quantify alterations (gain or loss) in function of the sensory systems which detect and mediate these phenomena in both man and animals, and potentially discriminate peripheral and central sensitisation.
- It has been postulated that evaluation of QST parameters may predict response to analgesics, ultimately increasing the individualisation of treatment for pain.
- However, while there do appear to be correlations between QST measures and responses to analgesics in man, there is currently insufficient evidence to recommend QST to direct clinical treatments".
    - *Hunt J et al (2019) Quantitative sensory testing in dogs with painful disease: A window to pain mechanisms Review Vet J 243,33-41*

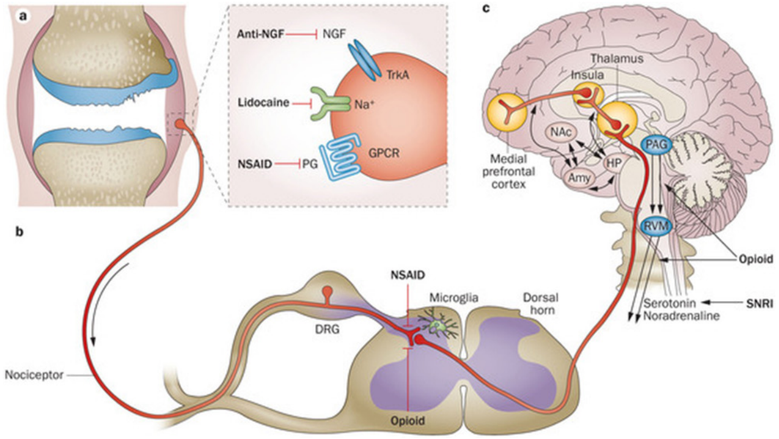
Animal Pain as a model for human pain?

- Spontaneous painful disease in companion animals can facilitate the development of chronic pain therapies for humans and in so doing drive the discovery of therapeutic interventions where there are common targets. The opportunities and limitations of naturally occurring, spontaneous OA as models of human OA pain is currently under consideration.
    - *Lascelles BDX et al. (2018) Spontaneous painful disease in companion animals can facilitate the development of chronic pain therapies for humans. Osteoarthritis & Cartilage 26, 2, 175-183*
    - *Cimino Brown D (2017) What can we learn from osteoarthritis pain in companion animals? Clin Exp Rheumatol. 35 Suppl 107,5,53-58*

How not to progress?

- There are significant concerns about the long-term use of opioids in canine and feline patients. There are multiple adverse effects, including opioid-induced hyperalgesia and the potential of opioids to suppress the immune response and thereby to increase the vulnerability to infections. Whilst not widely used in Europe, there is an increasing rate of prescription in the USA, apparently following the opioid epidemic that has plagued the human healthcare system. It would be reasonable to state that opioids should NOT be considered for long term analgesia in our patients.
    - *Clarke DL et al. (2019) Trends in Opioid Prescribing and Dispensing by Veterinarians in Pennsylvania JAMA Netw Open4;2(1): e186950*

<u>New and revisited therapeutics:</u>



http://www.nature.com/nrrheum/journal/v9/n11/images_article/nrrheum.2013.138-f1.jpg

Capsaicin

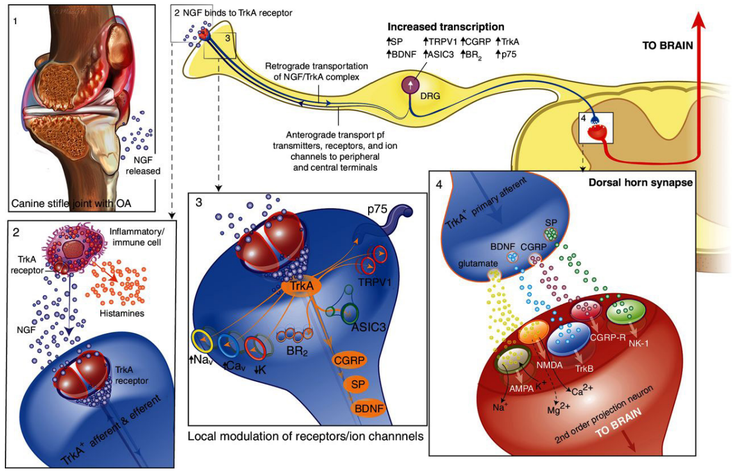
- Chemical compound responsible for the burning sensation felt when you eat chilli
- Topical capsaicin cream or (8%) patch
- Mechanism of action was thought to be by depletion of substance P
- More likely is 'receptor de-functionalization' involving several mechanisms
- Includes altered expression of receptor TRPV1
- No clinical dog data, this is a synopsis of human data : CNTX-4975 (trans-capsaicin) injection provides clinically meaningful pain reduction in subjects with painful intermetatarsal neuroma (Morton's neuroma): a randomized, double-blind, placebo-controlled, dose-ranging study | Cochrane Library (supplied by Dr A Ordman)

EP4 receptor – antagonists

- Non-cyclooxygenase (COX) inhibiting NSAID
- Prostaglandin receptor antagonist
- Acts as a blocker of the EP4 receptor which is responsible for the expression of pain and inflammation in osteoarthritis
- Unique targeted mode of action
- No significant serological or histopathological abnormalities detected in a safety study at up to 15 x the target dose for 9 months
- Indicated for the control of pain associated with mild to moderate OA in dogs
- No limit to treatment duration
- The safety of the veterinary medicinal product has not been established in dogs under 9 months of age and in dogs weighing less than 3.6 kg (DATA FROM ELANCO)
    - *Kirkby Shaw, K., Rausch-Derra, L., and Rhodes, L. (2016) Grapiprant: an EP4 prostaglandin receptor antagonist and novel therapy for pain and inflammation. Vet. Med. Sci. 2, 3-9.*
    - *Rausch-Derra, L., Huebner, M., and Rhodes, L. (2015) Evaluation of the safety of long-term, daily oral administration of grapiprant, a novel drug for treatment of osteoarthritis pain and inflammation, in healthy dogs. Am. J. Vet. Res. 76,10, 853-859.*
    - *Rausch-Derra, L., Rhodes, L., Freshwater, L., et al. (2016) Pharmacokinetic comparison of oral tablet and suspension formulations of grapiprant, a novel therapeutic for the pain and inflammation of osteoarthritis in dogs. J. Vet. Pharmcol. Ther. Mar 29.*
    - *Rausch-Derra, L., Huebner, M., Wofford, J., et al. (2016) A prospective, randomized, masked, placebo-controlled multisite clinical study of grapiprant, an EP4 prostaglandin receptor antagonist (PRA), in dogs with osteoarthritis. J. Vet. Int. Med. 30, 756-763.*
    - *Lebkowska-Wieruszewska B, De Vito V, Owen H, Poapholatep A, Giorgi M. (2017) Pharmacokinetics of grapiprant, a selective EP4 prostaglandin PGE receptor antagonist, after 2 mg/kg oral and i.v. administrations in cats. J Vet Pharmacol Ther. 40, 6, e11-e15.*

Anti-NGF antibodies

- Nerve growth factor (NGF) is essential for the survival of sensory and sympathetic neurons during development
- In the adult, NGF and its interaction with tropomyosin kinase A receptor (TrkA) has been found to play a critical role in nociception and nervous system plasticity in pain conditions
- Retrograde transport of TrkA/NGF complex to DRG promotes transcription
- Increase in nociceptors and ion channels
- Increased nociception
- Canine and feline anti-NGF monoclonal antibodies licensed in UK



Masataka Enomoto et al. Veterinary Record (2019)184, 23

- *Recent publication: https://veterinaryrecord.bmj.com/content/184/1/20.info*
- *Contemporary mechanism review: https://veterinaryrecord.bmj.com/content/184/1/23*
- *See video: https://www.zoetisus.com/oa-pain/first-time-resolution.aspx/*

Resiniferatoxin

- Chemical compound produced by the resin spurge, a cactus-like plant found on the slopes of the Atlas Mountains in Morocco
- Pure resiniferatoxin carries a rating of 16,000,000,000 SHU (Scoville Heat Units); that is one-thousand times stronger than pure capsaicin
- Very potent TRPV1 agonist
- Increased efficacy and a long duration of action
- Can be delivered by a central route of administration through injection into the subarachnoid space around the lumbosacral spinal cord
- Administered peripherally into a region of skin or deep tissue where primary afferents nerves terminate, or directly into a nerve trunk or a dorsal root ganglion (mainly research settings)
- Central route is currently being evaluated as a treatment for intractable pain in patients with advanced cancer

Ziconotide

- N-type voltage gated calcium channel blocker
- Binds onto calcium channels in the dorsal horn of the spinal cord blocking the influx of calcium
- Isolated from the venom of a marine snail – Conus magnus
- Intra-thecal use only, delivered by a pump
- Does not lead to the development of addiction and tolerance
- Very limited current use in the UK

Compounds in clinical development

https://www.youtube.com/user/RoyalSocietyMedicine

YouTube videos from the January 2020 meeting: New developments in the pharmacological management of chronic pain: Problems and possibilities

Techniques in clinical development:

There are multiple interventional pain-relieving techniques under clinical development, many of which take their inspiration from current human practice. The obvious advantage of analgesia delivered at the site of the lesion is the lack of exposure of the animal to systemic side effects, which as discussed previously can be considerable.

This is not an exhaustive list, but techniques include:

- Ultrasound-guided paravertebral perineural injections of local anaesthetic and glucocorticoids
- Ultrasound guided fascial and perineural injections
- Intra-articular administration of autologous platelet therapy, glucocorticoids, stem cells and hyaluronic acid.
    - *Wolf JK et al. (2021) Ultrasound-guided paravertebral perineural glucocorticoid injection for signs of refractory cervical pain associated with foraminal intervertebral disk protrusion in four dogs. J Am Vet Med Assoc 258,9, 999-1006*

Nonpharmaceutical Approaches to Pain Management

This area is rapidly expanding, and the evidence base surrounding it is increasing, though sometimes with conflicting results. Physiotherapy input is widely sought to help improve function following spinal surgery.

Many of the techniques employed may have an analgesic effect.

- These include:
- TENS
- Massage
- Manipulation
- Exercise
- Acupuncture (VS only in UK)
- LASER

Drug monologues:

The following information provides quick clinical reference for the use of new or revisited systemic pharmacological options for use in chronic pain

Ketamine

Drug type:

- Ketamine is an analgesic and dissociative anaesthetic.
- Widely used in anaesthesia and acute pain management.
- Increasingly amount of research in people for chronic pain indications.

Mechanism of action:

- Ketamine acts on NMDA receptors as a predominant analgesic mechanism.

Indications:

- Anecdotally for chronic refractory pain.

Clinical use comments:

- Little evidence beyond anecdote.
- Ketamine has been used in conjunction with multiple analgesics.
- Ketamine can be used in dogs already receiving other NMDA antagonists (amantadine, memantine) and adverse effects from this are rarely seen.
- Ketamine continuous rate infusions for pain breakthrough where admission to hospital is required. E.g., septic arthritis in an OA patient.
- Ketamine subcutaneously is an option for outpatient cases with sub-optimal pain control.

Clinical side effects:

- Rare. The dose is low (0.5 mg/kg SC).
- Most owners report that the dog sleeps well after the injection.
- Any excitement can be controlled by low dose alpha-2-agonist administration.
- Low dose will have minimal effect on cardiac myocytes so can be used in cases with cardiac disease.

Potential dosing:

- Ketamine 0.5 mg/kg SC repeated PRN (often 7-14 days)

Costs and other considerations:

- Inexpensive as an outpatient

Useful links and further reading:

- https://www.zeropainphilosophy.com/post/subcutaneous-ketamine-for-analgesia
- https://www.cebm.ox.ac.uk/news/views/low-dose-ketamine-can-be-effective-in-reducing-post-operative-pain

Pentosan Polysulphate (Cartrophen)

Drug type

- Semi-synthetic polymer of pentose carbohydrates
- Disease modifying drug OA drug (DMOAD)

Mechanism of action:

- Binds to damaged cartilage.
- Stimulates production of new glycosaminoglycans.
- Inhibits proteolytic enzymes.

Indications:

- Licensed as a disease modifying drug

Clinical use comments:

- Manufacturer recommends monitoring PCV/TS
- Recommended to withdraw NSAIDS/steroids.
- Likelihood of a problem in a dog with no history of bleeding disorder receiving COX-2 selective drugs is low. Personally, cost of removing NSAIDS in terms of discomfort usually outweighs risk of continuing with them but advise the owner of this.

Clinical side effects:

- Do not use in septic arthritis.
- Potential to cause spontaneous bleeding due to heparin like action.
- Do not use in animals with bleeding disorders

Potential dosing:

- S/C: 3mg/kg q 5-7 days on 4 occasions.
- I/A: 10-20mg/joint (not septic joints).

Costs and other considerations:

- Trials and experience show that clinical response generally lasts between 3-12 months (following a full course of injections) and each patient should be assessed on an individual basis
- Each course of injections is 4 injections, with 5-7 days between each injection.

Useful links and further reading:

- https://caninearthritis.co.uk/cam-conversation-with-cam-hannah-capon-about-cartrophen-vet/

Cannabidiol

Drug type

- Cannabidiol - CBD
- Cannabinoid is an umbrella term covering Cannabidiol (CBD), Tetrahydrocannabinol (THC), Cannabinol (CBN) and many others.

Mechanism of action

- Endocannabinoids have a homeostatic role in the body achieving balance in systems e.g., descending pain inhibitory pathways. They are involved in motor coordination, memory, pain modulation, appetite, neuroprotection, and immunomodulation.
- Five endocannabinoids have been identified so far including anandamide and 2-arachidonoylglycerol. There are two types of G protein coupled cannabinoid receptors type 1 receptors (CB1R) and type 2 receptors (CB2R).
- CBD has an extremely low affinity and shows little agonist activity at the G protein-coupled endocannabinoid system receptors, CB1R and CB2R.
- CBD may exert clinical effects by modulating the endocannabinoid receptor system – it may be allosteric modulator of the endocannabinoid receptors, influencing compounds that bind to the receptors - it impacts multiple target molecules.

Indications

- Substantial number of human clinical trials investigating a range of pathologies.
- Three products with specific licenses in people:
  - Epidyolex is a pure CBD product with a trace of THC present as an impurity only, granted NICE approval for use on the NHS for two specific types of childhood epilepsy.
- Ongoing research into potential benefit in OA in dogs.

Clinical Use Comments

- CBD oils available on the high street may contain no cannabinoids at all; less than 50% of the stated CBD content; solvents or heavy metals at concentrations above that permitted in food stuffs. Some contain illegal levels of THC and another cannabidiol CBN.

Clinical side effects

- CBD is metabolized by cytochrome P450 enzymes, specifically CYP2C and CYP3A. This gives the potential for interactions with co-administered medicines.
- CBD may either reduce or prolong the effect of medicines – depending upon their pharmacokinetics.
  - These include anaesthetics and sedatives; certain antibiotics; anti- epileptic drugs; selective serotonin reuptake inhibitors (SSRIs); monoamine oxidase inhibitors (MAOIs); anti-arrhythmic medications; ageing and dementia drugs; cytotoxic drugs.
- Knowledge of these potential interactions is essential if CBD is to be prescribed.

Potential dosing

- Ingestion of oil results in a bioavailability of only 5-10% due to the first pass effect in the liver. Several authors suggest that the sublingual route may increase the bioavailability by bypassing the liver.
- From the available research we can conclude that CBD is most available if administered in oil after a meal.
- When dosing with cannabidiol the accepted protocol is to start low and go slow.

Costs and other considerations: IMPORTANT Law Applicable to the UK

- The legal situation regarding CBD for administration to animals is different to that regarding human use because of the VMD statement 2018.
- CBD as a food supplement can be sold in shops for people so long as no medicinal claims are made. It must not be available to purchase for animals anywhere.
- It can only be administered to an animal once it has been prescribed by a veterinary surgeon as an unlicensed medication.
- VMD statement on CBD published September 2018:
- "We consider that veterinary products containing Cannabidiol (CBD) are veterinary medicines and should be regulated as such. CBD products for use in animals now require a marketing authorisation before they can be sold or supplied in the UK. There are currently no CBD based products that have been granted a UK veterinary marketing authorisation."
- As there are currently no CBD products authorised in the UK for veterinary use, a veterinary surgeon may prescribe a legally obtained human CBD product under the provisions of the prescribing cascade. Administration of an unauthorised product containing CBD without a veterinary prescription is an offence under Regulation 8 of the VMR. Companies supplying CBD products for human use in line with the requirements of the Medicines and Healthcare products Regulatory Agency must not indicate or recommend their products for use on animals
- Vets who wish to prescribe CBD to a patient must take both the VMD statement and the cascade into consideration.
- The method of administration, quality and safety of the product and any potential drug interactions should be assessed

Useful links and further reading:

Menzies S & Clark L (2021) What is CBD, what can it do and why is it controversial? Vet Times. Parts I & II Vet Times CPD +
Wessmann A and BSAVA Scientific Committee (2021) Use of cannabidiol (CBD) in dogs and cats From: Scientific information sheets Use of cannabidiol (CBD) in dogs and cats | BSAVA Library
https://m.facebook.com/CAMarthritis/videos/220258939003839/ - Siobhan Menzies discussion with CAM founder Hannah Capon.
https://caninearthritis.co.uk/cam-conversation-with-elaine-mcnamara-about-the-highs-and-lows-of-cannabidiol-cbd-in-arthritic-dogs/

.

Pathophysiology of Pain: a short review

Federico Corletto, PhD, CertVA, Dipl ECVAA, FRCVS

Pain knowledge and research were revolutionised in 1965, when Melzack and Wall proposed the gate control theory of pain. They suggested that nociceptive and touch fibers were two separate entities, overcoming the "intensity theory" of pain, which synapse in different regions of the dorsal horn of the spinal cord, with a gate mechanism, located in the *substantia gelatinosa*, modulating transmission of sensory information to supraspinal structures. The gating mechanism is controlled by the relative activity of large and small fibers, with larger fibers inhibiting it, and small fibers controlling it. The gate would open when the overall signal reached a threshold, resulting in transmission of the nociceptive information. The activity of the gate was also affected by descending inhibitory pathways, originating supraspinally.
This simplistic theory explains well the events occurring in acute physiological pain, but has the enormous limitation of considering the nociceptive system an hard-wired entity, not taking into account neuroplasticity and its consequences. This theory cannot explain why and how hypersensitivity, a very common phenomenon, occurs. It does not take into account the complex control of pain by the cognitive state of an individual: catastrophising can increase perception of pain; hypnosis can modulate the "unpleasant" component of pain without affecting its intensity, placebo and nocebo are well known to treat or induce pain, without affecting the spinal cord mechanisms or the activity of nociceptors.

This short review will therefore focus on the events occurring at molecular and cellular level, leading to neuroplasticity, and therefore to neuropathic pain and chronic pain, in which spinal cord and brain structures undergo significant plasticity and alteration of their network dynamics, sometime in an unpredictable way. The molecular mechanisms involved in the activity of the most commonly used analgesic agents (opioids, alpha-2 agonists, NSAIDs) will not be mentioned.
The purpose of this review is to provide information that will be necessary to understand the pathophysiology of specific conditions, and the medical approach to chronic and neuropathic pain treatment. In this setting it is important to remember that while when a receptor or channel is identified it is the possible to target it specifically with agonists and antagonists, such channel may play a crucial role in other omeosthatic mechanisms, precluding its use as analgesic in a clinical setting. A typical example is represented by TRPV1, whose role in nociception is without doubt relevant, but use of agonists and antagonist has so far been shown to compromise also thermoregulation.

Anatomical overview

Nociception is the process detecting noxious (thermal, mechanical or chemical) stimuli by a population of specialised peripheral nerve fibers whose body is located in the dorsal root ganglion (DRG)- with the notable exception of trigeminal fibers whose body is located in the trigeminal ganglion. Nociceptors are free nerve endings (ie there is no dedicated "corpuscular sensing structure), and surprisingly we still have not identified structural differences from nociceptive and non nociceptive (normal sensation) nerve endings.
Nociceptive fiber can be:

- **myelinated Aδ** (medium diameter), are polymodal, mediating acute and well localised pain. Based on their threshold, they can be
    - o Type I: respond to mechanical stimuli and thermal stimuli above 50 C; they can decrease their threshold when tissues are injured (ie thermal hyperalgesia); normally they modulate first pinprick pain sensation.
    - o Type II: they respond to intense mechanical stimuli (high mechanical threshold), but have lower heat threshold (43 C); normally they modulate heat induced first pain sensation.
- **unmyelinated C** (small diameter), mediating poorly localised pain; most of them are polymodal. A proportion of the C fibers is made of so called "silent nociceptors", which are heat responsive and mechanically insensitive, but become mechanically sensitive after tissue injury, with NGF released in the "inflammatory soup" mediating the activation process. Interestingly, they also respond to some itch-inducing compounds, and express histamine receptors. Silent nociceptors contribute to mechanical hyperalgesia associated with inflammation.
  C nociceptors can be peptidergic or non-peptidergic, based on the the expression of neuropeptides (substance P, CGRP). The role in nociception of the non-peptidergic fibres, accounting for up to 50% of the C fibers, has not yet been fully understood, although they appear to be involved in developing inflammatory mechanical hypersensitivity.
  It should finally be pointed out that not all C fibers are nociceptors, some of them are involved in mediating the affective component of pleasant touch sensation. They respond very well to a slow caressing touch. This is very distinct from the light touch sensation mediated by Ab fibers.

Primary sensory neurons present “biochemical equivalence”, as they can send or receive information from either end. This is different from the prototypical neuron, in which axon and dendrite are two distinct entities. Primary afferent neurons, whose body is the DRG, can release neurotransmitters affecting peripheral local environment, and at the same time can “sense” neurotransmitters released by other cells in the laminae of the dorsal horn of the spinal cord. Peripheral released CGRP and substance P causes vasodilation and extravasation of proteins (neuroinflammation). Conversely, release of neurotransmitters or changes in local conditions in the DRG can affect sensitivity of the nociceptor. This allow targeting of both sites to treat pain.

Primary afferents project to the dorsal horn of the spinal cord, with a specific anatomical organisation. Aδ nociceptors project to the laminae I and V, while C nociceptors project to laminae I (mostly peptidergic) and II (non peptidergic). Aβ afferents project to the laminae III-V. Most noxious stimuli converge to lamina I, while non noxious stimulation converges to laminae III and IV, with lamina V receiving both noxious and non noxious afferents. Lamina V also receive inputs from C fibers via the second order WDR (Wide Dynamic Range) neurons. WDR neurons receive inputs from nociceptive and non-nociceptive sensitivity, cutaneous, muscular and visceral. They are thought to be the converging point of the visceral and somatic pain pathways, explaining referred and radiating pain. Due to their peculiar organisation, WDR neurons present not only excitatory receptive fields, but also inhibitory ones, generally located around the excitatory field. Mechanical stimuli, particularly those of low intensity, applied to the inhibitory filed of a WDR neuron will inhibit its activity. In practical terms, application of a nociceptive stimulus in a specific area will stimulate the receptive field of some WDR neurons, and at the same time the overlapping inhibitory fields of others, with the final output depending on the overall balance. For example, non noxious stimulation applied to a large body area may cause sufficient activation of the inhibitory fields of some WDR neurons to “mask” the noxious activation of adjacent WDR neurons. This explains the analgesia caused by rubbing or TENS, and fits well with the gate theory of pain. Similarly, it explains how nerve damage may affect the balance between inhibitory and receptive fields of adjacent WDR neurons, resulting in erroneous interpretation of non nociceptive signals or even spontaneous firing of some WDR neurons. Interestingly, WDR neurons are also inhibited by nociceptive stimulation of distant areas of the body, with a mechanism that involves activation of the reticular formation. While probably the physiological reason for this inhibition is to make sure the CNS focus on the injured area, removing the “background noise” caused by discharging of other WDR neurons, the important implication is that a noxious stimulus can decrease or completely abolish pain arising from another part of the body, activating this descending noxious inhibitory control (DNIC). Finally, WDR neurons play a crucial role in establishing “wind up” after their continuous exposure to nociceptive inputs, which activates the NMDA receptor (see later).

Neurons in the laminae I and V project information from the dorsal horn of the spinal cord to supraspinal structures, where they activate descending inhibitory pathways at the level of the periaqueductal grey and rostral ventral medulla and reach the structures involved in processing information to create the sensation of pain in all its component (the somatosensory cortex, the cingulate cortex and the insular cortex).

Molecular mechanism of transduction

The mechanisms underpinning transduction of a variety of noxious stimuli have been studied in detail, providing useful information to understand how the nociceptive system works and identifying possible therapeutic targets. Knock-out animal models are commonly used to characterise the role of a specific channel or receptor in nociception, comparing the different behavioural response of the wild population and those of the receptor/channel deficient animal.
The Transient Receptor Potential (TRP) ion channel family and its role in cold, heat, inflammation and pain sensation has been investigated in depth. Noxious heat and cold are detected by TRPV1 and TRPA1/TRPM8 respectively.
TRPV1 is expressed by most nociceptors sensitive to heat, can be stimulated by capsaicin (creating a heat sensation) and anandamide (endogenous CB1 agonist); its response is affected by the chemical mediators of the inflammatory soup, explaining the thermal hyperalgesia observed after a tissue injury. TRPV1 knock out mice not only show reduced (but not absent, due to the activity of other TRPV channels) response to heat, but also reduced or absent thermal hyperalgesia after tissue injury, suggesting that TRPV1 plays a vital role in converging chemical and thermal stimuli.
TRPM8 and TRPA1 are channels sensitive to cold and menthol and while the former appears to be involved in cold induced pain, the latter seems to be involved prevalently in cold sensitivity. TRPA1 is also activated by chemicals capable of covalently binding to thiol groups and also by reactive oxygen species. Among these, worth of mention are acrolein (present in tear gas and smoke), formalin vapours, thiosulfinates (garlic, onion), isothiocyanates (mustard), and isoflurane. Activation of TRPA1 by these compounds explain the pain and inflammation they are able to induce.
Surprisingly, while there is general consensus on the fibres involved in mechanoception (Aδ and C for pain, Aβ for normal vibration and light pressure) there is no general consensus on the specific mechanism of transduction. The existence of a mechanosensitive channel opened by pressure has been postulated, but most studies have failed to identify conclusively the identity of such channel, hampering attempts to target it therapeutically. Acid Sensitive Ion Channels (ASIC) have been identified as pressure transducers in *C. elegans,* but studies in ASIC-deficient mice have unfortunately failed to demonstrate impairment of mechanoception. Conversely, ASICs respond to acidification, and their role in pain induced by peripheral inflammation, bone cancer and ischaemic pain has been well demonstrated. ASIC3 channels are expressed in fibers innervating the cardiac and skeletal muscle, and are considered crucial to transduce cardiac or muscoloscheletal pain.
The ability of TRPV2 to respond to stretch (osmotic) has made it an interesting candidate for mechanotransduction. It is expressed in Aδ fibres responding to both thermal and mechanical stimuli, but despite TRPV2 deficient mice showing compromised blood pressure, voiding, they maintain normal mechanoception.
Other possible mechanotransducer investigated without success are the TRPA1 channel and the potassium channel subfamily K.

Pain signal conduction

The most known player in generation and transmission of the action potential generated peripherally in the nociceptor is without doubt the family of the voltage gated sodium channels (Nav). Loss of function of Nav 1.7 causes inability to detect noxious stimuli, and an increase in its function has been linked to paroxysmal spontaneous pain in humans. Interestingly, while mice not expressing of Nav1.7 in C nociceptosr show, as expected, reduced acute nociception and inflammatory mechanical and thermal hypersensitivity, they retain pain induced by nerve injury, suggesting that the spontaneous ectopic discharge induced by this condition is involving a different Nav. The link between Nav and inflammatory pain make then a suitable target for analgesics, and the effect of serotonin and NAdr reuptake inhibitors on neuropathic pain is likely to depend, at least in part, on their effect on voltage gated sodium channels.
At the other end of the nociceptor, voltage gated calcium channels (Cav) play a fundamental role in releasing neurotransmitter at synaptic level. N and T Calcium channels are expressed in the presynaptic terminal of nociceptive C fibers, and are upregulated by nerve injury or metabolic neuropathies. If this does not appear to be immediately relevant, consider that intrathecal ziconotide, a N type calcium channel blocker, has been investigated as possible treatment for cancer pain. Further, consider that the α2δ subunit of the calcium channel, controlling its kinetic of activation, is upregulated after nerve injury and selectively targeted by gabapentinoids.

From nociceptive to neuropathic pain

Now that we have identified the key players in the nociceptive process, the next step is to investigate how they contribute to developing and maintaining pathological pain.
Neuropathic pain may result peripherally from a damage to nerve fibers, causing spontaneous discharge, alterations in conduction and release of neurotransmitters.
Peripheral sensitisation is a process leading to changes in the local environment of the nerve fibers. It is driven by non neural cells (inflammatory response with accumulation of leukocytes and platelets), releasing molecules like cytokines (IL-1β, IL-6, TNFα), prostaglandins, growth factors, substance P, VGEF, CGRP, ATP, protons, just to mention a few, producing the so called “inflammatory soup”. Nociceptors present receptor to recognise most of these molecules, and this interaction increases excitability, resulting in mechanical and thermal hyperalgesia. NGF, in particular, is recognised by a specific receptor (TrKA) present on peptidergic C nociceptors; binding produces hypersensitivity to heat and mechanical stimuli, mediated by activation of MAPK (mitogen activated protein kinase) and PIP3 (phosphatoinositide-3-kinase), resulting in increased expression of target proteins, such as TRPV1. After internalization of the NGF-TrKA complex, NGF is transported in endosomes to the DRG, where it causes increased transcription and expression of pronociceptive proteins (substance P, TRPV1, Nav). Strategic targeting of TNF and NGF with antibodies has been used to treat pain resulting from immunomediated disease and osteoarthritis, respectively, without affecting normal sensation.

The central nervous system is the location for what is considered the most crucial event in starting the cascade of events leading to pathological pain: central sensitisation. Central sensitisation is the process leading to increased responsiveness of nociceptors in the central nervous system, enhancing nociceptive transmission. Three key players have been identified for which there is general consensus on their crucial role in establishing central sensitisation: the NMDA receptor, loss of tonic inhibition, and glial-neuronal interaction.
The increased nociceptive input form persisting stimulation of nociceptors results in increased release of glutamate at the first synapsis. Normally glutamate binds to the AMPA and Kainate receptors, but the increased neurotransmitter release depolarises postsynaptic neurons, activating silent NMDA receptors (NMDAR). Activation of the NMDAR increases intracellular calcium, facilitating synaptic transmission. Substance P, released with glutamate by peptidergic C nocicpetors, binds to it NK1 receptor, also contributing to increased calcium influx and central sensitisation. The resulting increase in cytosolic calcium activates other signalling pathways (via intracellular kinases), increasing release of important factors such as CGRP and BDNF. Targeting directly NK1 receptor administering SP-saporin intrathecally has resulted in a time-dependent anti nociceptive effect in dogs with spontaneous osteosarcoma, confirming the role of SP as powerfulmodulator of nociception. The duration of the increased synaptic transmission initiated by NMDAR activation may, under certain conditions, outlast the duration of the stimulus that caused it, resulting in genuine Long Term Potentiation. Central sensitisation results in facilitation of transmission of the nociceptive stimulus form the first to the second order neuron, but also contributes to creating an area of allodynia surrounding the primary injury, due to converging of normal and nociceptive stimuli in WDR neurons in the dorsal horn of the spinal cord.
Loss of GABAergic and glycinergic inhibition by interneurons in the dorsal horn of the spinal cord is a well known mechanism to increase pain perception, already described by Malzack and Wall. While it was believed that the loss of inhibition was caused to apoptosis of inhibitory interneurons, more recent studies suggest that the GABAerigc and glycinergic activity of such neuron is maintained, and it is the response of nocicpetors to be affected. According to this theory, peripheral nerve injury downregulates the K/Cl cotransporter (KCC2), resulting in a shift of the chloride gradient, such that GABAergic stimulation results in depolarization of the neuron, instead of hyperpolarization. The exact mechanism, which will be explained later, involves activation of the microglia. It is interesting to point out that normal sensation, modulated by Aβ fibres, converges on these inhibitory interneurons, normally inhibiting nociceptive discharge. An effect of reversal of GABAergic inhibition on secondary neurons is that stimulation of such inhibitory neurons by Aβ fibers will result in stimulation of nociception, instead of its inhibition, resulting in allodynia. At the same time, spinal release of PGE2 stimulates the prostaglandin EP2 receptor (do not get excited- grapiprant is specific for EP4 receptor) on excitatory interneurons and projection neurons, causing phosphorylation of a subunit of the glycine receptor, thus making the neuron less sensitive to glycinergic inhibition.
Finally, microglia seems to play a fundamental role in establishing the central sensitisation and leading to neuropathic pain. Injured nerves release Colony Stimulating Factor 1 (CSF1) and ATP in the dorsal horn of the spinal cord. The resident microglia detects such molecules that bind to specific receptors (CSF1R and P2 purinergic, respectively) and within hours migrates and accumulate in proximity of the termination zone of the injured nerve, showing a phenotype change (from long branching “sensing” to plump “active” with short processes). The activated microglia releases a cohort of mediators, including TNF-α, ILs, and BDNF, triggering a series of events, previously outlined, leading to central sensitisation and LTP. TNF, for example, increases both NMDA and AMPA response to glutamate, while IL-1β contributes to decreasing GABA and glycine mediated inhibition. It is

interesting to point out that nociception resulting from inflammatory tissue injury is not sufficient to activate microglia, suggesting that it is the actual damage to the fibre, not its activation that triggers this response.
Microglia activation in neuropathic pain is not limited to the dorsal horn of the spinal cord. Experimental studies have demonstrated microgliosis in the thalamus, amygdala, nucleus accumbens, periaqueductal grey, and ventral tegmental area after peripheral nerve injury. It is not clear how this activation occurrs, but targeting microglia in the ventral tegmental area restored normal GABAerigc inhibition in interneurons in this location. PET studies in humans, using markers of microglia/astroglia activation has demonstrated increased expression in some brain regions of patients with peripheral nerve injury or chronic back pain, supporting a clinical correlate for animal studies.
Microglia may also play an important role in opioid tolerance: microglia activation in the dorsal horn of the spinal cord and in some brain regions has been demonstrated in chronically opioid treated rodents; interfering with microglia has been shown to reduce tolerance and opioid induced hyperalgesia in these animal models.
While microglia plays a fundamental role in developing central sensitisation, it is unlikely that it is maintaining neuropathic pain. Animal models have shown that microgliosis and microglia activation subside a few weeks after the initial injury, when neuropathic pain still persists. Further, direct microglia stimulation in normal conditions results in hypersensitivity, but not neuropathic pain. The time course of astrogliosis (persisting months) may suggest that it may be this cell type, capable of modifying the local environment in the spinal cord, that maintains central sensitisation and persistent pain. Pharmacological inhibition of astrocytes resulted in reduction of neuropathic pain intensity and duration, although the toxins used were not very specific. The role of astrocytes in sustaining pain is supported also by animal studies showing that their stimulation results in mechanical allodynia. At molecular level peripheral nerve injury causes increase JNK signalling in astrocytes, initiating transcription of inflammatory mediators able to support central sensitisation, so it is plausible that these cells may play an active role in maintaining the spinal cord changes underpinning neuropathic and chronic pain, becoming a possible target for therapeutic interventions.

References available on request.

Pain and Chiari-like malformation: pathophysiological mechanisms and treatment options

Clare Rusbridge, BVMS, PhD, Dipl ECVN, FRCVS, RCVS and European Specialist in Veterinary

Introduction

Chiari-like malformation (CM) is a complex developmental condition of the skull and craniocervical vertebrae characterized by a conformational change and overcrowding of the brain and cervical spinal cord, particularly at the craniospinal junction. Obstruction to cerebrospinal fluid (CSF) channels can result in pain and a tendency for fluid cavitation of the spinal cord termed syringomyelia (SM). The cavities (syrinx or syringes) contain CSF like fluid which can expand and can cause irreversible damage to the spinal cord resulting in clinical signs of pain and neurological deficits.

Pathogenesis

The fundamental abnormality is brachycephaly with skull bone insufficiency as a consequence of early fusion of skull sutures (craniosynostosis). In addition, dogs with CM have reduction in facial bony tissue with a loss of the frontal sinus and short muzzle. This given them a more defined "stop". The "stop" is the pronounced angle between the nasal/maxilla bones and the frontal bones which is a defining feature of domesticated dogs and absent in wolves. The skull insufficiency results in brain overcrowding with secondary hindbrain herniation. Importantly, some predisposed breeds such as the Cavalier King Charles spaniel (CKCS) also have comparatively big brains – their brain is similar in size to a dog twice the weight. For review see references [1,2]. The overcrowding of the nervous tissue can result in 2 pathologies - 1) a pain syndrome (Chiari-like malformation pain on CM-P) and syringomyelia (SM). Syringomyelia describes fluid filled cavitation of the spinal cord (syrinx or syringes). Biochemically the fluid is very similar but is not identical to cerebrospinal fluid (CSF).

It is well established that brachycephalic dogs and cats are predisposed to cerebrospinal fluid (CSF) circulation disorders, such as ventriculomegaly, hydrocephalus, quadrigeminal cistern expansion, Chiari-like malformation, and syringomyelia. The reasons for this predisposition is multifactorial (for review see [3]) however likely pivotal factors are a combination of reduced CSF absorption and obstruction of CSF movement out of the ventricular system (ventriculomegaly and hydrocephalous) and between the cranial and spinal CSF compartments (syringomyelia).

CSF is produced by nervous tissue (60%) and the choroid plexus within the ventricles (40%). The primary site of CSF absorption is the lymphatics associated with the olfactory mucosa and the cranial base. It is hypothesized that a reduction in surface area of these regions in brachycephalic dogs impairs absorption[3,4]. Dogs with CM also have overcrowding at the junction between the cranial and spinal CSF compartment due to small volume caudal cranial fossa with flattened supraoccipital bone. The craniocervical vertebrae are closer or even invaginated into the skull reducing the volume of the craniospinal junction and the cisterna magnum.

SM associated with CM is predisposed by two morphological phenotypes (or combination of); the first by more extreme brachycephaly, and the second by more extreme craniocervical junction deformation [5,6]. Other factors likely important in the development of SM are reduced CSF absorption though nasal lymphatics [2,3], reduced venous drainage [3,7], altered neuroparenchymal compliance and conformation of the spinal canal and cord [8,9] The pathogenesis of spinal cord fluid cavitation secondary to CSF channel obstruction is debated; the most accepted theory is that CSF in the subarachnoid space fluid enters the spinal perivascular space and then the spinal cord because of a mismatch in timing between the arterial pulse peak pressure and CSF pulse peak pressure [10].

Predisposed toy brachycephalic breeds have a high prevalence of CM, but it is not always clinically relevant, and the spectrum covers 4 variations.

1. **CM-N** – Clinically normal dogs with an MRI appearance of CM but with no behavioural or clinical signs of pain.
2. **CM-P** – Dog has behavioural and clinical signs of pain with an MRI appearance of CM. SM may or may not be present. Compared to clinically normal dogs with CM (CM-N), dogs with CM-P have more extreme brachycephaly i.e. shorter cranial base, more craniofacial hypoplasia with greater neuroparenchyma disproportion and overcrowding 6
3. **SM-M** – Dog has syringomyelia but no syringomyelia specific signs. Typically, the syrinx is symmetrical, central and has a maximum transverse diameter of less than 4 mm (for CKCS – other breeds not quantified). Dog can be CM-N or have CM-P
4. **SM-S** – Dog has syringomyelia specific signs relating to spinal cord damage (phantom scratching, scoliosis, weakness or ataxia). The syringomyelia typically has a maximum transverse diameter greater than 4 mm and the localisation of the syrinx is consistent with the neuro-localisation for example thoracic limb weakness is associated with a large syrinx in the C6-T2 spinal segments. Dog can be CM-N or have CM-P.

Clinical signs

CM-P

Pain in CM-P is thought to relate to failure to equilibrate intracranial pressure due to obstruction of CSF pathways. Intracranial pressure is affected by the systolic pulse, venous drainage, the balance between CSF production and absorption and micro-gravitational effects for example when being lifted rapidly or with head position. Classically in humans, pain in CM is exacerbated by Valsalva, a brief increase in intrathoracic pressure, for example when coughing or with abdominal straining.

Signs of CM-P reported by owner or observed on clinical examination	
Common signs	**Signs described by owner**
Postural or Valsalva pain	Yelping described by owner as “out of nowhere”, spontaneous or when moving, whilst lying resting or asleep, when lifted under sternum or on rising. Refusing / hesitating / difficulty or vocalization when jumping or doing stairs. Change in greeting behaviour - yelping during or refusal to get up and greet owner. Sleeping elevated or unusual head posture (rule out Brachycephalic Obstructive Airway Syndrome as alternative explanation) Abnormal awake head / neck posture Yelping whilst straining to defecate.
Head pain	Head or ears scratching or rubbing (exclude skin and ear disease) Yelping whilst scratching head or ears Aversion to touch or grooming of the head and ears but tolerates touch or grooming elsewhere. Owner describes pain face - a grimacing facial expression suggesting pain Squinting / avoiding light (keratoconjunctivitis sicca ruled out)
Spinal pain	Hyperaesthetic to palpation in the cervical, thoracolumbar or caudal lumbar / lumbosacral region
Activity change	Described as exercise intolerant, unwilling to exercise, lethargic or sleeping more.
Sleep disruption	Described as being restless in the night or having disturbed sleep (rule out Brachycephalic Obstructive Airway Syndrome as alternative explanation)
Change in behaviour or demeanour	Becoming more timid, anxious, withdrawn or having uncharacteristic belligerence to other dogs / people.
Forelimb hypermetria	Subtle increased proximal joint movement giving a tendency to overshoot.
Flank, sternum or limb sensitivity	Owner reports that the dog has an aversion to touch of this body part and tolerates touch or grooming elsewhere. Licking paws without evidence of skin or orthopaedic disease.

SM specific signs are associated with wide syringes and include phantom scratching, scoliosis and sensory and motor signs (SM-S) [11]. The neurolocalisation is consistent with the syrinx location. Gait disturbances and paresis can be surprisingly mild even with wide SM from C2 to the lumbar segments. Typically, the thoracic limbs are weaker than the pelvic limbs reflecting central spinal cord damage. Other differentials should be considered if there is a non-ambulatory tetraparesis or severe paraparesis for example intervertebral disc disease, degenerative myelopathy or constrictive myelopathy. Likewise SM does not provide an explanation for diseases with a brain or cranial nerve neurolocalisation for example epilepsy, flycatching, facial nerve paralysis and vestibular disease. These unrelated conditions should be managed as separate diseases.

Clinical signs of clinically relevant syringomyelia (SM-S; maximum transverse width equal to or greater than four millimetres in CKCS)	
Clinical signs	**Details and neuro-localisation**
Phantom Scratching	Rhythmic scratching action towards neck, but not contacting the skin, together with a curvature of the body and neck towards the foot. Induced by light rubbing to the neck or ear region and triggered by excitement, anxiety and exercise. Associated with a large mid-cervical syringe extending to the superficial dorsal horn ipsilateral to the scratching.
Scoliosis / cervicothoracic torticollis	Corkscrew deviation of neck associated with a large mid-cervical syringe extending to the superficial dorsal horn ipsilateral to lateral shoulder deviation and contralateral to the ventral head tilt.
Weakness	Thoracic limb and paraspinal muscle weakness associated with a large cervicothoracic syringe.
Thoracic limb muscle atrophy	Thoracic limb muscle atrophy associated with a large C5-T2 spinal segment syringe.
Postural responses decreased	As demonstrated by “hopping”, “hemi-walking” and “correction of knuckled-over paw” testing. Typically associated with a large C5-T2 spinal segment syringe. Thoracic limbs typically more affected than pelvic limbs. If severe paraparesis consider other differentials of spinal disease.

Diagnosis

Dogs can be presented at any age although most dogs with clinically relevant disease will show signs of CM-P or SM-S before four years of age.

MRI remains the only diagnostic test to support suspicion of CM-P and SM. When MRI is performed in predisposed breeds, CM is commonly reported, and SM can be an incidental finding. Care must be taken not to over diagnose; MRI results should be related to historical and clinical findings. For more details of MRI protocols to investigate CM and SM see[12]. A minimal diagnostic protocol for CM and SM should include sagittal imaging of brain and spinal cord to the caudal extent of the presyrinx / syrinx. At least one region of the spinal cord, typically a sagittal sequence of the cervical region, should have static T1-weighted and T2-weighted sequences to determine that the signal characteristics of the fluid filled cavity are identical to CSF and eliminate other causes of hyperintensity on T2-weighted images for example oedema associated with meningoencephalomyelitis of unknown origin. Transverse imaging should be obtained through the widest parts of the syringes in the C1-C5, C6-T2, T3-L3 and L4-S3 spinal segments to determine the maximum transverse width and position within the spinal cord including dorsal horn involvement. These findings are correlated with the neurolocalisation. Paramagnetic contrast enhancement is indicated if (i) there is evidence of a mass as intramedullary tumours can be cystic and should be distinguished from SM; (ii) if the cause of the CSF channel obstruction is not apparent; (iii) there is a presyrinx and need to eliminate other causes of spinal cord oedema.

Diagnosis of CM-P

CM-P is a diagnosis of exclusion suggested in a predisposed breed or type of dog that is presented with signs of postural and head pain. MRI features are listed below

Craniofacial and MRI features of CM-P	
Morphological change	Craniofacial and MRI features
Craniofacial hypoplasia	"Forehead" formed by the frontal bone overlying the brain with absent or minuscule frontal sinuses - Muzzle which is short in height and length Well-defined or indented stop - junction between nasal and maxilla forming an angle rather than a slope.
Rostrotentorial overcrowding	Rostral forebrain flattening - the forebrain shape changes from a rugby to a soccer football shape. Small, ventrally orientated olfactory bulbs Increased cranium height, especially in the occipital region
Reduction / obstruction of CSF channels	Reduction in cranial and spinal subarachnoid space Ventriculomegaly of all ventricles and cisterns, except the cisterna magna which is reduced
Skull base shortening	Shortening of the basicranium especially the presphenoid bone
Caudotentorial overcrowding	Rostrotentorial neuroparenchyma is displaced dorsocaudally reducing the functional caudotentorial space Small caudal cranial fossa Supraoccipital bone short and flat Opisthion (dorsal foramen magnum) rostral with respect to the occipital crest
Cerebellar vermal indentation and foramen magnum herniation	Cerebellum loses its rounded shape and is displaced into the foramen magnu*m*

Diagnosis of clinically relevant SM (SM-S)

The finding of SM implies a fluid filled cavity related to disturbance of CSF flow, spinal cord tethering or intramedullary tumour. The cause of SM should be determined[12]. SM is not an appropriate description for myelomalacia or cystic lesions. Non-inflammatory spinal cord oedema, as distinct from cavities containing free fluid, is referred to as presyrinx (presyringomyelia). Presyrinx most commonly affects the dorsal and ventral columns of the spinal cord and can eventually progress to SM. CNS inflammatory diseases can also cause spinal cord oedema and is an important differential for this change. As SM can be an incidental finding an assessment should be made as to whether the location and severity of the syrinx would account for the signs.

MRI features of SM associated with CM	
MRI feature	**Notes**
More extreme brachycephaly as for CM-P	As previous
Craniovertebral junction malformation.	Atlas is closer to the skull with acute angulation of the odontoid peg relative to the skull base (cervical flexure)
Craniospinal junction kinking or elevation	Rostrocaudal shortening and reduction in volume of the craniovertebral junction results in a concertina like flexure of nervous tissue at the junction between skull and spine.
Syrinx maximum transverse width	Measured from the widest part of the syrinx on transverse images Myelopathic signs in CKCS are associated with a syrinx transverse width of four millimetres or more (SM-S)
Syrinx fluid characteristics	Fluid signal-void sign within syrinx cavity indicates pulsatile or turbulent flow and a sign of an "active" and filling syrinx more likely to expand. Fluid signal-void sign is appreciated on T2W images as "dark" hypointense regions within the "white" hyperintense syringe
Syrinx position in spinal cord and neurological signs	Phantom scratching - mid cervical syrinx and extension of the syrinx into the superficial dorsal horn (2 or 10 o'clock position on the outer rim of the spinal cord) ipsilateral to the scratching. Rubbing the dermatome associated with that spinal cord segment induces the scratching action. Cervicotorticollis / scoliosis - mid cervical syrinx and extension of the syrinx into the superficial dorsal horn (edge of the spinal cord in the 2 or 10 o'clock position) contralateral to the head tilt/ twist. Proprioceptive deficits – wide syrinx that involves the dorsal funiculus Thoracic limb paresis – wide cervicothoracic junction syrinx that extends into ventral horn Thoracic lordosis – wide thoracic syrinx
Spinal cord outline	Spinal cord outline expanded by the syrinx is filling actively and more likely clinically relevant. A quiescent syrinx is centrally located, elliptical on sagittal images and symmetrical, usually circular on transverse images and results in little or no change to the outline of the spinal cord.

Other diagnostic tests

CSF analysis should be performed if there is a suspicion of CNS inflammatory disease particularly if 1) C-reactive protein is elevated 2) there is spinal cord oedema (presyrinx) rather than distant cavities 3) marked pain especially if multifocal or induced on cervical ventroflexion (atlantoaxial joint normal). However, CM and SM can be associated with elevated CSF protein due to stagnation of flow (Froin's syndrome) and cells counts can be marginally elevated with neutrophils present [13,14].

Prognosis

Although syrinx width can increase over time, the rate of increase is not constant. Many syringes rapidly expand within months (or even days) and then remain remarkably unchanged over years having achieved a hydrodynamic equilibrium. Clinical signs will progress in approximately 75% of dogs and approximately 15% will be euthanised because of CM-P and SM-S [15,16]. Despite progressive signs, many dogs with signs of pain and phantom scratching respond to medical management and are considered by their owners to have an acceptable quality of life. Dogs that are presented with SM-S before three years of age have a poorer prognosis and are more likely to develop severe weakness which is more difficult to treat. Cervicotorticollis can slowly improve despite persistence of the syrinx.

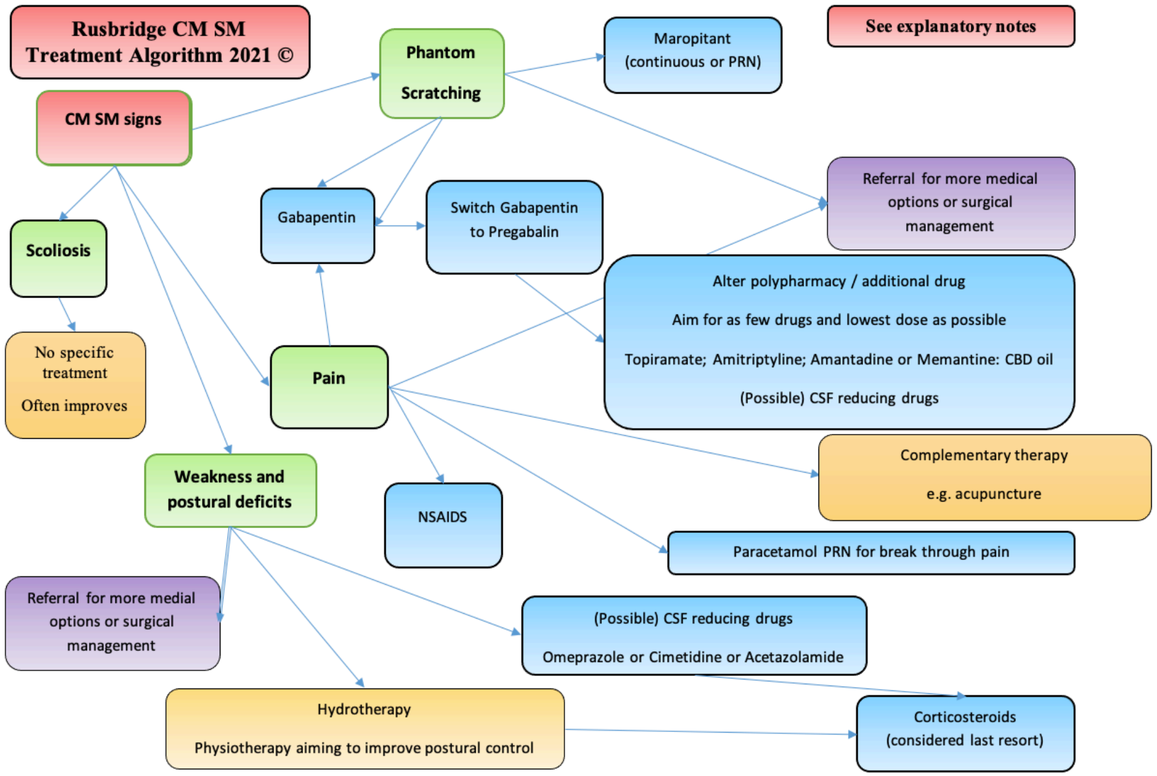
Medical management of CM-P and SM-S

A possible treatment algorithm is detailed below [15,17,18]. If an animal remains in pain, then other adjuvant analgesics, acupuncture, physical and physiotherapy may be useful. Anecdotally, a positive response to antacids such as cimetidine or omeprazole is reported. The principle is that that these drugs reduce CSF production thus reducing the driving force contributing to CM-P and SM however there is poor evidence that these drugs achieve a therapeutic choroid plexus concentration or effect CSF production[19,20]. Exercise should be encouraged, and excessive weight

gain discouraged. Hydrotherapy can be useful for some patients especially those with weakness or proprioceptive deficits. NK-1R antagonists such as Maropitant can be useful in short term to reduce phantom scratching.

Surgical management

There are three recognised surgical options for management of CM-P and SM-S: Craniocervical decompression surgery; ventricular to peritoneal shunting and syringo to pleural or subarachnoid shunting. Although good clinical improvement is reported, no surgical series has provided MRI evidence of sustained and substantial postoperative syringe collapse. If the postoperative MRI reveals a syrinx which has expanded the spinal cord outline, then there is active syrinx filling. Documenting that syrinx is static is not proof of surgical efficacy as many syringes achieve a hydrodynamic equilibrium. Likewise, surgical efficacy is not proved by stabilisation or improvement of clinical signs as this can occur with medical management. As the syrinx is likely to persist, surgery is more clearly indicated and most likely to be considered successful in dogs with CM-P (with or without SM) that have responded incompletely or not at all to medical management. Those dogs generally have a reduction in medication requirement and number of "bad days"



Explanatory notes - Unlicensed drugs used in the medical management of CM-Pain and SM-S

Drug	Dose
Analgesics	
NSAIDS	As per data sheet
Paracetamol (Acetamino-phen)	10mg/kg PRN up to TID (NOT CATS)
Adjuvant analgesics	
Gabapentin	10-20mg/kg BID / TID
Pregabalin	5-10mg/kg BID / TID.
Topiramate	10mg/kg TID (DOG) 2.5-10mg/kg BID (CAT)
Amantadine	3-5mg/kg PO SID
Memantine	0.3 – 1 mg/kg BID
Amitriptyline	0.25 – 2 mg/kg PO SID / BID
NK-1R antagonists (phantom scratching -unlicenced)	
Maropitant	2mg/kg PO SID – long term use not studied. Currently advised for "bad scratching days" up to 14 days in duration
(Possible) CSF reducing drugs	
Omeprazole	0.5-1.5mg/kg PO SID / BID
Cimetidine	5-7mg/kg PO TID
Acetazolamide	4-8 mg/kg SID
Corticosteroids	
Prednisone / Prednisolone / methylprednisolone	0.5mg/kg PO SID then decrease to lowest possible ideally alternate day dose that controls signs
Cannabinoids	
Cannabidiol (CBD oil / hemp extract)	2mg/kg BID

PRN - pro re nata (as needed), PO – per os (by mouth); SID – once daily, BID – twice daily, TID- three times daily.

Important points

- None of drugs listed above are licensed for veterinary medicine (with exception of NSAIDs and cimetidine).
- Doses are that used by author. Unless otherwise indicated start at the low end of the dose range and make increases based on effect and absence of adverse effects.
- All drugs should be prescribed by a veterinary surgeon who should refer to a formulary for drug adverse effects / drug interactions / titration and tapering details.
- Effect assessed over a 2 to 4-week period except amantadine, memantine and amitriptyline which require at least 4 weeks to assess effectiveness.
- Assess haematology and biochemistry before starting drugs and reassess at a minimum annually for animal receiving long term medication.
- Gabapentin and pregabalin are Schedule 3 controlled drugs under the Misuse of Drugs Regulations 2001, and Class C of the Misuse of Drugs Act 1971.
- The effect of omeprazole and cimetidine on CSF production is unproven, the benefit anecdotal and recently disputed by recent studies 19.

- Dose of CBD oil is based on the only published canine study21 that assessed CBD oil for pain associated with osteoarthritis. Most commercial preparations do not contain enough compound to be able to achieve this dose easily. The UK Veterinary Medicine Directorate considers that veterinary products containing cannabidiol are veterinary medicines and therefore can only be administered with a veterinary prescription.

Genetic factors and breeding advice

CM is a complex trait and the tendency for SM involves additional genetic factors [22-24]. Although there is moderately high heritability, the late onset nature means that screening for the disorder is challenging. Ideally predisposed breeds would have MRI screening from 12 months at age (before breeding) and after 5 years old (after breeding). Breed-wide screening and contribution to an estimated breeding value scheme could then be used to predict the risk of SM in descendants. Many European Kennel Clubs enforce or recommend screening of predisposed breeds and breeding according to guidelines [25]. However screening for CM-P is not yet available and because of the complexity of the disorder is likely to require a machine leaning solution to determine an objective measure using an simple artificial intelligence tool [26].

Further reading list and references

1. Rusbridge C. New considerations about Chiari-like malformation, syringomyelia and their management. In Practice 2020;42:252-267.
2. Knowler SP, Galea GL, Rusbridge C. Morphogenesis of Canine Chiari Malformation and Secondary Syringomyelia: Disorders of Cerebrospinal Fluid Circulation. Frontiers in Veterinary Science 2018;5.
3. Rusbridge C, Knowler P. The Need for Head Space: Brachycephaly and Cerebrospinal Fluid Disorders. Life 2021;11:139.
4. Mollanji R, Bozanovic-Sosic R, Silver I, et al. Intracranial pressure accommodation is impaired by blocking pathways leading to extracranial lymphatics. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 2001;280:R1573-R1581.
5. Knowler SP, Kiviranta AM, McFadyen AK, et al. Craniometric Analysis of the Hindbrain and Craniocervical Junction of Chihuahua, Affenpinscher and Cavalier King Charles Spaniel Dogs With and Without Syringomyelia Secondary to Chiari-Like Malformation. PloS one 2017;12:e0169898.
6. Knowler SP, Cross C, Griffiths S, et al. Use of Morphometric Mapping to Characterise Symptomatic Chiari-Like Malformation, Secondary Syringomyelia and Associated Brachycephaly in the Cavalier King Charles Spaniel. PloS one 2017;12:e0170315.
7. Fenn J, Schmidt MJ, Simpson H, et al. Venous sinus volume in the caudal cranial fossa in Cavalier King Charles spaniels with syringomyelia. Vet J 2013;197:896-897.
8. Cirovic S, Lloyd R, Jovanovik J, et al. Computer simulation of syringomyelia in dogs. BMC veterinary research 2018;14:82.
9. Sparks CR, Robertson I, Olby NJ. Morphometric analysis of spinal cord termination in Cavalier King Charles Spaniels. Journal of Veterinary Internal Medicine 2019;33:717-725.
10. Stoodley M. The Filling Mechanism. In: Flint G, Rusbridge C, eds. Syringomyelia: A Disorder of CSF Circulation. Berlin, Heidelberg: Springer Berlin Heidelberg; 2014:87-101.
11. Rusbridge C, McFadyen AK, Knower SP. Behavioral and clinical signs of Chiari-like malformation-associated pain and syringomyelia in Cavalier King Charles spaniels. Journal of Veterinary Internal Medicine 2019;33:2138-2150.
12. Rusbridge C, Stringer F, Knowler SP. Clinical Application of Diagnostic Imaging of Chiari-Like Malformation and Syringomyelia. Frontiers in Veterinary Science 2018;5.
13. Whittaker DE, English K, McGonnell IM, et al. Evaluation of cerebrospinal fluid in Cavalier King Charles Spaniel dogs diagnosed with Chiari-like malformation with or without concurrent syringomyelia. Journal of veterinary diagnostic investigation : official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc 2011;23:302-307.
14. Freeman AC, Platt SR, Kent M, et al. Chiari-Like Malformation and Syringomyelia in American Brussels Griffon Dogs. Journal of Veterinary Internal Medicine 2014;28:1551-1559.
15. Plessas IN, Rusbridge C, Driver CJ, et al. Long-term outcome of Cavalier King Charles spaniel dogs with clinical signs associated with Chiari-like malformation and syringomyelia. The Veterinary record 2012.
16. Thofner MS, Stougaard CL, Westrup U, et al. Prevalence and heritability of symptomatic syringomyelia in Cavalier King Charles Spaniels and long-term outcome in symptomatic and asymptomatic littermates. Journal of veterinary internal medicine / American College of Veterinary Internal Medicine 2015;29:243-250.
17. Plessas IN, Volk HA, Rusbridge C, et al. Comparison of gabapentin versus topiramate on clinically affected dogs with Chiari-like malformation and syringomyelia. Veterinary Record 2015;177.
18. Sanchis-Mora S, Chang YM, Abeyesinghe SM, et al. Pregabalin for the treatment of syringomyelia-associated neuropathic pain in dogs: A randomised, placebo-controlled, double-masked clinical trial. The Veterinary Journal 2019;250:55-62.
19. Girod M, Allerton F, Gommeren K, et al. Evaluation of the effect of oral omeprazole on canine cerebrospinal fluid production: A pilot study. Vet J 2016;209:119-124.
20. Girod M, Allerton F, Vangrinsven E, et al. CSF omeprazole concentration and albumin quotient following high dose intravenous omeprazole in dogs. Research in veterinary science 2019;125:266-271.
21 Gamble L-J, Boesch JM, Frye CW, et al. Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs. Frontiers in Veterinary Science 2018;5.
22. Kibar Z, Dubé MP, Knowler SP, et al. Preliminary results from syringomyelia (SM) genome wide scans in cavalier King Charles spaniel kindred and directions for future research. Chiari-like malformation and Syringomyelia in the Cavalier King Charles Spaniel 2007:179.
23. Lemay P, Knowler SP, Bouasker S, et al. Quantitative Trait Loci (QTL) Study Identifies Novel Genomic Regions Associated to Chiari-Like Malformation in Griffon Bruxellois Dogs. PloS one 2014;9:e89816.
24. Ancot F, Lemay P, Knowler SP, et al. A genome-wide association study identifies candidate loci associated to syringomyelia secondary to Chiari-like malformation in Cavalier King Charles Spaniels. BMC genetics 2018;19:16.
25. BVA T. Appendix 1 Breeding recommendations until relevant EBVs are available. In: British Veterinary Association/ Kennel Club Chiari malformation / Syringomyelia (CM/SM) Scheme. http://www.bva.co.uk/public/documents/CM-SM_breeding_recommendations.pdf: BVA, The; 2012.
26. Spiteri M, Knowler SP, Rusbridge C, et al. Using machine learning to understand neuromorphological change and image-based biomarker identification in Cavalier King Charles Spaniels with Chiari-like malformation-associated pain and syringomyelia. Journal of Veterinary Internal Medicine 2019;0.

A riddle wrapped in a mystery inside an enigma: Lumbosacral neuropathic and discogenic pain

Frank Steffen, Prof.Dr.med.vet., Dipl ECVN
Vetsuisse faculty of the University of Zurich, Switzerland

Both lumbosacral neuropathic and discogenic pain syndromes are accepted clinical entities in people. In dogs, these pain sources are poorly described and difficult to diagnose because of lack of patient description and because numerous structures within the degenerated spinal segment can be painful. This presentation is intended to summarize the facts of these algesic phenomena.

Radicular pain is defined by its mechanism as pain evoked by stimulation of the sensory root or its dorsal root ganglion (DRG). Pathophysiologic processes of radicular pain can be divided broadly into (1) mechanical deformation and compression and (2) inflammatory reactions both resulting in nociceptive pain.

Mechanical compression is the most frequent pain source in dogs with degenerative lumbosacral disease. Typically, pain is elicited during physical activities, specifically when the ls junction is extended. Clinically, compression of sensory nerve structures can be aggravated specifically with the lordosis test because this manoeuvre results in narrowing of central canal and foramina.

Inflammation is a key process that causes several degenerating spinal structures to be painful. Nucleus pulposus is a driver of inflammation around the nerve root affecting its electrophysiologic function. Multiple inflammatory mediators and cytokines such as nitric oxide, prostaglandine E, various types of interleukins, phospholipase A2 and TNF-α are present in degenerated discs or are produced by migrating leukocytes. Most of these inflammatory mediators have greater activity in presence of an extruded, sequestrated disc rather than in subligamentous disc protrusions. Besides local stimulation of sensory nerve endings, inflammatory changes in the epidural space may set off a cascade of events leading to sensitization of the nerve root. This correlates with the clinical observation that dogs with extruded lumbosacral discs are much more painful than those with protrusions only.

Disc material harvested during surgery does not only contain inflammatory mediators. Also, increased levels of the neurotransmitter glutamate have been found in herniated discs. Infusion of radiolabeled glutamate into the rat epidural space resulted in significant radiolabeling of the DRG. It was suggested that glutamate originating from disc proteoglycan may diffuse into the DRG and elicite radicular pain syndromes.

Neuropathic pain (NP) is an important mimic of radicular pain. It is generally believed that NP is caused by changes in expression of the function of receptors, enzymes and voltage-dependent ion channels in peripheral nerves and dorsal root ganglion (DRG) neurons; central pain is generated by activity in 2nd or 3rd order neurons of the nociceptive system. After nerve injury, DRG neurons become more excitable and exhibit ectopic firing. Various molecular mechanisms are associated with NP including downregulation of GABA and opioid receptors, up-regulation of insensitive Na-Channels within axons and sensory cell bodies, central sensitization, and A-fibre phenotype switching, all of which can result in perceived noxious stimulation of non-noxious sensory information. The clinical manifestations of NP are chronic in nature and often characterized by hyperesthesia, allodynia and intermittent spontaneous/shooting pain. Recognition of these algesic manifestations in dogs requires careful observation and interpretation as objective measurements are not available. NP may develop after the initiating event (compressive or inflammatory) has resolved. Typically, NP is unresponsive to anti-inflammatory medication and opioids. Thus, response to therapy is an important diagnostic information in dogs (moreover because either electrophysiologic and imaging findings may be normal in patients with NP). Gabapentin, Pregabalin and Amitryptiline are the drugs of choice for treatment of NP. Gabapentin prevents the release of glutamate in the dorsal horn via interaction with the α2δ subunit of voltage-gated calcium channels (VGCC). While there is only anecdotal evidence for efficacy of gabapentin in dogs an anatomical study documents presence of of α2δ subunits in dorsal root ganglia of puppies and adult dogs demonstrating its role in signal processing. Multilabeling studies showed coexpression of α2δ, substance P and calcitonin gene-related protein (CGRP) implying that these neurons are involved in peptidergic nociception (Rosati et al. 2012). Chronic compression of nerve roots results in thickening of those structures due to interfascicular fibroblast proliferation and collagen type II formation. Albeit also motor axons can be affected functionally and on imaging the dorsal root and DRG are more severly affected clinically and in diagnostic imaging. Also, a recent electrodiagnostic study performed in dogs with painful lumbosacral foraminal stenosis found a delay in the onset of cord dorsum potentials as the most reliable diagnostic result (Harcourt-Brown et al., 2019). The origin of pain in swollen nerve roots is most likely multimodal, mechanical and neuropathic because there is marked improvement following surgical decompression but some dogs require also gabapentin to control algesic signs. Inflammation does not seem to be a characateristic feature of nerve root enlargement in those DLSS patients because only few inflammatory cells have been found during histopathological examination in nerve root biopsies. However, this does not exclude the possibility of molecular inflammatory processes (presence of inflammatory cytokines and mediators). Diagnosis of nerve root referred NP is not only hampered by the inability of dogs to report their sensations but also the absence of reliable diagnostic imaging features. A human imaging study using nerve-root anesthesia reported that nerve root enlargement had a positive predictive value of 80% for radicular pain. While we have found clinical signs of lumbosacral disease were also highly associated with thickened L7 and S1 nerve roots, this finding does not correlate with presence of NP in canines. In a majority of dogs with abnormal nerve roots clinical signs improve after decompression alone and only a few continue to be painful and then improve with medication against NP. Currently, the diagnosis of lumbosacral neuropathic pain is based on careful collection of clinical observations and therpeutical trials only.

Discogenic pain (DP) is the most common type of chronic low back pain in people accounting for 20-40% of cases. The term internal disc disruption (IDD) has been proposed which implies that discogenic pain is caused by disc degeneration and non-nerve root referred pain. IDD is a separate clinical entity that is different from compressive variants of degenerative disc disease such as disc herniations and painful segmental hypermobility. Pathologic

features of painful discs include formation of zones of vascularized granulation tissue with extensive innervation into annular fissures. Cytokines present in degenerated IVDs (TNF-alpha, interleukins, Nerve growth factor) induce ingrowth of sensory nerves. Another mechanism for generation of discogenic pain is an endplate damage, in which the pathogenesis is consistent with that of annular injuries: ingrowth of blood capillaries through defects is followed by ingrowth of sensory nerve endings. Mechanical stimulation of these sensory nerves in the hypermobile degenerated IVD is thought to be painful. In the only veterinary study investigating nerve fibers within adult canine lumbar discs (sampled from dogs without clinical signs), they were found to be confined only to the outer layers of the annulus in immunohistochemical examinations using protein gene product 9.5 as a marker (Willenegger et al 2005). In other species nerve endings have been found to extend down into the nucleus pulposus (man, rats and rabbits). Because no study was performed to document nerve endings to penetrate deep into the annulus fibrosus in affected dogs there are controversial opinions about existence of DP in dogs.

Mechanical stimulation of nerve endings is not the only source of pain. Peng et al (2015) postulated that inflammation is the key that differentiates symptomatic from asymptomatic disc degeneration. Intradiscal inflammation has been demonstrated also in canine degenerated discs. PGE2 levels and CCL2 levels in degenerated and herniated IVDs were significantly higher compared with non-degenerated and non-herniated IVDs (Willems et al. 2016) supporting the hypothesis that chemical stimulation of nerve endings can be a source of DP. In summary, DP can be regarded as confluence of innervation, inflammation and mechanical hypermobility. To demonstrate pathophysiological evidence that discogenic pain is a clinical entity also in dogs investigations must reveal presence of both sensory innervation/nociceptive substances and inflammation in degenerated discs of dogs with lumbar pain without nerve root compression. Our group has sampled degenerated discs with macroscopic defects suspicious for nerve ingrowth and healthy discs serving as normal controls. Various antibodies against IVD structures associated with discogenic pain were tested including Substance P and calcitonin- gene related peptide (CRGP), nerve growth factor (NFG), pan-neuronal marker (TuJ1), neuron-specific enolase, synaptophysin, vimentin (marker for mesenchymal cells) and blood vessel staining (CD31). In summary, all stainings failed to provide robust evidence for presence of gene products or cell types associated with DP. Problems included lack of clear separation of positive and negative controls, co-staining of chondrocyte like cells (CLC), presence of unspecific staining within defects in AF. Although, some stainings worked well in individual samples it did not in others.

Likewise, clinical diagnosis of DP is challenging. Provocation discography in people is the only available means to identify painful discs. Because disc puncture and pressurized injection increase the risk for accelerated disc degeneration alternative non-invasive diagnostic tests using MRI were investigated and those may also apply in dogs. T2 mapping utilizes the T2 values for quantification of moisture content and collagen breakdown. A clinical study demonstrated a correlation between degeneration of the posterior annulus fibrosus and chronic low back pain in people. Therefore, T2 mapping was suggested as a quantitative measure for diagnosing DP. High-intensity zones (HIZ) seen in the dorsal annulus of lumbosacral discs on T2W MRI are sensitive indicators of IDD. A recent metaanalysis found that the HIZ on lumbar T2W images can be an effective index for prediction of discogenic low back pain. However, as some discs with HIZ are not painful on discography caution is indicated. HIZ are also common in dogs with clinical signs of low back pain and degenerated lumbosacral discs (34/50 in one of our clinical studies on DLS). In absence of nerve root compression this imaging feature may serve as a marker for DP.

Similar to the problem of NP, response to treatment against DP may provide at least indirect evidence that the entity exists in dogs. In people, various treatment options are available. First-line recommendations include nonspecific back exercises. More targeted management techniques include physical therapy and acupuncture. Epidural steroid injections are not recommended in recent guidelines, but intradiscal injection of methylene blue to ablate nerve endings were used and found to be significantly more effective compared to placebo treatment. Also, injection of protein rich plasma (PRP) was found to be beneficial in a preliminary study. In dogs, clinical improvement was achieved by reduction of back pain after intradiscal application of a COX-2 inhibitor in 9 of 10 dogs with chronic disc degeneration, as was shown by clinical examination and owner questionnaires. In 3 of 10 dogs, back pain recurred after 3 months. This study showed safety and effectiveness of intradiscal injections in vivo with a thermoresponsive PCLA-PEG-PCLA hydrogel loaded with celecoxib (Tellegen et al., 2018). In an experimental setting with induced disc degeneration in Beagles, intradiscal delivery of sustained released formulation of corticosteroids was clinically safe but did not affect positively affect Pfirrman grade, T2 mapping values, collagen and Glycosaminoglycanes compared to controls. NGF, a biomarker of DP, was decreased in nucleus pulposus tissue after treatment with triamcinolone acetonide (Rudnik-Jansen et al. 2019).

Among regenerative therapies only mesenchymal stem cell treatment has been applied clinically to both people and dogs. Altough some small case series reported improved function and pain the overall strength of evidence for efficacy and safety was low. In dogs, the clinical effects of MSC injection could not be evaluated reliably because clinically affected DLSS dogs were treated with decompressive surgeries concomitantly. Surgical fusion-stabilization surgeries represent the most invasive option to manage DP. While the potentially painful disc can be removed it remains unclear if clinical improvement is attributed to immobilization of the affected segment.

Many pain sources are present in dogs with lumbosacral degeneration and various treatment options are available. However, specific definition of the origin of pain in order to apply a targeted treatment is not possible because absence of quantitative and qualitative measures. Critical awareness of the possibility of neuropathic and discogenic pain syndromes may help to avoid both over- and undertreatment in clinical patients.

Moore SA. Managing neuropathic pain in dogs. Front Vet Sci 3:12, 2016

Rosati et al. Developmental changes in voltage-gated calcium channel α(2)δ-subunit expression in the canine dorsal root ganglion. Dev Neurosci 2012; 34(5)

Ohtori et al. Pathomechanisms of discogenic low back pain in humans and animal models. Spine J 2015; 15(6)

Willems et al. Inflammatory profiles in canine intervertebral disc degeneration. BMC Vet Res. 2016 Jan 13;12:10

Tellegen et al. Intradiscal application of a PCLA-PEG-PCLA hydrogel loaded with celecoxib for the treatment of back pain in canines: What's in it for humans? J Tissue Eng Regen Med 2018; 12(3)

Fujii et al. Discogenic back pain: literature review of definition, diagnosis, and treatment. JBMR Plus, 2019

Teraguchi et al. The association of high-intensity zones and low back pain: a systematic review. Scoliosis and spinal disord. 218, 13:22

Rudnik-Jansen et al. Safety of intradiscal delivery of triamcinolone acetonide by a poly(esteramide) microsphere platform in a large animal model of intervertebral disc degeneration. The Spine Journal 2019 (19), 905-919

Steffen et alTreatment of Naturally Degenerated Canine Lumbosacral Intervertebral Discs with Autologous Mesenchymal Stromal Cells and Collagen Microcarriers: A Prospective Clinical Study. Cell Transplant. 2019 28:201-211

Cannabinoids: just fashion or real opportunity?

Renato Vellucci, MD

Author affiliations: Palliative Care and Pain Therapy Unit, University Hospital of Careggi
Corresponding author: Renato Vellucci, MD, Palliative Care and Pain Therapy Unit, University Hospital of Careggi

For centuries, cannabis has been used for medicinal use. The Emperor Fu His note that Cannabis was very popular medicine, which possessed both yin and yang. Shennong Ben Cao Jing encyclopedia, which dates back to 2900 BC in China, recommended the seeds as treatment for pain. During the last decade, interest in cannabis in medicine has been increasing, and during recent years, interest in the use of cannabis in clinical practice has being of growing. From biological point of view, delta-9-tetrahydrocannabinol is the only pharmacologically and toxicologically most relevant and best studied metabolite of cannabis, but is necessary remember the polypharmaceutical potential of the plant due to the presence of hundreds of biologically active compounds. 480 chemical entities are present in cannabis plant Cannabis. In order to be brief I will simply mention Apigenin, witch is the characterized anxiolytic agent of Matricaria chamomilla L. and provides beneficial suppression of TNF-α(Tumor Necrotic Factor-α), whether in concert with THC 1 or counteracting THC. Cannflavin A witch represents a stronger inhibitor of cyclooxygenase enzymes and lipoxygenase enzymes than THC. Flavonoids, witch could modulate the pharmacokinetics of THC via a mechanism shared by cannabidiol (Inhibition of P450 3A11 and 3A4). What we learn from literature, smoked cannabis for neuropathic pain suggests that inhaled cannabis results in short term benefits for chronic neuropathic pain with a NNT of 5.6, CRI95%. Patients treated report Short term benefits for neuropathic pain, but the author denounce lack evidence regarding: sustained long-term benefits, risks in the community setting, small number of included studies and participants, and weak ability to draw firm conclusions. Long term studies are needed to confirm the safety and effectiveness of inhaled cannabis for chronic neuropathic pain in the community. From some meta-analysis on neuropathic pain and cannabis emerges as treatment effects were generally modest, one study did not meet study target for clinical significance, was observed a limited treatment duration, and adverse events like paranoia, psychosis, anxiety, depersonalization, worsened short-term memory, impaired judgment and driving, appetite stimulation with weight gain. The authors suggest a strong need to study well the efficacy and safety of medical cannabis. The conclusion, of recent meta-analysis about the efficacy of cannabis to improve cancer related pain, was that there is no high-quality evidence for the efficacy of oromucosal nabiximols, consider cannabinoids after therapeutic trial of two or more established agents, 2019 German guideline on palliative care fails to mention cannabinoids in the section pain management, and in the absence of high-quality evidence for benefit, the use of cannabis-based medicines should be at the discretion of a pain specialist, no evidence-based argument can be made for the use of medical cannabis o nabilone. Many chronic pain patients considering medical cannabis anticipate disapproval from their friends and family. It is not uncommon for patients to avoid disclosing their medical cannabis use to their loved ones altogether, despite experiencing significant improvements in their pain management and quality of life. These concerns are rooted in societal stigmatization of cannabis and can often be mitigated by enabling patients to medicalize their approach to disclosure, by explaining to friends and family that cannabis has been prescribed to them as a medicine which is used to treat a variety of conditions. Patients may avoid some of the stigmatization associated with use of medical cannabis. Empowering patients with evidence-based knowledge will significantly facilitate this process. To conclude could be necessary to define the role of THC compared to CBD. Cannabis can alleviate the patient's suffering, but we had to reduce the risk to transform the treatment in a stigma. It is still incumbent the risk of the relapses of the Italian law 187, which does not allow an easy social reintegration of patients treated with THC. All authors agree on the strong need to study the efficacy and safety of medical cannabis, defining the community risks, and the chronic effect of cannabis use.

Future perspectives in the management of chronic pain in human medicine

Renato Vellucci, MD

Author affiliations: Palliative Care and Pain Therapy Unit, University Hospital of Careggi
Corresponding author: Renato Vellucci, MD, Palliative Care and Pain Therapy Unit, University Hospital of Careggi

20% of adults in Europe and 26% in Italy are affected by chronic pain, the relevance of such epidemiological data makes this a public health problem. Pain is the symptom most frequently reported by adults and is the cause of 40% of the visits carried out in the primary medicine clinic in Italy. Acute pain is a symptom of great importance, protective against current, potential risks and to facilitate natural healing, often promotes the carrying out of clinical and instrumental insights that can guide towards a diagnosis of disease. Despite the pain performs these multiple informational tasks, when it loses this adaptive primary function and perseveres, it can become a real chronic disease of great impact on people's quality of life. Today, the scenario of chronic pain management is unsatisfactory. The large variability of the effects of the drugs for chronic pain management introduce the idea of patient-tailored healthcare prevention and therapy. This is the base of personalized treatment of pain, which foresees the use of molecular data to better classify disease, to facilitate the growth and endorsement of new targeted therapies, to treat patients with more specificity and efficacy but fewer adverse events. Efforts in the pharmacogenomics (PGx) discoveries have been assisted by nationally accessible reference databases which classify and annotate genomic variation. Genes can influence pharmacodynamics for variations in drug target receptors and downstream signal transduction. In addition, genes influence pharmacokinetics impact drug metabolism, altering the relationship between drug dose and steadystate ematic drug concentrations. The successful adoption of PGx into routine clinical care requires multiple efforts like the creation of multidisciplinary consortiums and databases, but could represent the future for tailored medicine for chronic pain patients. Another topic is suggested by recent studies about Mesenchymal stem cells. The great value of cell therapy over the past few decades was demonstrated for the treatment of various degenerative diseases in combination with pain. In particular mesenchymal stem cells could play a regenerative role not through their differentiation potential, but through their paracrine factors of the extracellular vesicle including exosomes. The exosomes are nanosized membrane-bound extracellular vesicles, not only involved in cell-to-cell communication but also in the development of tissue injury repair. Further mesenchymal stem cells play a role in local immune regulation, responding to synovial membrane injury and inflammation, secreting various chemokines which attract various immune regulatory cells. With the growing clinical data and future investigational data is not unrealistic to believe that these forms of approach may one day support or replace the current therapies and act to provide longer relief and greater clinical benefit.

Oral Abstracts

INCREASED RESTING STATE CONNECTIVITY IN THE ANTERIOR DEFAULT MODE NETWORK OF IDIOPATHIC EPILEPTIC DOGS

K.M. Beckmann[1], A. Wang-Leandro[2], H. Richter[2,3], R.N. Bektas[4], F. Steffen[1], M. Dennler[2], I. Carrera[5], S. Haller[6,7]

[1] University of Zurich, Clinic of Small Animal Surgery, Neurology Department, Switzerland
[2] University Zurich, Clinic for Diagnostic Imaging, Department of Diagnostics and Clinical Services, Switzerland
[3] University Bonn, Clinic for Neuroradiology, Germany
[4] University Zurich, Section of Anaesthesiology, Department of Diagnostics and Clinical Services, Switzerland
[5] Willows Veterinary Centre and Referral Service, United Kingdom
[6] Uppsala University, Department of Surgical Sciences, Radiology, Sweden
[7] University of Geneva, Faculty of Medicine, Switzerland

Epilepsy is increasingly recognized as a network disorder rather than a disorder of isolated epileptic zones. Resting state functional magnetic resonance imaging is a none-invasive method to investigate brain connectivity. In human epilepsy and rodent models, altered functional connectivity in different large-scale brain networks have been identified. Since large-scale brain networks have been consistently identified in anesthetised dogs, application of this technique on canine epilepsy research is promising.

The aim of the present study was to investigate differences in resting state networks of epileptic dogs compared to healthy controls. We hypothesize that epileptic dogs show altered large-scale networks compared to healthy control dogs.

A group of 17 dogs affected by idiopathic epilepsy, 11 Border Collies and 6 Greater Swiss Mountain Dogs, was compared to 20 healthy beagle dogs under a standardized sevoflurane anesthesia protocol. Group level independent component analysis with dimensionality of 20 components, dual regression analysis and two-sample t-test were performed. Significantly increased connectivity at the anterior default mode network (DMN) of idiopathic epileptic dogs compared to healthy control dogs (p= 0.00060). No significant differences were found at the posterior DMN, primary visual, higher order visual, auditory and somatosensory networks.

The DMN is an important higher order brain network and its dysfunction has been found in human epilepsy, but also in epileptic-comorbidities such as anxiety and depression. Altered anterior DMN connectivity suggests synaptic reorganization and possibly compensatory mechanisms in canine idiopathic epilepsy and may indicate a target for further advanced computational neuroimaging.

MIR-134: A NEW THERAPEUTIC TARGET FOR DRUG-RESISTANT IDIOPATHIC EPILEPSY IN DOGS?

Rodrigo Gutierrez-Quintana[1], Cristina Ruedell Reschke[2], Aoife Campbell[2], Andrea Tipold[3], Florian Hansmann[4], Holger Volk[3], Frances McLauchlan[5], Roberto José-López[1], Catherine Stalin[1], Adriana Kaczmarska[1], David Henshall[2]

[1] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, UK
[2] Physiology and Medical Physics, Royal College of Surgeons Ireland
[3] Department of Small animal Medicine and Surgery, University of Veterinary Medicine Hannover, Germany
[4] Department of Veterinary Pathology, University of Veterinary Medicine Hannover, Germany
[5] Abbey Veterinary Group, UK.

Current antiseizure drugs (ASD) provide symptomatic control of seizures in only two-thirds of patients and do not change the underlying pathophysiology. Recently, microRNAs (miR) have emerged as potential novel targets for seizure control and disease-modification in drug-resistant epilepsy. miR-134 is up-regulated in rodents after prolonged or repeated seizures and in brain tissue form humans with drug-resistant temporal lobe epilepsy. MicroRNAs can be specifically targeted using antisense oligonucleotides and inhibiting miR-134 has shown potent and long-lasting anticonvulsant and neuroprotective effects in rodent epilepsy models. We aim of to assess miR-134 as a circulating biomarker of drug-resistant epilepsy in dogs.

Plasma samples from seven healthy dogs and 14 dogs with a tier II confidence level for idiopathic epilepsy (IE) were used. Seven IE dogs were responsive to ASD and seven were drug-resistant (less than 50% reduction of seizures despite at least two ASD). RNA was extracted using the miRCURY RNA isolation kit for biofluids (Exiqon). Levels of miR-134 were assessed by individual Taqman miRNA by RT-qPCR on QuantStudio 12 K Flex PCR system and expressed relative to miR-16. ANOVA with post hoc test was used for groups comparison.

Results revealed plasma levels of miR-134 were significantly higher ($p=0.0034$) in dogs with drug-resistant epilepsy compared to controls and also considerably higher than in dogs responsive to ASD.

This confirms that changes in miR-134 expression are present in canine IE and supports miR-134 as biomarker of drug-resistant epilepsy in dogs and as an interesting therapeutic target for seizure control and disease-modification in drug-resistant cases.

RISK FACTORS ASSOCIATED WITH SHORT-TERM MORTALITY AND RECURRENCE OF STATUS EPILEPTICUS IN DOGS

R. Fentem[1]*, A. de Stefani[2], R. Gutierrez Quintana[3], E. Alcoverro[4], G.M.C. Jones[2], P. Amengual-Batle[3], R. Gonçalves[1]

[1] Small Animal Teaching Hospital, School of Veterinary Science, University of Liverpool, UK
[2] Queen Mother Hospital for Animals, Royal Veterinary College, University of London, UK
[3] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, UK
[4] Chestergates Veterinary Specialists, UK

Background: Status epilepticus (SE) is a neurological emergency associated with serious consequences for both the patient and owner. Data regarding risk factors for short-term mortality or recurrence in patients with SE is limited.

Objective: To identify risk factors associated with short-term mortality (euthanasia or spontaneous death) and with recurrence of SE in dogs.

Animals: 130 client-owned dogs presented in status epilepticus.

Methods: Retrospective multicentre study using data collected from medical records of dogs presented in SE to the contributing institutions. Multivariable logistic regression analysis was performed using a manual backwards stepwise approach to identify risk factors associated with short-term mortality and with recurrence of SE after discharge.

Results: The short-term mortality for patients in this study was 32.3%. Factors significantly associated with short-term mortality included the presence of structural disease, the presence of SE prior to admission at the referral centre and the increasing duration of hospitalisation. SE recurred in 27% of dogs which survived to discharge. Factors significantly associated with recurrence of SE included a prior history of pharmacoresistant epilepsy and the predominance of a focal seizure phenotype.

Clinical significance: The results from this study may be used to inform clinicians and dog owners regarding risk factors for both short-term mortality and recurrence in canine patients with SE.

Ethical approval for use of data was granted by the Ethics Committee of the University of Liverpool (VREC522) and Royal Veterinary College, University of London (URN SR2019-0324)

THE PHARMACOKINETICS OF SINGLE ORAL DOSE EXTENDED-RELEASE TOPIRAMATE AND ADVERSE EFFECTS AFTER MULTI-DOSE ADMINISTRATION IN HEALTHY CATS

L.T. Graham[1], K.D. Foss[1], K.M. Fleming[1], D.W. Hague[1], J.M. Reinhart[1], Z. Li[2]

[1] Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois Urbana-Champaign, United States of America
[2] Roy J. Carver Biotechnology Center, University of Illinois Urbana-Champaign, United States of America

Extended-release topiramate is an anticonvulsant approved for use in humans, which is administered once daily and manufactured in capsules that can be opened and sprinkled on food. A prospective study was designed to establish pharmacokinetic parameters and safety after multi-dose administration in eight healthy cats. After ensuring systemic health, baseline plasma samples were obtained followed by administration of 5 mg/kg (n= 4) or 10 mg/kg (n = 4) extended release topiramate sprinkled on food. Plasma sampling occurred up to 84 hours post-administration and concentrations were measured in all samples using liquid chromatography mass spectrometry. Based on these data, steady state predictions were performed to determine the most appropriate dosage and frequency required to achieve a minimum target concentration of 5 ug/mL after multidose administration. After a wash-out period, all cats were then administered 10 mg/kg extended release topiramate sprinkled on food once daily for 30 days. Weekly blood gas, physical examination, and intraocular pressures were obtained. A baseline plasma sample was obtained on day 30 prior to administration of the final dose, followed by 24 hours of plasma sampling. No significant adverse effects were noted during the study and the extended-release topiramate plasma concentration was greater than 5 ug/mL at all sampling time points in all participants after 30 days of administration. In conclusion, once daily administration of 10 mg/kg extended release topiramate is adequate to achieve a plasma concentration of 5 ug/mL without causing significant adverse effects after 30 days of administration.

Ethical permission was obtained for this study.

SOUNDS OF SEIZURES-ACOUSTIC INFORMATION ENABLES IMMEDIATE RECOGNITION AND DETECTION OF GENERALIZED TONIC-CLONIC SEIZURES IN DOGS

S. Meller[1], A. Zamansky[2], A. Sinitca[3], D. Kaplun[3], N. Meyerhoff[1], V. Stein[4], A. Tipold[1] & H. A. Volk[1]

[1] Department of Small Animal Medicine & Surgery, University of Veterinary Medicine Hannover, Germany
[2] Department of Information Systems, University of Haifa, Israel
[3] Department of Automation and Control Processes, Saint Petersburg State Electrotechnical University, Russia
[4] Department for Clinical Veterinary Medicine, University of Bern, Switzerland

Epilepsy is the most common chronic neurological disease in humans and dogs. Seizures greatly impact patients' and caretakers' quality of life. One of the caretakers' major concerns is that seizures may remain unnoticed or may be noticed too late. There is need for reliable detection of seizures in order to apply quick emergency treatment for preventing further seizure evolution resulting in cluster seizures or status epilepticus. Artificial intelligence may represent a new tool to overcome this gap. A crucial step in this direction is the creation of quality datasets and computational tools for investigating seizure-related audio, video, and sensor signals.

A dataset of 42 audio tracks of videos of dogs with generalized tonic-clonic epileptic seizures was collected and annotated. 138 statistical features were used and 9 classifier types using 4474 sound samples with the duration of 1 second each were investigated.

The obtained classifiers were evaluated with k-fold cross-validation and automatic hyperparameter tuning, reaching balanced accuracy of above 70%.

Classical machine learning methods show promising results in the detection of epileptic seizure sounds, providing a potential basis for the development of an alert and detection system for domestic and clinical environments. In addition, such systems could significantly improve the detection of seizure frequency and semiology to measure therapeutic effectiveness in more scientific settings. Employing various advanced deep learning techniques and neural networks has even greater potential to increase accuracy; however, larger datasets are needed. Research was partially funded by RFBR and MOST according to the research project No 19-57- 06007.

COMPARISON OF BRAIN METABOLITES BETWEEN IDIOPATHIC EPILEPTIC DOGS AND HEALTHY CONTROL DOGS WITH SINGLE VOXEL PROTON MAGNETIC RESONANCE SPECTROSCOPY OF THE THALAMUS

N. Mauri[1,2], H. Richter[2], N. Zoelch[3], K. Beckmann[4]

[1] Vetimage Diagnostik GmbH, Oberentfelden, Switzerland
[2] University of Zurich, Vetsuisse Faculty, Clinic for Diagnostic Imaging, Department of Diagnostics and Clinical Services, Switzerland
[3] University of Zurich, Institute of Forensic Medicine, Department of Forensic Medicine and Imaging, Switzerland
[4] University of Zurich, Vetsuisse Faculty, Neurology Service, Department of Small Animal Surgery, Switzerland

Magnetic resonance spectroscopy (MRS) has been used to characterise ictal and inter-ictal metabolic abnormalities in humans with epilepsy. In veterinary medicine, several advantageous applications of MRS in epileptic and non-epileptic dogs have been presented. However, especially for the investigation of canine epilepsy, MRS published data is limited.
The purpose of this case-control study was to assess and compare thalamic MRS-Spectra in dogs with idiopathic epilepsy (IE) and healthy control dogs. We hypothesized that epileptic dogs, show elevated glutamate-glutamine (Glx) and reduced N-acetyl-aspartate (NAA) thalamic concentration compared to controls, similar to humans with idiopathic generalized epilepsy.
MRS of the thalamus was performed in 31 IE dogs and 25 healthy control dogs during a retrospective (2015-2019) and a prospective (2019-2021) part of this study. Single voxel proton MRS of the thalamus was performed with a 3-Tesla MRI using an optimized protocol (PRESS-localisation, TE=31 ms, TR=2000 ms, NSA=240). Metabolite concentrations were estimated with an automated data processing spectral fitting algorithm using water signal as reference, and compared between IE dogs and controls using a Wilcoxon unpaired two-sample test.
Dogs affected by IE showed statistically significant elevated thalamic Glx concentrations (Cohen's-d=-0.728). However, no statistically significant difference in NAA between IE dogs and controls was detected.
In conclusion, preliminary results of this study show that dogs affected by IE have increased Glx, but no decrease in NAA thalamic concentration compared to healthy controls. These findings support the application of MRS for further investigation of canine epilepsy.

Keywords: MRS, [1H] MRS, N-acetyl aspartate, glutamate, glutamine, brain, canine.

Nico Mauri ORCID ID: 0000-0001-8980-4053
Henning Richter ORCID ID: 0000-0003-3696-6993
Niklaus Zoelch ORCID ID: 0000-0002-9722-7783
Katrin Beckmann ORCID ID: 0000-0002-1823-7845

The study was authorized by the cantonal ethical committee (Zürich, Switzerland).

The submitting author, Nico Mauri, is a resident in Diagnostic Imaging (ECVDI).

SURFACE ELECTROENCEPHALOGRAPHY ALLOWS TO RECORD EVENT RELATED POTENTIALS DURING QUANTITATIVE SENSORY TESTING IN AWAKE CATS

A. Castel[1], A. Delsart[2], C. Otis[2] and E. Troncy[2]

[1] Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Montreal, Saint-Hyacinthe, QC, CANADA
[2] Department of Biomedical Sciences, Faculty of Veterinary Medicine, University of Montreal, Saint-Hyacinthe, QC, CANADA

Quantitative sensory testing (temporal summation number following mechanical stimulation (MS) or application of an acetone drop on a paw), allow to assess rather objectively, mechanical and cold allodynia associated with chronic pain but cannot evaluate the mechanisms associated with pain perception and modulation at the cortical level. We hypothesize that the recording of event related potentials (ERPs) measuring superficial cortical activity in areas involved in pain processing following MS and thermal (TS) stimulations, is feasible in awake cats using surface electroencephalography (sEEG).

Eight sEEG electrodes were placed on the skull of six healthy research cats to record sEEG activity before and during either repeated MS or TS (pinprick or an acetone drop on the dorsum of a front paw, respectively). The number of MS tolerated and the latency to observe a behavioral response after TS were recorded. The method of principal component analysis was used to decompose the EEG traces of each trial at each electrode site into basic waveforms (principal components) followed by an analysis of variance to detect if the stimulations generated a specific component. A generalized linear mixed model allowed to detect any electrode site with unique activity generated by the stimulations.

The number of tolerated MS was similar to previous reports (mean 26.4 [18-30]). TS did not elicit any significant reaction. Awake sEEG were well tolerated and allowed recording of ERPs in the Cz area following MS and TS. sEEG could allow to evaluate cortical activity associated with allodynia in awake cats with chronic pain.

A NOVEL LATERAL APPROACH TO THE C7 AND C8 SPINAL NERVES AND NERVE ROOTS FOR RESECTION OF MALIGNANT PERIPHERAL NERVE SHEATH NEOPLASIA IN TWO DOGS

O. Marsh[1,a], N. Shimizu[2], S.Mason[3] and A. Uriarte[1]

[1] Southfields Veterinary Specialists, Neurology Service, UK
[2] Southfields Veterinary Specialists, Surgery Service, UK
[3] Southfields Veterinary Specialists, Oncology Service, UK
[a] Oliver Marsh is a neurology resident in training

Peripheral nerve sheath tumours are malignant mesenchymal tumours that commonly cause neuropathic pain. Surgery with or without adjuvant radiotherapy, or radiotherapy alone, is recommended. Excellent access is required for excision with clear margins, improving prognosis. The surgical approach to the C7 and C8 spinal nerves and nerve roots is complicated by the scapula and possible intra-thoracic tumoral extension. Here, we outline a novel surgical procedure in two dogs to resect brachial plexus masses with rib and intrathoracic involvement that extended into the C6-C7 intervertebral foramen in one case and the C7-T1 intervertebral foramen in the other.
Each patient was placed and secured in lateral recumbency. Forequarter limb amputation with first rib removal and distal resection of the affected spinal nerves allowed excision of the intrathoracic and brachial plexus portion of the mass. The table was then tilted 20° towards the vertical plane to improve access to the intervertebral foramina. The C6-T1 vertebrae were approached laterally by dissecting the sternothyroideus muscle, distracting the superficial scalenus muscle and removing the deep scalenus muscle from its vertebral attachments. C6-C7 or C7-T1 hemilaminectomies were performed. The C7 or C8 nerve root was resected 1mm distal to its spinal cord origin. Both dogs subsequently received adjuvant radiotherapy.
The procedure allowed excellent visualisation and access to intervertebral foramina and nerve roots without complications. At the time of writing, one case was pain-free nine months after surgery and the other remained comfortable for four months before developing a lung mass.

Note on ethical approval: the work described involved owned animals. Established internationally-recognised high standards of veterinary care (‘best practice’) were always followed. Ethical approval from a committee was therefore not specifically required.

SPINAL ARACHNOID DIVERTICULA CONFORMATIONAL VARIATIONS IN DOGS

J.M. Frias, S. De Decker, A. De Stefani, F. Llabres-Diaz

Department of Clinical Science and Services, Royal Veterinary College, University of London, Hatfield, UK

The description of spinal arachnoid diverticula (SAD) conformations and their clinical implications are poorly characterized in dogs. This retrospective cross-sectional study was conducted to describe variations of SAD conformations in dogs and to identify if there is an association between SAD conformation and age, time to referral, brachycephalic conformation, body weight, localisation, syringomyelia (SM) presence/localisation in relation to SAD, presence of vertebral malformation/intervertebral disc disease at the site of SAD, treatment, short-term and long-term outcome (4 weeks and more than 6 months from diagnosis, respectively).

Sixty-two dogs were included (12 cervical and 50 thoracolumbar SAD). All dogs with a cervical SAD had a cranial tethered conformation and were not included in the statistical analysis. Half of the dogs with a thoracolumbar SAD were cranial tethered and the other half caudal tethered. All dogs with the presence of SM and caudal tethered SAD had a cranial positioned SM (n=22) and all dogs with SM and a cranial tethered SAD (n=19) had a caudal positioned SM. Furthermore, the difference of SM absolute length was statistically significant (P=.018) between caudal (21.05mm$\pm$19.84) and the cranial (13.5mm$\pm$11.9) tethered thoracolumbar SAD. The difference of SM length/L2 vertebra ratio was statistically significant (P=.018) between caudal (1.44$\pm$1.45) and cranial (1.1$\pm$0.81) tethered thoracolumbar SAD. Only the short-term outcome was statistically significant (P=.045); the caudal tethered conformation was found to have better outcome regardless of treatment.

SAD conformation in dogs can influence SM formation. A possible link between short-term outcome and SAD conformation was found, but further research is warranted.

SPINAL SUBARACHNOID WEBS - ARE THEY A VARIANT OF SUBARACHNOID DYVERTICULA IN DOGS?

E. Bersan[1,2], T. Maddox[1], E. Ricci[3], J. Mortimer[1], R. Goncalves[1]

[1] Dept. of Small Animal Clinical Science, Small Animal Teaching Hospital, University of Liverpool, UK
[2] Unita' Operativa di Neurologia e Neurochirurgia, Malpensa Veterinary Clinic AniCura, IT
[3] Dept. of Veterinary Pathology and Public Health, Veterinary Pathology Diagnostic Service, University of Liverpool, UK

Subarachnoid webs (SAW) are described in human medical literature, thought to represent a variant of subarachnoid diverticula (SAD). A definitive diagnosis is often difficult from pre-operative images, needing the aid of intra-operative modalities such as ultrasonography. The ultrasound appearance of SAW is characterised by longitudinal membranes of subarachnoid tissue that obstruct the subarachnoid space. The primary objective of this retrospective study was to determine if SAW exist in dogs. We also aimed to evaluate the value of intraoperative ultrasonography during decompressive surgery in cases of SAD/SAW, comparing ultrasound images with pre-operative magnetic resonance imaging data.

The study population comprised 12 dogs that underwent MRI and intra-operative ultrasonography. Based on the MRI study, the point of greatest dilation of the subarachnoid space was at T10 vertebral body (5/12), T12 (4/12) and T11 (3/12). All dogs underwent dorsal laminectomy. Durotomy was performed in all cases followed by focal durectomy in 11 cases. Five dogs underwent subsequent spinal stabilisation.

Images were independently reviewed by 2 radiologists. A consensus diagnosis of SAW was found in 8 cases, 4 cases were classified as SAD. Surgical planning was modified and extended based on the intra-operative ultrasonography findings resulting in a more extensive approach involving more than 1 vertebral body in 7 cases.

In conclusion, dilations of the subarachnoid space showing ultrasound characteristics compatible with the medical descriptions of SAW were found in multiple dogs. In all cases, intraoperative ultrasonography provided essential information to establish a definitive diagnosis, appropriate surgical margins and debridement of adhesions.

TRAUMATIC AND IATROGENIC SCIATIC NERVE INJURY IN THIRTY-NINE DOGS AND TEN CATS: CLINICAL AND ELECTRODIAGNOSTIC FINDINGS

Dell'Apa D.[1], Auletta L.[2,] Okonji S.[3], Cauduro A.[4], Dondi M.[1], Opreni M.[4], Gandini G.[3], Bianchi E.[1]

[1] Dept. Of Veterinary Science, University of Parma, Italy
[2] IBB CNR, Naples, Italy
[3] Dept. Of Veterinary Medical Science University of Bologna, Italy
[4] Neurovet Professional Association, Milano, Italy

Aim of the study was to retrospectively evaluate clinical and electrodiagnostic findings of dogs and cats with traumatic and iatrogenic lesions of the sciatic nerve.
Patients visited in the period 2006-2020 that underwent neurologic examination and electrodiagnostics were included. A grading scale was applied to results of motor nerve conduction (MNCS) based on amplitudes of CMAPs. These data were compared to clinical findings like absence/presence of nociception in the peroneal and tibial nerves using contingency tables.
Thirty-nine dogs and 10 cats (23 males, 26 females) met the inclusion criteria. Injuries were caused by trauma (51%), surgical procedures (44.9%) and injections (4.1%).
Electrodiagnostics were suggestive of neurotmesis in 23 nerves (16 peroneal, 7 tibial). Peroneal and tibial nerve were affected in 83% (41/49) and 92% (45/49) of the patients respectively.
Of the 39 subjects with both nerves injured, 19 had a prevalent peroneal and 3 a prevalent tibial involvement. Nociception was absent in 5/7 tibial and in 16/16 peroneal nerves that had absent CMAPs (neurotmesis). Nociception was absent also in 5/6 tibial and 8/14 peroneal nerves that had severely reduced amplitudes of CMAPs (<1 mV). A significant association between the grading scale and nociception was found for both the tibial and peroneal nerve (P=0.006 and P=0.001 respectively).
Different types of trauma and orthopedic procedures can cause injury and dysfunction of the sciatic nerve. Peroneal is often more severely affected than tibial. Electrodiagnostics appear to be superior to neurological evaluation in differentiating neurotmesis form severe axonotmesis, that may carry a better prognosis.

VALVELESS VENTRICULOPERITONEAL SHUNT IN DOGS AND CATS - CLINICAL EXPERIENCE AFTER 20 YEARS

R. F. Schamall, J. Almeida, K. Schmidt

Clínica Veterinária Petrópolis - Petrópolis - RJ - Brazil

We report our experience in the treatment of hydrocephalus in dogs and cats, using valveless ventriculoperitoneal shunt technique. We believe that, due to the anatomical particularities of these species, the use of a CSF valve as a flow regulator device is not necessary. Twenty-two dogs and two cats with primary or secondary hydrocephalus (three of them also associated with quadrigeminal cysts) were treated. The surgical procedure was the same as traditional technique, except for the absence of a valve. Complications were: three obstructions in the first month after surgery, two cases of infection and two cases of concentric pachymeningeal fibrosis (obstructing the intraventricular end of the tube). A severe case of subdural haemorrhage was the only intraoperative complication. Twenty animals achieved a normal life and four animals died in the first week after surgery, by causes unrelated to the technique. These results suggests that the valve is unnecessary and, besides adding cost and complexity, reportedly causes unnecessary complications. The complications found in our series was related to the shunt technique and not due the absence of the valve. In no patient was noted, at least clinically, the occurrence of hyperdrainage syndrome. The low morbidity and mortality indicate the safety of this modification of the traditional valvulated technique. We hope these data provides a proof of concept for its clinical utilization.

COMPARISON OF NEUROTRANSMITTERS CONCENTRATION IN CANINE CEREBROSPINAL FLUID, BLOOD, AND URINE SAMPLES MEASURED VIA HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

S. Meller[1], R. Hildebrandt[1], M. Gramer[2], F. Richter Assencio[2] & H. A. Volk[1]

[1] Department of Small Animal Medicine & Surgery, University of Veterinary Medicine Hannover, Germany
[2] Department of Pharmacology, Toxicology & Pharmacy, University of Veterinary Medicine Hannover, Germany

The coordinated interplay between neurotransmitters is crucial for the physiological functioning of the central nervous system. It is thought that neurotransmitter do not penetrate the blood brain barrier. However, in humans, urinary neurotransmitter analysis for mood disorders like anxiety and depression is used in practice. The aim of the current study was to compare neurotransmitter concentrations across body fluids. This is the first canine study evaluating how neurotransmitter concentrations in cerebrospinal fluid (CSF), serum, and urine are associated with each other, providing new insights into the canine neurotransmitter metabolism.

CSF, serum, and urine were collected from 8 beagle dogs at three different time points (2 weeks apart) under general anesthesia. The samples were stored at -80°C before high-performance liquid chromatography was performed for analysis. Significant neurotransmitters from the group of amino acids and catecholamines were measured.

Twenty-four CSF, blood, and urine samples were collected. Concentrations of serine, glycine, and norepinephrine were significantly positively correlated between all assessed body fluids. Aspartate concentrations only correlated positively in CSF and serum. No significant negative correlations were revealed.

The mirroring of concentration profiles of neurotransmitters in different body fluids offers new opportunities to study non-invasively behavioural disorders which have recently gained great importance in veterinary medicine. However, it is important to state that neurotransmitters can also be produced by peripheral organ systems and the microbiome, which makes further research necessary.

APPLICATION AND ACCURACY OF A MAGNETIC RESONANCE IMAGING-GUIDED NEURONAVIGATION SYSTEM FOR BRAIN BIOPSY IN SMALL ANIMALS

C.C. Yang, Y.P. Chang

Institute of Veterinary Clinical Science, School of Veterinary Medicine, National Taiwan University, Taiwan

The image-guided stereotactic technique can display the location of surgical instrument and biopsy target in real-time, allowing to perform minimal invasive brain biopsy with reduced risks. RETINA® is a frameless stereotactic navigation system, but its application in dogs and cats hasn't been investigated.

Using canine and feline cadavers, a study was conducted to evaluate its accuracy. Phantom lesions were created at various regions and depths in the brain. Eight fiducial markers composed of titanium screws and plastic cylinders filled with diluted gadolinium, were installed at the outer table of frontal sinus and zygomatic arch in each cadaver. T1-weighted turbo field echo three-dimensional MR images in 1-mm thickness were imported into the RETINA®. After placing the reference tracker on the dental bite block, the infrared camera was applied to register the head and the images through detecting the spatial relationship between fiducial markers and reference tracker. The path to the targeted lesion was determined in real-time, and 0.2 µl of diluted gadolinium was injected at each target. Coordinates of navigated target-point and the center of gadolinium deposition were established in repeated MR images. The distance between these coordinates was defined as targeting error.

In total, 64 lesions were targeted. The mean targeting error was 2.87 mm $\pm$ 0.82 mm. Lesion location, path length, and operator's experiences did not significantly affect the accuracy. The feasibility and accuracy of this navigation system support its clinical application for brain lesions of diameter > 3.07 mm in dogs and cats.

OPTIMISATION OF CEREBROSPINAL FLUID METABOLOMICS

F. Verdoodt[1,3], L.Y. Hemeryck[2], L. Vanhaecke[2], L. Van Ham[3], M. Hesta[1], S.F.M. Bhatti[3]

[1] Equine and Companion Animal Nutrition, Department of Morphology, Imaging, Orthopedics, Rehabilitation and Nutrition, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[2] Laboratory of Chemical Analysis, Department of Veterinary Public Health and Food Safety; Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[3] Small Animal Department, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

In veterinary medicine there is increasing interest for omics methodologies. Metabolomics is one of the more recent methods where the individual's biological phenotype is characterised, by integrating host-related and external factors (e.g. diet, microbial community). Fingerprinting of the canine cerebrospinal fluid (CSF) metabolome can lead to new discoveries of clinical biomarkers and may increase knowledge of the pathophysiology of multiple neurological diseases. However, at present there is no optimised and validated extraction protocol for metabolomics in CSF.

The objective of this study was to establish a validated protocol for CSF metabolomics. Therefore, CSF samples from healthy Beagles were analysed with ultrahigh performance liquid chromatography coupled to high resolution mass spectrometry (UHPLC-HRMS). This platform is considered the gold standard for metabolomics analysis. The extraction was optimised through a design of experiments, using JMP 15 software (SAS, UK). First a 2^4 factorial design was established with 19 experiments to assess four factors: volume, type of solvent, centrifugation time, usage of a filter. In a second phase, response surface modelling was applied to optimise yield. The extraction of a broad range of polar metabolites, including e.g. amino acids, ketones and carbohydrates was envisioned and evaluated. Preliminary data indicate a reliable detection of tryptophan and kynurenine. These metabolites are known to play a role in the microbiota-gut-brain axis (MGBA).

In conclusion, this validated protocol is an important step toward standardised metabolomics research in veterinary neurology. It can help unravel the role of MGBA in multiple conditions, such as canine cognitive dysfunction and idiopathic epilepsy.

OLIGOCLONAL BANDS IN DOGS WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN (MUO)

J.K. Prümmer[1], V.M. Stein[1], E. Marti[2], A. Lutterotti[3], G. Schüpbach[4], T. Buch[5], A. Maiolini[1]

[1] Division of Clinical Neurology
[2] Division of Clinical Immunology
[3] Department of Neurology
[4] Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Switzerland
[5] Institute of Laboratory Animal Science, University of Zurich, Switzerland

Meningoencephalitis of unknown origin (MUO) is an inflammatory disease of the canine central nervous system (CNS) that shares several characteristics with multiple sclerosis (MS), an inflammatory disease of the human CNS. In approximately 95 % of MS patients, ≥ two immunoglobulin G (IgG) oligoclonal bands (OCBs) are detectable exclusively in the cerebrospinal fluid (CSF).

The aim of this study was to detect OCBs in CSF and serum in a population of dogs with different diseases (MUO, intervertebral disc disease (IVDD), idiopathic epilepsy (IE), intracranial neoplasia (IN), steroid-responsive meningitis-arteritis (SRMA), and diseases outside the CNS). We hypothesized that, analogous to MS, a high proportion of dogs with a clinical diagnosis of MUO have ≥ two OCBs in the CSF (=OCB-positive).

121 paired CSF and serum samples were assessed via isoelectric focusing and immunoblot (MUO n=28, IVDD n=23, IE n=18, IN n=23, SRMA n=13, non-CNS n=16). Presence of an OCB-positive result was significantly higher in dogs with MUO (57 %) compared to all other groups (22 % in IN, 6 % in IE, 15 % in SRMA, 13 % in IVDD, and 0 % in the non-CNS group). Dogs with MUO were 9.9 times more likely to have an OCB-positive CSF result than the group of all other diseases.

This result underlines the analogy of MUO in dogs and MS in humans. MUO or one of its subtypes could serve as a translational animal model for MS studies.

IS CEREBROSPINAL FLUID ANALYSIS USEFUL IN SUSPECTED INTRACRANIAL DISEASE WITH NORMAL MAGNETIC RESONANCE IMAGING?

S. Monteiro[1], L. De Risio[2], L. Alves[1], A.E. Vanhaesebrouck[1]

[1] Department of Veterinary Medicine, University of Cambridge, UK
[2] Linnaeus Group, UK.

Cerebrospinal fluid (CSF) analysis is a common diagnostic tool used to characterise different neurological disease processes and, when not demonstrating any cytological or biochemical changes, increase the confidence in the diagnosis of idiopathic epilepsy.

This retrospective study investigated whether CSF analysis altered the likelihood of diagnosing dogs and cats with intracranial disease in the presence of unremarkable magnetic resonance imaging (MRI). Additionally, the usefulness of CSF analysis with normal and abnormal neurological examination findings was investigated. Clinical, imaging and laboratory records of patients that underwent brain MRI and CSF analysis at two veterinary neurology centres were collected.

Five hundred and ninety-six dogs and cats (536 and 60 respectively) with suspected intracranial disease, CSF analysis and an unremarkable MRI, were included. Eighteen animals (3%) had abnormal CSF, with 50% presenting pleocytosis (with or without an elevated protein count) and 50% hyperproteinoraquia only. Fourteen of these 18 (78%) animals presented with an abnormal neurological examination. In 4 of these, diagnosis and treatment changed based on CSF findings - two dogs were diagnosed with idiopathic cerebellitis, one with meningoencephalitis of unknown origin and one with suspected pachymeningitis. In one case with normal neurological examination and a history of vestibular disease, mildly inflammatory CSF led to short-term treatment with corticosteroids.

In this population of patients with normal MRI and neurological examination, it is unlikely that CSF analysis will reveal an undiagnosed intracranial condition. However, CSF evaluation should be considered as a valuable diagnostic tool in animals with an abnormal neurological examination consistent with intracranial disease.

CLINICAL OUTCOME OF SUBCLINICAL BACTERIURIA IN DOGS FOLLOWING SURGICAL DECOMPRESSION OF HANSEN TYPE I THORACOLUMBAR INTERVERTEBRAL DISC HERNIATION

K. Siu[1], H. Rylander[2], C. Obernberger[2], N. Pfaff[3], F. Hartmann[2], M. Wood[2], K. Viviano[2]

[1] Colorado State University, Fort Collins, CO, USA
[2] University of Wisconsin-Madison, Dept. of Medical Sciences, School of Veterinary Medicine, Madison, Wisconsin, USA
[3] Urgent Care Associate, SAGE Veterinary Centers, Dublin CA, USA

Thoracolumbar intervertebral disc herniation Hansen type I (IVDH Hansen Type I) is a common cause of acute spinal cord injury in dogs. Surgical decompression is the recommended treatment. Secondary urinary dysfunction and subclinical bacteriuria (SBU) have been documented in veterinary patients; antimicrobial therapy is not the current standard of care in human patients with symptomatic bacteriuria. While studies have looked at the prevalence of SBU in dogs, no studies have followed these patients to see whether they develop clinical signs. The aim of this study was to describe the clinical outcome, in the absence of antimicrobial intervention, of SBU in dogs following surgical decompression of IVDH Hansen type I.

Twenty client owned dogs that underwent surgical decompression for IVDH Hansen type I were included in this prospective study. Urinalysis, urine culture, neurologic status, urination status and blood work were evaluated at presentation, discharge, 2 weeks post-operatively and 4-6 weeks post-operatively.

Five dogs had bacteriuria at 4 days (n=1), 2 weeks (4), 4-6 weeks (4), and 9 weeks (1) after surgery. The bacteriuria resolved without any treatment in one dog. Four dogs were treated with antibiotics after persistent bacteriuria at 2 months (1), 4 months (1), and 6 months (2). Incontinence, the only clinical sign in 3 dogs, resolved with treatment. Two dogs did not have clinical signs of bacteriuria.

This study suggests that patients who develop bacteriuria post-operatively should be closely monitored and may not require intervention. Signs of clinical bacteriuria may be limited to new onset of incontinence.

ALTERATION OF Th17 AND TREG CELLS IN DOGS IN THE ACUTE PHASE OF PAINFUL INTERVERTEBRAL DISC HERNIATION

P. Can[1], K. Warzecha[2], R. Carlson[2], J. Nessler[2], A. Tipold[2]

[1] Department of Surgery, Faculty of Veterinary Medicine, University of Ankara, Ankara, Turkey. 2Department of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany.

Intervertebral disc herniation (IVDH) can be associated with neuropathic and inflammatory pain. Neuropathic pain has been suggested to be influenced by the proinflammatory immune response and experimentally and in human studies by alteration of Th17 and Treg cells. In the current study, we hypothesized that the Th17/Treg balance may be altered in dogs with painful IVDH when compared with non-painful IVDH.

Pain was evaluated subjectively during the neurological examination in 52 dogs. The absolute numbers of Th17 and FOXP3 + Treg cells were quantified using a multicolor flow cytometry in blood samples in the acute phase of the disease before surgical treatment. Th17, Treg cells and Th17/Treg ratio were compared statistically between patients with painful (n= 40) and non-painful (n= 12) IVDH, and between ambulatory (n= 16) and non-ambulatory (n= 24) painful IVDH.

There was no statistically significant difference between Tcell values of painful and non-painful dogs ($p>0.05$). Although the mean values of Th17, Treg and Th17/Treg ratio of the non-ambulatory painful IVDH patients increased compared to ambulatory ones, this increase was found statistically insignificant. Rising Th17 cell numbers were accompanied with increased values of Treg cells.

The results of this study show that alteration of T cell subsets might be related with the severity of the inflammation rather than pain in the acute phase of IVDH.

PAEDIATRIC NEUROLOGICAL DISORDERS IN DOGS AND CATS: A RETROSPECTIVE MULTICENTRIC STUDY OF 888 CASES (2003-2019)

A. Cloquell[1,2], R. José-López[1], F. del Ry[2], I. Mateo[2,3], M. Czopowicz[4], R. Gutierrez-Quintana[1]

[1] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, Glasgow United Kingdom
[2] Hospital Veterinario de la Universidad Alfonso X el Sabio, Madrid, Spain
[3] Hospital Veterinario Vetsia, Madrid, Spain
[4] Division of Veterinary Epidemiology and Economics, Institute of Veterinary Medicine, Warsaw University of Life Sciences – SGGW, Warsaw, Poland

Neurological disorders in young animals pose different considerations as to etiology and therapeutic decisions compared with adults. The age of patients can be useful determining the list of differential diagnoses, however, epidemiological studies in young-age dogs and cats with neurological diseases are lacking.
Dogs and cats younger than 12 months of age presented to three referral hospitals were included in this retrospective study.
Eight hundred and eighty-eight patients met the inclusion criteria. Patients younger than 12 months represented 6.5% of all neurological consultations. Cats were significantly younger than dogs (median of 5.1 months vs. 6.7 months; $p<0.001$). Forebrain and intracranial diffuse was the most common neuroanatomical localization in both species. Lower motor neuron signs were more common in cats ($p<0.001$). No diagnosis was achieved in 22% dogs and 27% of cats. Different reasons for the lack of diagnosis were recorded. Among dogs with definitive diagnosis, the most common were congenital anomaly (19%), inflammatory/non-infectious (17%) and trauma (10%). French bulldogs, Chihuahuas, and Pugs were significantly overrepresented for congenital anomalies; Boxers were predisposed to inflammatory/non-infectious diseases, and Yorkshire terriers, crossbreeds and Chihuahuas were predominant in the trauma group. In cats, the most common diagnoses were trauma (26%), inflammatory-infectious (15%) and congenital anomaly (11%).
As generally accepted, congenital, inflammatory and traumatic diseases were overrepresented in the juvenile population of both species. Inability to reach a diagnosis was common, and the causes were multifactorial. Epidemiological data presented here assists with determination of the list of differential diagnoses for young dogs and cats with neurologic signs.

Key words: epidemiology, young, feline, canine, neurolocalisation, neurological diseases.

DIFFUSION TENSOR IMAGING IN SYRINGOMYELIA SECONDARY TO CHIARI MALFORMATION IN CAVALIER KING CHARLES SPANIEL. PRELIMINARY STUDY

A. Banasik[1], K. Owsińska-Schmidt[2], W. Krupińska[1], A. Zimny[3], M. Wrzosek[2,4]

[1] Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Poland
[2] Department of Internal Diseases with a Clinic for Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Poland
[3] Department of General and Interventional Radiology and Neuroradiology, Wroclaw Medical University, Poland
[4] Center of Experimental Diagnostics and Innovative Biomedical Technologies, Wrocław University of Environmental and Life Sciences, Poland

The aim of this study was to find a correlation between clinical assessment and diffusion tensor imaging (DTI) values in the course of Syringomyelia.
Sixteen Cavalier King Charles Spaniel dogs, (eight in the symptomatic and eight in the asymptomatic group), 6-70 months of age (mean 36), 3.5-9.5 kg (mean 7.2), were qualified for the research. All animals underwent the same study protocol that included a clinical and neurological examination followed by MRI examination. DTI was performed with a 1,5 Tesla magnetic resonance scanner (Philips, Ingenia). Two DTI parameters: fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were measured. Measurement of FA and ADC values was made by drawing regions of interest (ROIs) at the level of three intervertebral spaces (C1-C4) in both sympthomatic and asympthomatic group. Image post-processing was done using the Fiber Trak package (Philips Ingenia workstation).
Statistical analysis showed no significant differences in FA and ADC values between the symptomatic and asymptomatic groups. However, decreased FA values were observed in ROI-2 and ROI-3 in the symptomatic group compared to the asymptomatic group. Compared to the asymptomatic group, in the symptomatic group in ROI-1 the same ADC values were observed, while in ROI-2 and ROI-3 an increase in ADC values was noted.
Findings suggest that DTI could be a helpful technique in the study of syringomyelia in Cavalier King Charles Spaniel, in contest of anticipation of eventual development of clinical symptoms in young dogs. DTI values measurements may provide more objective spinal cord microstructure and indirectly also status assessment.

FORAMEN MAGNUM DECOMPRESSION AND MODIFIED CRANIOPLASTY USING TITANIUM MESH PLATE IN SMALL DOGS WITH CAUDAL OCCIPITAL MALFORMATION SYNDROME AND SYRINGOMYELIA

Y. Nakano[1], Y. Nozue[1], K. Nakata[1], S. Kimura[1, 2], H. Kamishina[1, 2]

[1] Dept. of Neurology and Neurosurgery, Animal Medical Center of Gifu University, Gifu
[2] The United Graduate School of Veterinary Sciences, Gifu University, Gifu, Japan

Foramen magnum decompression (FMD) is one of the surgical treatments of Chiari malformation type 1 in humans. FMD is also a treatment option for caudal occipital malformation syndrome (COMS) and syringomyelia in dogs. Cranioplasty (CP) is combined with FMD to prevent postoperative scar tissue formation that compresses the FMD site. However, adequate decompression may not be achieved in small-breed dogs with reported surgical procedures because of the potential risk of damage of the transvers sinus. We performed modified FMD+CP in small-breed dogs and retrospectively investigated the clinical outcomes and complications.

Informed consent was obtained from owners of all dogs prior to surgeries. We performed modified FMD+CP in 5 dogs with COMS and syringomyelia. The occipital bone was removed widely with a great care not to damage the transvers sinus. A pre-contoured titanium mesh plate was placed over the bone defect and secured to the parietal and temporal bones with screws. Procedures were completed without any intraoperative complication in all dogs. Complete resolution of clinical signs was seen in 2 dogs. Cerebellar symptoms such as ataxia and hypermetria remained in three dogs, but QOL of these dogs was improved and the owners were satisfied with the outcome. Three-month postoperative follow-up MRI performed in 3 dogs revealed considerable reduction of the syrinx size.

In conclusion, modified FMD+CP is a safe procedure and leads to considerable reduction of the syrinx in small-breed dogs. This procedure is expected to reduce the risk of recurrence of foramen magnum compression and syrinx formation by postoperative scar tissues.

EVALUATING THE BENEFIT OF CONTRAST MAGNETIC RESONANCE (MR) IMAGES IN DETECTING SPINAL CORD PATHOLOGY: A RETROSPECTIVE STUDY

E. Robinson[1] & P. Freeman[1]

[1] Department of Veterinary Medicine, Queen's Veterinary School Hospital, Cambridge, UK

Gadolinium based intravenous (IV) contrast medium is commonly used in MRI to better characterize underlying pathology. Although possible to detect a previously unidentified lesion, evidence suggests this is unlikely following brain studies.

The objective of this study was to assess whether the administration of contrast media following normal pre-contrast MR sequences is beneficial for detecting a previously unidentified lesion in the vertebral canal.

The MRI database (June 2010 - April 2021) of a large referral hospital was searched for patients with spinal cord imaging where post-contrast MR sequences were acquired. Case details including signalment and neurological examination findings were recorded. Each individual imaging report was assessed to determine if a lesion was visible prior to contrast administration, and those cases were excluded. Cases where no lesion was visible on pre-contrast T1 and T2W sagittal and transverse images were then checked for evidence of a lesion visible on post-contrast T1W images.

375 animals were identified, where 354 showed abnormalities affecting one or more elements of the vertebral canal visible on the pre-contrast MR images. 21 cases were reported normal on pre-contrast images, of which 19 were also reported as normal on post-contrast sequences. Mild contrast enhancement was seen in 2 cases: 1 was considered artefactual, and 1 altered interpretation.

It appears unlikely that contrast medium will detect a lesion in the vertebral canal when pre-contrast images are normal. However, more cases are required with normal pre-contrast images, and imaging reports may not be reliable as a method of assessing this data.

JUVENILE-ONSET MOTOR POLYNEUROPATHY IN 15 CATS

N. Van Caenegem[1], T. Troupel[1], A. Jeandel[2], H. Vandenberghe[3], V. Mayousse[4], S. Blot[1]

[1] Ecole nationale vétérinaire d'Alfort, Univ Paris Est Créteil, INSERM, IMRB, Maisons-Alfort, France
[2] Centre Hospitalier Vétérinaire Pommery, Reims, France
[3] Bristol Veterinary Specialists at Highcroft, CVS Referrals, UK
[4] Centre Hospitalier Vétérinaire des Cordeliers, Meaux, France

Juvenile-onset motor polyneuropathy in cats is infrequently described in the literature and seemed breed-related (Bengal, Siberian, and Snowshoe cats).
This retrospective case series included cats presented with (1) age of presentation < 2 years; (2) acute onset of clinical weakness consistent with polyneuropathy; (3) no evident cause such as diabetes mellitus; (4) electrodiagnostic examination consistent with motor polyneuropathy. Medical records, electrodiagnostic findings, muscle and nerve biopsies were reviewed. Owners were contacted by phone at the time of the study.
Fifteen cats (5 females and 10 males) were included. Nine cats were purebred (Abyssinian, Bengal, Birman, British Shorthair, Devon Rex, Persian, Ragdoll, Siamese). The median age at the presentation was 7 months old. All cats presented reluctance to jump and to stand, and a plantigrade stance. Electromyography showed spontaneous abnormal activity with positive sharp waves and fibrillation potentials in all cats (100% in pelvic limbs, 93% in thoracic limbs). Nerve conduction study was consistent with generalized motor axonal and demyelinating polyneuropathy. Muscle histology was consistent with denervation in all samples. Common peroneal nerve histology was abnormal in 6/8 cats. The median follow up was 7 months. All cats achieved clinical remission. Five cats received corticosteroids: four after the diagnosis and one due to sluggish recovery. Only one cat relapsed after every corticosteroid's discontinuation. The median remission latency after electrodiagnostic examination in other cats was 4 weeks.
This study described a case series of juvenile-onset motor polyneuropathy of unknown origin. Our results indicate that young cats of every breed could be affected.

Submitting author: neurology resident.

MECHANICAL NOCICEPTIVE THRESHOLDS AND ASSESSMENT OF DESCENDING INHIBITORY CONTROLS IN HEALTHY CATS AND THOSE WITH DIABETES MELLITUS

Ruel H.L.M.[1], Bruneau V.[2], Conversy B.[2], Steagall P.V.[1]

[1] Department of Clinical sciences, Faculty of Veterinary Medicine, Université de Montréal, Canada
[2] Centre Hospitalier Universitaire Vétérinaire, Saint-Hyacinthe, Canada

This study aimed to evaluate mechanical nociceptive thresholds (MNT) between cats with diabetes mellitus (DM_{cats}) and healthy controls, and to assess the diffuse noxious inhibitory controls (DNIC) of both groups.
Eight cats with diabetes mellitus and twelve healthy controls were included in a prospective, randomized, blinded study after owner's written consent. MNT (N) were measured using a sharp-tipped 4-cm polypropylene probe to apply increasing pressure bilaterally against the metatarsal pad until paw withdrawal, or when a cut-off was reached (10 N) (Bioseb; MNT_{bio}). MNT were also measured through inflation of a modified blood pressure bladder to the cat's pelvic limb (Topcat Metrology; MNT_{top}). Stimuli were performed in a randomized order by an observer unaware of the cat's condition. The DNIC was assessed by comparing MNT_{top} before and after the application of a conditioning stimulus (inflated blood pressure cuff around the humerus 200 mmHg for 1 minute). A t-test, Spearman's and Pearson's tests were used ($p < 0.05$).
MNT_{bio} of controls were significantly lower (2.1 $\pm$ 0.7N) than those of DM_{cats} (3.6 $\pm$ 1.2N). MNT_{bio} were significantly higher in male (3.3 $\pm$ 1.3N) than in female cats (2.1 $\pm$ 0,4N). DNIC and MNT_{top} were not different between groups. There was a positive correlation (rho = 0.52) between body weight and left tarsus MNT_{bio}.
These results suggest the presence of hypoalgesia in the lower extremities of DM_{cats} and potential loss of sensory function as demonstrated in humans with pain-related diabetic neuropathy. The methodology could not assess the DNIC in healthy and DM_{cats}.

This study was approved by the local animal care committee of the Faculty of Veterinary Medicine, Université de Montréal (19/20-Rech-2035).

Acknowledgements: This study was funded by a Natural Sciences and Engineering Research Council of Canada Discovery grant. Dr. Hélène Ruel was the recipient of the MITACS Research Training Scholarship. The authors want to acknowledge M. Tristan Juette for the statistical analysis.

Flash Presentations

AN EPISODIC MOVEMENT DISORDER IN JUVENILE WEIMARANERS

M. Green[1], M. Lowrie[1], R. Gutierrez-Quintana[2], K. Faller[3], K. Bossens[4], C. Rusbridge[5]

[1] Dovecote Veterinary Hospital, Derby, United Kingdom
[2] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, Glasgow, United Kingdom
[3] The Royal (Dick) School of Veterinary Studies, The University of Edinburgh, Edinburgh, United Kingdom
[4] Veterinary Referral Centre Orion, Herentals, Belgium
[5] Fitzpatrick Referrals, Godalming, United Kingdom

The aim of this retrospective case series was to document an episodic movement disorder in juvenile Weimaraners.

Six Weimaraner dogs were presented for episodes of abnormal gait characterised by increased muscle tone, ataxia and hypermetria, leading to occasional collapse. Abnormal movements consisted of high frequency chorea, predominantly affecting the pelvic limbs, almost becoming ballistic at times. Kyphosis and low head carriage were also consistent features. Age of onset was 3 to 7 months. Excitement or exercise were reported to trigger the abnormal episodes, which could occur multiple times daily with a duration of 5 to 15 minutes. Two dogs displayed intermittent anisocoria associated with the episodes. Based on the episode phenomenology, a paroxysmal dyskinesia was considered most likely.

Resting neurological examination was unremarkable, although the reported abnormalities were elicited by short periods of exercise or excitement in 3/6 dogs. Results of diagnostics including haematology, biochemistry, magnetic resonance imaging, cerebrospinal fluid analysis and electrophysiology were unremarkable. Organic acid testing in one dog revealed evidence of lower production or decreased metabolism of the neurotransmitters serotonin, norepinephrine, epinephrine and dopamine. Treatment with fluoxetine in 3/6 dogs and acetazolamide in 1/6 dogs resulted in a dramatic reduction in episode frequency in all cases.

This episodic movement disorder in Weimaraners appears to share some features of episodic ataxias (EAs) in humans. However, the lack of inter-ictal abnormalities such as myokymia or nystagmus make this less likely. A paroxysmal kinesogenic dyskinesia like that reported in the German shorthaired pointer seems a more appropriate classification.

ORTHOSTATIC TREMOR IN DOGS: 60 CASES (2003-2020)

T. Liatis[1], R. Gutierrez-Quintana[1], L. Mari[2,3], M. Czopowicz[4], D. Polidoro[5], S. Bhatti[5], F. Cozzi[6], F. Tirrito[6], J. Brocal[1,3], R. José-López[1], A. Kaczmarska[1], R. Cappello[7], G. Harris[8], L. Alves[8], C. Rusbridge[9], J.H. Rossmeisl[10]

[1] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, Glasgow, UK
[2] Small Animal Referral Centre, Animal Health Trust, Newmarket, UK
[3] Wear Referrals, Stockton-on-Tees, UK
[4] Division of Veterinary Epidemiology and Economics, Institute of Veterinary Medicine, Warsaw University of Life Sciences – SGGW, Warsaw, Poland
[5] Small Animal Teaching Hospital, Small Animal Department, Faculty of Veterinary Medicine, Ghent University, Ghent, Belgium
[6] Clinica Neurologica Veterinaria NVA, Milan, Italy
[7] North Downs Specialist Referrals, Bletchingley, UK
[8] The Queen's Veterinary School Hospital, Department of Veterinary Medicine, University of Cambridge, Cambridge, UK
[9] Fitzpatrick Referrals Orthopaedics and Neurology, Eashing, UK
[10] Department of Small Animal Clinical Sciences, Virginia-Maryland College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg, USA

Orthostatic tremor (OT) is a movement disorder characterized by high frequency (13-18 Hz) involuntary, rhythmic, sinusoidal movements affecting predominantly the limbs when standing, which are relieved when sitting, lying or walking. OT can be primary (POT) when a sole sign or OT-Plus when concomitant with another neurological disease.

Multicenter retrospective case-series study aiming to expand current knowledge on canine OT. Inclusion criteria was conscious electromyography of a >12 Hz frequency.

Fifty-three cases were diagnosed with POT. Giant breeds represented the majority of cases (44/53); the rest were large (8/53) and medium (1/53). Breeds affected were Great Dane (21/53), Newfoundland (9/53), Retriever (7/53; 4 Labrador, 2 Labrador-cross, 1 Golden Retriever), Irish Wolfhound (6/53), Mastiff (6/53) and other (4/53). All dogs were younger than 2-year-old at onset of signs, except for Retrievers. The major presenting complaint was shaky limbs when standing (45/53). Tremor generalisation was noticed in 62.3% of dogs. Tremors usually affected all limbs (75%), while pelvic limb form or head/trunk involvement were less common. Tremors improved, mainly partially, in 84.9% of dogs treated with phenobarbital, primidone, gabapentin, pregabalin or clonazepam. In Retrievers, remission was less likely. OT-Plus was seen in seven dogs diagnosed with: cervical spondylomyelopathy (n=3), intervertebral disc protrusion (n=1), vascular encephalopathy (n=2) and subclinical neuropathy (n=1; Labrador). In vascular encephalopathy and subclinical neuropathy cases, OT was considered secondary.

POT is a progressive disease of young, purebred, giant/large-breed dogs which responds partially to medications. Retrievers manifest a less-pharmacoresponsive older-dog POT, whilst one manifested OT-Plus associated with subclinical neuropathy.

A CASE SERIES OF THREE DOGS PRESENTING WITH NEUROLOGICAL DEFICITS DUE TO SUSPECTED NUTRITIONAL SECONDARY HYPERPARATHYROIDISM AFTER BEING FED AN EXCLUSIVE DIET OF BARF (BIOLOGICALLY APPROPRIATE RAW FOOD) DIET

L. Nowak[1], S. van Loon[2], N. Bergknut[3]

[1] The IVC Evidensia Referral Hospital Helsingborg, Sweden
[2] The IVC Evidensia Referral Hospital in Waalwijk, The Netherlands
[3] The IVC Evidensia Referral Hospital in Waalwijk, The Netherlands

Nutritional secondary hyperparathyroidism is a well described disease in dogs. Puppies of large breed dogs seem to be highly susceptible due to an elevated calcium requirement. Imbalanced feeding can cause osteoclastic bone resorption with cortical thinning, pathological fractures, and fibrous tissue replacement of bone.
Three pups (from unrelated litters) of medium to large breeds were investigated due to acute onset of pain and difficulties walking. Two of them progressed rapidly with neurological deficits including non-ambulatory para- and tetra paresis respectively. All three pups showed reduced radiodensity of the skeleton. One pup had a CT scan of the lumbar and pelvic area displaying pathological folding fractures of the pelvis and abnormal curvature of the sacrum.
All the three pups had normal blood levels of Calcium. Two of the pups had normal serum phosphor, the third had a slight elevation. All the dogs were fed diets mainly consisting of raw meat.
Two pups were euthanized, and one was subjected to a post-mortem examination, revealing diffuse and severe cortical bone resorption, bone fibrosis and diffuse hyperplasia and hypertrophy of the parathyroid glands. The third pup rapidly responded to pain medication and alternation to a commercial diet.
This case series highlights the risk of young dogs developing severe neurological deficits, with acute onset of pain and paresis, due to nutritional secondary hyperparathyroidism when fed mainly a raw meat diet. Therefore, it is strongly recommended to give a commercial and properly balanced diet to all dogs, especially growing pups of large breeds.

THE EFFECTS OF EXERCISE RESTRICTION ON DOGS AND THEIR OWNERS: A PILOT STUDY

Gemma Walmsley[1,2], Laura Hill[2], Rebecca Fonseka[2], Hannah Robinson[2], Carri Westgarth[3]

[1] Department of Muscouloskeletal Biology, Institute of Lifecourse and Medical Sciences
[2] Department of Veterinary Science, Small Animal Teaching Hospital
[3] Department of Livestock and One Health, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Leahurst, Neston, Cheshire, UK

The mental and physical health benefits of regular exercise are well documented for humans and dogs. Lack of exercise is a risk factor for canine obesity, poor physical health and undesirable behaviour. Exercise restriction is often recommended for conservative and post-operative management of orthopaedic and neurological conditions in veterinary patients, yet the impact of exercise restriction on dogs and their owners is poorly documented.
Two questionnaire-based studies employing closed and open questions were carried out first targeting clients of the Small Animal Teaching Hospital (SATH) whose pets were required to undergo a period of exercise restriction ≥ 4 weeks and a second surveyed veterinary surgeons in neurology and orthopaedic services. We found that 40% of owners with dogs on restricted exercise found this difficult and a range of effects on the dogs and their owners were reported. The majority of veterinary surgeons who regularly recommend rest also felt 50-75% of dogs and owners struggle with exercise restriction and it has a large effect on their quality of life. We also carried out a wider internet survey of dog owners and they reported a significant reduction in dog quality of life and effects on mental well-being of both dogs and their owners during exercise restriction.
In conclusion, there are mental/behavioural and physical consequences for many dogs and their owners from a period of exercise restriction. Further research will aim to identify which dogs/owners are at risk and how to prevent the negative effects of exercise restriction without affecting recovery.

VERTEBRAL AND ENDPLATE CHANGES IN DOGS WITH SUSPECTED FIBROCARTILAGENOUS EMBOLIC MYELOPATHY

C. Llanos[1], R. Dennis[2], M.A. Genain[3], L. Alves[3]

[1] Dept. Diagnostic Imaging, Southfields Veterinary Specialists, United Kingdom
[2] Dept. Diagnostic Imaging, Dick White Referrals, United Kingdom
[3] Dept. Neurology and Diagnostic Imaging, The Queen's Veterinary School Hospital, University of Cambridge, United Kingdom.

Fibrocartilaginous embolic myelopathy (FCEM) is a frequently diagnosed disease in dogs characterised by ischemic infarction of the spinal cord due to fibrocartilaginous material embolization. Endplate signal intensity changes such as Schmorl´s nodes and vertebral body marrow adjacent to the endplates changes (Modic changes) have been described both in human and dogs.
An observational cohort multicentre retrospective study was conducted to describe and characterise vertebral and endplate changes and its prevalence in dogs presented with MRI features of FCEM and compare those changes with a control group of dogs presented with presumptive acute non-compressive nucleus pulposus extrusion (ANNPE). Additionally, vertebral and end plate changes were compared between high field and low field MRI studies.
Vertebrae closely related to the spinal cord lesion was analysed using MRI. One vertebra cranial and one caudal to the affected region was also analysed. The disc space closest to the suspected FCEM/ANNPE was recorded, stating if the endplate (cranial or caudal) was normal or abnormal. If abnormal, focal (including Schmorl's nodes) or diffuse irregularities was recorded. Modic changes if present will be categorized according to described current literature.
A total of 77 dogs with suspected FCEM and 46 dogs with suspected ANNPE were reviewed.
All dogs from the ANNPE groups failed to show any vertebral or endplate changes. 4/78 dogs showed Modic changes in the FCEM group.
In conclusion, the results of this study suggest that dogs with suspected ANNPE do not appear to show vertebral or endplate changes on MRI. Dogs with suspected FCEM rarely show changes on MRI.

Ethical approval
This study was approved by the ethical committee of the University of Cambridge.

USEFULNESS OF FOLLOW UP MRI IN DOGS WITH DISCOSPONDYLITIS: A RETROSPECTIVE EVALUATION

M.I. de Freitas[1], E. Vettorato[2], G.B. Cherubini[1], A. Caine[3]

Dick White Referrals

[1] Neurology and Neurosurgery department
[2] Anaesthesia department
[3] Diagnostic Imaging department, Suffolk, U.K.

The usefulness of follow-up Magnetic Resonance Imaging (MRI-2) to assist clinical decision making in dogs treated for discospondylitis is unknown. This cross-sectional retrospective study investigated the features of MRI-2 in dogs treated for discospondylitis, and if MRI-2 can predict the presence or absence of clinical signs. Dogs were included if they met the criteria for diagnosis of discospondylitis and if they underwent MRI-2 a minimum of 28 days following initial MRI (MRI-1). After comparing MRI-1 and MRI-2 images, an observer, blinded to the dog's clinical signs, subjectively classified the discospondylitis as active or inactive in two separate occasions. A second observer categorized dogs as symptomatic or asymptomatic, based on the presence or absence of clinical signs at the time of MRI-2. Data were analysed using Fisher's Exact or McNemar tests; logistic regression was performed.

A total of 25 dogs were included: 16 dogs were asymptomatic and 9 were symptomatic. Based on MRI-2, 20/25 (80%) and 18/25 (72%) dogs were considered to have active discospondylitis on the first and second assessment, respectively ($p = 0.62$). No MRI-2 features were predictive of the dogs' clinical status.

The sensitivity and specificity of active and inactive discospondylitis to predict symptomatic or asymptomatic dogs were 40% (21.88 – 61.34) and 80% (37.55 – 98.97), after first assessment, and 38.9% (20.31 – 61.38) and 71.4% (35.89 – 94.92) on second assessment.

The clinical status of dogs treated for discospondylitis cannot be predicted by MRI-2, with no evidence to recommend routine use to guide clinical decision making, particularly in asymptomatic patients.

A NEW FORM OF HEREDITARY ATAXIA IN AUSTRALIAN SHEPHERD. PHENOTYPIC AND GENETIC CHARACTERIZATION

Catherine Escriou[1], Nelly Laurent[1], Thibaut Troupel[2], Vidhya Jagannathan[3], Eglantine Noblet[1], Stéphane Blot[2], Tosso Leeb[3], Marie Abitbol[1,4]

[1] Univ Lyon, VetAgro Sup, Campus vétérinaire de Lyon, Marcy l'Etoile, France
[2] Ecole nationale vétérinaire d'Alfort, 94700, Maisons-Alfort, France
[3] Institute of Genetics, Vetsuisse Faculty, University of Bern, Bern, Switzerland
[4] Institut NeuroMyoGene, CNRS UMR5310, INSERM U1217, Faculté de Médecine, Rockefeller, Université Claude Bernard Lyon I, Lyon, France

Hereditary ataxia are extremely common among dog breeds with numerous and various etiologies. We describe a new form of hereditary ataxia to our knowledge neither reported in four related Australian shepherds.

Phenotype

Owners noticed first signs between 4 months to 19 months (mean 9.5 months). They described bunny hoping, wobbly and stiff gait on pelvic limbs, difficulties to walk up or down the stairs and to get up. Neurological examination at that stage revealed moderate ataxia more obvious on pelvic limbs with slight hypermetria, slight to no proprioceptive deficits on pelvic limbs and discrete intention tremors for some dogs. These motors symptoms worsened progressively, and dogs were no more able to walk without help from the age of 30 months to 44 months. Neurological examination at this stage revealed tetraparesis/tetraplegia with severe spasticity on pelvic limbs, proprioceptive deficits on four limbs and absent menace response for some dogs. Neuroanatomical diagnosis was diffuse/multifocal central nervous system lesion. MRI (brain and spinal cord) was unremarkable at 21 months but revealed a cerebellar atrophy at 60 months. Two dogs were euthanized at 30 and 39 months, brain histology revealed diffuse demyelination and oligodendrogliosis.

Genetics

Pedigree analysis revealed autosomic recessive transmission. Pangenomic analysis (whole genome sequencing) identified a single frameshift variant that was predicted to be deleterious. All affected dogs were genotyped homozygous for the variant. Obligate carriers were heterozygous.

Additional analyses are ongoing to better characterize the pathogenesis of the disease.

HEAD TURN: A STUDY OF NEUROLOCALISATION

A. Nagendran A.[1], R. Jose-Lopez[2], A. Suñol[3], J. Brocal[4], R. Gonçalves[1]

[1] Institute of Infection, Veterinary and Ecological Sciences, Small Animal Teaching Hospital, University of Liverpool, United Kingdom
[2] Veterinary Clinical Services, Small Animal Hospital, University of Glasgow, United Kingdom
[3] Royal (Dick) School of Veterinary Studies and the Roslin Institute, University of Edinburgh, Roslin, UK
[4] Wear Referrals Veterinary Hospital, Derby, UK

Head turn and pleurothotonus have been two interchangeable terms that are frequently used to describe postural abnormalities as part of a neurological examination in veterinary patients. The presence of these abnormal signs has traditionally been attributable to lesions affecting the prosencephalon. The aims of this study were to identify whether lesions in other locations of the central nervous system (CNS) can cause a similar presentation.

Dogs were prospectively included if they had photographic or video evidence of head turn. All cases were required to have signalment, neurological examination and advanced imaging. Animals were excluded if the imaging findings represented multifocal pathology.

Forty-four dogs met the inclusion criteria. Imaging localisation was made to forebrain [23/44], brainstem [8/44], cerebellum [5/44] and cervical spinal cord (C1-C5) [7/44]. Within the forebrain cases, 10/23 were localised to diencephalon, 8/23 to cerebral cortex and 5/23 a combination of the two areas. Localisation on neurological examination was correct in 21/23 forebrain cases, 6/8 brainstem cases, 6/7 cervical cases and 5/5 cerebellar cases. An ipsiversive head turn was identified in 22/23 forebrain cases, 7/8 of the brainstem cases, 5/5 of cerebellum cases. An aversive head turn was identified in 6/7 cervical cases. Concurrent pleurothotonous was identified in 7/7 cervical cases, 4/8 brainstem cases, 10/23 forebrain cases and 0/5 cerebellum cases.

In this study, we have identified further anatomical sites that could elicit a head turn. Therefore the presence of a head turn, alongside the rest of the neurological examination, should not preclude other neurolocalisations other than forebrain.

URINARY NEUROTRANSMITTER PATTERNS ARE ALTERED IN CANINE EPILEPSY

T. Schmidt[1], S. Meller[1], S.R. Talbot[2], B.A. Berk[3,4], T.H. Law[4], S.L. Hobbs[4], R.M.A. Packer[4], H.A. Volk[1]

[1] Dept. of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany
[2] Institute for Laboratory Animal Science, Hannover Medical School, Hannover, Germany
[3] BrainCheck.Pet – Tierärztliche Praxis für Epilepsie, Sachsenstraße, Mannheim, Germany
[4] Dept. of Clinical Science and Services, Royal Veterinary College, Hatfield, UK

Epilepsy is the most common chronic neurological disease in humans and dogs. Epilepsy is thought to be caused by an imbalance of excitatory and inhibitory neurotransmission. The primary pathway of neurotransmitter elimination is via the urine. In human medicine, non-invasive urinary neurotransmitter analysis is used for the management of medical conditions such as depression and attention-deficit hyperactivity disorder, but not as yet for epilepsy.

The aim of the current study was to investigate if urinary neurotransmitter profiles differ between dogs with epilepsy and controls. A total of 223 urine samples were analysed from 63 dogs diagnosed with idiopathic epilepsy (IE) and 127 healthy control dogs without epilepsy. The quantification of seven urinary neurotransmitters was performed utilising High-performance liquid chromatography Triple Quadrupole MS/MS technology.

A significant difference between urinary neurotransmitter levels (glycine, serotonin, norepinephrine/epinephrine ratio, gamma-aminobutyrate/glutamate ratio) of dogs suffering from IE and the control group was found, when sex and neutering status were accounted for.

The results of this study indicate that the imbalances in the neurotransmitter system which causes epileptic seizures may lead to altered neurotransmitter elimination in the urine of affected dogs and may serve as biomarkers for diagnostics and treatment monitoring. More research on this topic needs to be undertaken to better understand the association of neurotransmitter deviations in the brain and their association with urine neurotransmitter concentrations in dogs with IE.

THE REIBERGRAM IN NEUROLOGICAL DISEASES OF DOGS

M. Püschel[1], F. Freise[2], R. Carlson[1], A. Tipold[1], J. Neßler[1]

[1] Dept. of Small Animal Medicine and Surgery
[2] Institute for Biometry, Epidemiology, and Information Processing, University of Veterinary Medicine Hanover, Germany

In various neurological diseases the total protein content in cerebrospinal fluid (CSF) might be increased. To distinguish blood-CSF barrier dysfunction (BD) and intrathecal immunoglobulin (Ig) synthesis (ITS) albumin, mainly produced extracranially, can be used as a reference marker for BD. But hitherto used linear regression models are insufficient in detecting ITS or BD.
In the present study a hyperbolic quotient graph (="Reibergram") was developed based on albumin CSF/serum quotients (QAlb) and IgA CSF/serum quotients (QIgA) from 6 healthy Beagles and 38 client-owned dogs with diseases in which an isolated BD was suspected. Quantile regression resulted in the hyperbolic curve,
$QLim\ (IgA) = 0.13 \sqrt{((QAlb)^2 + 11.9 \cdot 10^{-6})} - 1.01 \cdot 10^{-3}$, where QLim (IgA) describes the upper limit of physiological value of QIgA. The upper physiological value of QAlb was calculated with a 95% confidence interval and is 2.22. Both lines QAlb and QLim (IgA) were transferred into a graph, where they divide the diagram into four sections: normal, isolated BD, isolated ITS of IgA and combined BD & ITS of IgA. The canine Reibergram was validated with 118 dogs suffering from various neurological diseases and detects diseases with suspected BD with a sensitivity and specificity of 81% and 89% respectively, and diseases with suspected ITS of IgA with a sensitivity of 85% and specificity of 88%.
The canine IgA Reibergram allows the clinician to draw conclusions about the function of the blood-CSF barrier and ITS of IgA and might aid as an additional tool in the diagnostics of neurological diseases in dogs.

EVALUATION OF THE EFFECT OF PHENOBARBITAL ADMINISTRATION ON BIOCHEMISTRY PROFILE WITH FOCUS ON SERUM LIVER CONCENTRATIONS IN CATS WITH EPILEPSY: A MULTI-CENTER STUDY

M. Hermans[1], M. Charalambous[1], A. Pakozdy[2], U. Eisl-Glantschnigg[2], J. Neßler[3], S.A.E. Van Meervenne[4], G. Serrano[1], I. Cornelis[1], L. Van Ham[1], D. Paepe[1], B.J.G. Broeckx[5], S.F.M. Bhatti[1]

[1] Small Animal Department, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[2] Clinical Unit of Internal Medicine Small Animals, University of Veterinary Medicine, Vienna, Austria
[3] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Hannover, Germany
[4] AniCura Kalmar Animal Clinic, Kalmar, Sweden
[5] Laboratory of Animal Genetics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

Phenobarbital (PB) is the most common antiseizure drug (ASD) used for the management of feline epilepsy. In dogs, PB is known to cause serum liver enzyme induction and hepatotoxicity especially after long-term administration or high serum PB concentrations. In cats, insufficient evidence is available to draw similar conclusions. The aim of this study was to evaluate the effect of PB administration on the serum biochemistry profile in cats with epilepsy.

Medical records of four veterinary center were retrospectively reviewed for cats with epilepsy receiving PB treatment. Serum alkaline phosphatase, alanine transferase (ALT), aspartate transaminase and gamma-glutamyl transferase activities and total bilirubin, bile acids, glucose, albumin, total protein, urea and creatinine concentrations before and during PB administration were recorded. Serum PB concentration was also recorded, when available.

Thirty-three cats with a median age of 3 years met the inclusion criteria. Idiopathic or structural epilepsy was diagnosed in 25 (76%) and 8 (24%) cats, respectively. The follow-up period ranged from 1 to 62 months. No statistically significant increase in serum liver enzymes and other evaluated biochemistry parameters was found comparing parameters at baseline to parameters during PB treatment.

PB administration did only result in serum hepatic enzyme induction in a minority of cats and no increase was found for the other biochemical abnormalities in cats. This strengthens the safety profile of PB as an ASD in cats.

FELINE TEMPORAL LOBE EPILEPSY: SEVEN CASES OF HIPPOCAMPAL AND PIRIFORM LOBE NECROSIS IN ENGLAND AND LITERATURE REVIEW

B. Scalia[1], A. Caine[1], R. Pittaway[1], G. B. Cherubini[1]

[1] Dick White Referrals, Six Mile Bottom, UK

Feline hippocampal and piriform lobe necrosis is an uncommon acute epileptic condition resembling human autoimmune limbic encephalitis and temporal lobe epilepsy. Seizures are typically focal and feature uni- or bilateral orofacial or head twitching, hypersalivation, lip smacking, mydriasis, vocalisation and motionless staring, with inter-ictal behavioural changes such as unprovoked aggression and rapid running. Emerging evidence supports an autoimmune aetiology, although disruption of hippocampal architecture secondary to brain neoplasia has also been recognised. Most commonly, however, the underlying cause remains unknown. Diagnosis is achieved clinically and with brain MRI; electroencephalography and voltage-gated potassium channel-complex autoantibodies are currently subject of research. Affected cats are frequently refractory to conventional antiepileptic treatment.

Seven cases of feline hippocampal and piriform lobe necrosis are described with particular emphasis on clinical, radiographic and histopathological correlations. The MRI abnormalities varied from case to case, with T2W hyperintensity and enlargement of the hippocampi commonly identified, accompanied by variable degrees of contrast enhancement. Fibrillary astrocytoma and lymphoma were diagnosed post mortem in two cats. Considering the existing literature, our cases and the fact that different aetiologies have been associated with similar presentations, the hippocampus and piriform lobe are proposed as neuroanatomical localisation for focal seizures with orofacial involvement in cats, regardless of aetiology.

Following review of the literature and comparisons with human medicine, potential complicating factors such as pyrexia and peri-ictal urinary dysfunction are also discussed.

This work involved the use of non-experimental animals only and established internationally recognised high standards of individual veterinary clinical patient care were followed, therefore ethical approval was not required.

The study was carried out during the submitting author’s Neurology Internship, which has just been completed. The submitting author will begin his ECVN residency in July 2021.

CONCENTRATION OF C REACTIVE PROTEIN IN SERUM AND CEREBROSPINAL FLUID IN DOGS WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN OR STEROID RESPONSIVE MENINGITIS ARTERITIS

R. Cavalerie[1], S. Beurlet[2], S. Piazza[1]

[1] Neurology and neurosurgery department, Small animal Referral Centre Languedocia, France
[2] VEBIO Veterinary laboratory, France

Meningoencephalitis of unknown origin (MUO) and steroid responsive meningitis arteritis (SRMA) are the two most frequent noninfectious inflammatory disorders affecting canine central nervous system. C reactive protein (CRP) is frequently measured in dogs' serum with SRMA to support the diagnosis and monitor the treatment response. To our current knowledge, CRP concentration has never specifically been studied in MUO cases.

A prospective observational study, still in progress, is designed to evaluate CRP concentrations in serum and cerebrospinal fluid (CSF) of dogs suspected suffering from MUO (n=18) or SRMA (n=12). The dosages are performed at time of diagnosis and during the follow-up when possible.

Preliminary results show normal measurements of CRP in both serum and CSF in all MUO cases at time of diagnosis and at follow-up (between 5 and 7 months). At initial presentation, CRP concentration was moderately to severely elevated in blood in all cases of SRMA with a median value of 120,2 +/- 83,4 mg/L, whereas it was inferior to 7 mg/L (considered as normal) in CSF in all cases. MUO cases frequently display normal blood cell count or biochemistry profile as well as normal CRP concentrations in serum and CSF, which could correlate with a confined inflammation to the central nervous system in this noninfectious inflammatory condition. Results concerning CRP concentration in serum in SRMA cases are consistent with previous studies.

In conclusion, CRP concentrations in serum and CSF aren't useful in the diagnosis of MUO, and evaluation of CRP in CSF in dogs with suspected SRMA doesn't seem to be a reliable marker of inflammation compared to serum CRP.

COMPARISON OF SERUM CK AND AST LEVELS IN CANINE PROTOZOAL MENINGOENCEPHALITIS AND NON-INFECTIOUS MENINGOENCEPHALITIS

Jones Bs & Harcourt-Brown Tr.

Langford Vets Small Animal Hospital, Bristol, BS40 5DU, United Kingdom

Creatine Kinase (CK) and aspartate transaminase (AST) are two enzymes whose serum concentrations can be elevated with myositis associated with canine Toxoplasma and Neospora infection.

We hypothesised that serum concentrations of CK and AST can be used as a rapid screen for predicting a positive serology with Toxoplasma gondii or Neospora caninum in dogs compared to those with non-infectious meningoencephalitis.

Retrospective case-control study - 80 dogs with meningoencephalitis based on magnetic resonance imaging and cerebrospinal fluid analysis. Serological cut-offs (>1:800 IFA for Neospora and >1:400 IgG or/and >1:64 IgM for Toxoplasma) categorized dogs as infected (n=21, all Neosporosis) or non-infected (n=59). Concentrations of CK and AST between infected and non-infected groups were compared with Mann-Whitney-U and ROC analysis.

Serum CK and AST concentrations were significantly increased (p<.0001) in dogs with a positive serology for Neospora [CK 1334 U/l (281-3633) and AST 124 U/l (59-333)] compared to non-infectious cases [CK 215 U/l (69-683) and AST 36 U/l (19-139)]. A CK cut-off at 485U/l had a 95.24% sensitivity and 96.61% specificity with a negative predicative value of >99%. An AST cut-off at 57.50U/l had a 94.44% sensitivity and 85.71% specificity with a negative predicative value of 99%.

In conclusion serum CK and AST concentrations can be used as an indicator for increasing the level of suspicion for active clinical infection in dogs with Neospora whilst awaiting serological tests for dogs with a meningoencephalitis.

APPLICATION OF MACHINE LEARNING TO GUIDE THE CLINICAL REASONING IN DOGS PRESENTING WITH SEIZURES AND A NORMAL INTER-ICTAL NEUROLOGICAL EXAMINATION

C. Smith[1], T. Harcourt-Brown[1,2], M. Bailey[2]

[1] Langford Veterinary Services, Neurology, United Kingdom.
[2] University of Bristol, Veterinary Sciences, United Kingdom.

Background Brain MRI is currently recommended for inter-ictally normal epileptic dogs if they are less than 6 months or older than 6 years of age. This range is based on small datasets and does not take into account other factors such as breed that may improve its accuracy.

Objectives: To assess the ability of machine learning tools (decision trees and random forests) to improve these recommendations.

Animals: 326 dogs presenting with generalised seizures and a normal inter-ictal neurological examination.

Methods: Retrospective study using machine learning algorithms to formulate a decision tree and random forest for the clinical reasoning of dogs presenting with seizures.

Results: Dogs presenting with an age of first seizure of <416 weeks (8 years) have a 9% chance of clinically significant abnormalities on MRI. This is decreased to 4% when certain breeds were excluded. Age at first seizure and breed are the most clinically relevant factors for the clinical reasoning of dogs presenting with seizures.

Conclusions: and clinical importance This retrospective study provides a novel diagnostic approach to the investigation of seizures in dogs with a normal inter-ictal neurological examination. We suggest an age of >8 years should be considered as the main determinant for performing an MRI scan in dogs presenting for seizures with a normal inter-ictal neurological examination.

USE OF 3D-PRINTING TECHNOLOGY TO CREATE A SIMULATOR FOR CEREBROSPINAL FLUID SAMPLING AT THE LUMBAR SUBARACHNOID SPACE

M. Madden[1], R. Collins[2], T. Schwarz[1], A. Suñol[1]

[1] Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK.
[2] Edinburgh College of Art, University of Edinburgh, Edinburgh, UK.

Cerebrospinal fluid (CSF) sampling at the lumbar subarachnoid space (LSS) is technically challenging to learn. Currently, training relies on cadaver availability or performance within a clinical scenario. This study aims to develop an affordable, realistic simulator to train in this technique. Using 3D-printing technology, we produced an anatomically precise model of the lumbosacral vertebral column of a healthy, adult dog. The model was augmented with synthetic materials and a fluidic system to permit successful collection of CSF. The simulator was validated by experts, who rated it highly across multiple criteria. Final year students were recruited to take part in practical sessions using either the simulator (N=16) or a cadaver (N=16). Performance was recorded for each participant and feedback was obtained using an anonymous online survey. Student performance was similar between groups (p=0.39), with 87.5% and 68.75% of students in the simulator and cadaver group, respectively, successfully placing the needle into the LSS. All successful students in the simulator group were able to obtain a CSF sample, compared to none in the cadaver group. No difference in the number of attempts was detected between groups (p=0.7), with the majority of students taking more than 3 attempts. User experience was similar between groups, with 93.8% of students in each group rating the session as a positive learning experience. In summary, we demonstrate the validity of a novel, low-cost and reproducible simulator, which can be used for teaching CSF sampling at the LSS.

UTILITY OF A FLEXED NECK SAGITTAL MRI SEQUENCE PRIOR TO CSF SAMPLING FROM THE CEREBELLOMEDULLARY CISTERN IN DOGS

D. Sivolapenko[1], J. Duncan[1], C. Eivers[2], T. Liuti[1], K. Marioni-Henry[1]

[1] Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK
[2] Veterinary Specialists Auckland, Imaging Service, Auckland, New Zealand

Cerebrospinal fluid (CSF) collection from the cerebellomedullary cistern (CM) of dogs with congenital or acquired cerebellar herniation could lead to serious complications. It is anecdotally more challenging in large brachycephalic breeds possibly due to the increased distance between the skin and CM. The first objective of this study was to assess whether flexed-neck sagittal MRI sequences would assist in the decision-making process of collecting CSF from the CM. The second objective was to examine the dimensions of the CM measured in neutral and flexed views, and whether cranial index (CI), skull height and body weight correlated with the distance of the CM from the skin surface. Forty-one dogs of various breeds were included in the study. Mild cerebellar herniation was detected in 23/41 (56%) of the flexed-neck views versus none in the neutral views. The CM area was significantly larger in flexed-neck views than in neutral views ($p<0.05$). In 29% of the cases (12/41) the trajectory of the needle intersected the cerebellar vermis. There was a positive correlation between the distance of the CM from the skin and body weight ($p<0.05$) and skull height ($p<0.05$), but not with the CI ($p=0.23$). These findings suggest that performing a cisternal CSF collection in large dogs with an increased skull height and body weight may be more challenging and that a flexed view could help in assessing the degree of cerebellar herniation and planning the procedure; further studies will be necessary to confirm these findings in a larger population of dogs.

NONINVASIVE MONITORING OF INTRACRANIAL PRESSURE WAVES USING BCMM 2000 BRAIN4CARE MONITOR IN DOGS WITH MYELOPATHIES UNDERGOING MYELOGRAPHY

M.V. Bahr Arias[1], N.L.F.C. Rocha[1], D.E. Bortolucci[1], G.S. Cardoso[1]

[1] Dept of Veterinary Clinics, State University of Londrina, Londrina, Paraná, Brazil

Monitoring of intracranial pressure (ICP) is essential in the evaluation and treatment of neurologic diseases; however, this procedure is rarely performed because of the complications and limitations of the available techniques. A noninvasive ICP monitoring device (ICP-Ni) has been used in humans to analyze cerebral complacency, with good results. The device detects cranium deformations via a strain gauge sensor, registering ICP waves. These waves have three peaks and the P2/P1 ratio is related with cerebral complacency. The objective of this study was to determine whether the BCMM-2000 Brain4care monitor detects changes in ICP dynamics caused by contrast injection into the subarachnoid space in dogs undergoing myelography.

This study was approved by the Ethics Committee for the Use of Animals (n. 10052.2018.88). The ICP-Ni was monitored in 6 dogs with myelopathies before (M1), during (M2), and after (M3) contrast (iohexol) injection into the subarachnoid space. Cerebrospinal fluid was collected for analysis prior to contrast injection. Subarachnoid pressure (PS) was simultaneously monitored in 3/6 dogs. Correlation between both methods was performed using Pearson's coefficient. The P2/P1 was greater at M2 for both monitoring methods ($p<0.05$). At M3, values were similar to M1, due to return of brain complacency. There was a strong correlation ($r = 0.73$, $p = 0.027$) between both ICP monitoring methods. Speed of contrast administration, degree of spinal cord compression, and volume of CSF previously collected may affect P2/P1 ratio.

The BCMM-2000 Brain4care monitor was effective in detecting changes in ICP dynamics in dogs undergoing myelography.

DO HASTE MRI SEQUENCE FINDINGS CORRELATE WITH CLINICAL SIGNS IN DOGS WITH THORACOLUMBAR DISC EXTRUSIONS?

S.H. Khan[1], P. Freeman[1]

[1] Queen's Veterinary School Hospital, Cambridge, United Kingdom

Thoracolumbar intervertebral disc extrusions are a common reason for veterinary hospital admission. Whilst multiple factors, including degree and length of compression and rate of onset of clinical signs, have been tested for correlation with clinical severity, no factor has been reliably shown to correlate with severity. Half-Fourier Acquisition Single-Shot Turbo Spin Echo (HASTE) MRI sequences highlight the dorsal and ventral CSF columns and have been used to highlight spinal cord swelling in dogs with thoracolumbar disc extrusions. This welling has been used as a predictor of progressive ascending-descending myelomalacia but has not been correlated with neurological grade.

Dogs less than 15kg who were non-ambulatory due to suspected thoracolumbar intervertebral disc extrusions were prospectively recruited for a study into conservative management. MRI studies were undertaken under sedation including HASTE sequences. The length of CSF disruption was then divided by the length of the L2 vertebra and compared to clinical severity.

No statistically significant difference was demonstrated between the mean CSF disruption and neurological grade ($p=0.1694$) but there was a significant difference in the mean CSF disruption in those who retained deep pain perception and those who did not ($p=0.02054$). Time to loss of ambulation was also found to not be correlated with CSF disruption ($p=0.9519$)

In conclusion, the length of CSF disruption of HASTE MRI sequences in dogs less than 15kg suffering from intervertebral disc extrusions may be correlated with a loss of deep pain perception.

LONG TERM OUTCOME IN DOGS WITH COMPLETE SENSORY AND MOTOR LOSS FOLLOWING THORACOLUMBAR INTERVERTEBRAL DISC HERNIATION

A. Barriere[1], S. Martin[1], F-X. Liebel[1], K. Lazzerini[1], T. Harcourt- Brown[1], A. Fadda[1]

[1] Langford Veterinary Services, University of Bristol, Langford, Bristol, United Kingdom

Current veterinary research on spinal cord injury secondary to thoracolumbar intervertebral disc herniation (TL-IVDH) in dogs, mainly focuses on factors influencing functional recovery, but the fate of dogs left with persistent sensory and motor loss remains uncertain and little information exists on the impact of such disability on Owners. Outcome evaluation of a questionnaire-based survey focused on survival of 39 dogs suffering complete sensory and motor loss after TL-IVDH and factors impacting both dogs and Owners' life is provided.

Preliminary results indicate that despite not regaining motor or sensory function, 78% of dogs were still alive one year after discharge. The remaining were euthanized, due to a perceived decreased quality of life (QOL) and not to associated morbidities. Morbidities were mainly related to feet injury, cleanliness (>50%) and urinary tract infections (44.4%). Conversely, bladder management and wheels were well tolerated in most patients. Whilst overall QOL of paralyzed and incontinent pets is perceived as very good, Owner's QOL is profoundly impacted, due to sacrifice of personal time and house cleanliness. For 44.5% of Owners the worry of their pet suffering remains a stressful factor. 61% of respondents had to adapt their home to pet's needs. Whilst 88.8% of owners found discharge information very useful, 50% additionally turned to web resources and social media.

Although uncommonly, disability remains a reason for euthanasia. Accurate and up to date information on nursing care and logistical aspects should be prioritized at discharge to ensure a more manageable life with a disabled pet.

SAFETY OF EARLY POSTOPERATIVE HYDROTHERAPY IN DOGS UNDERGOING THORACOLUMBAR HEMILAMINECTOMY

A. Mojarradi[1], S. De Decker[2], C. Bäckström[1], N. Bergknut[3]

[1] The IVC Evidensia Referral Hospital in Helsingborg, Sweden
[2] Dept. of Clinical Science and Services, Royal Veterinary College, University of London, United Kingdom
[3] The IVC Evidensia Referral Hospital in Waalwijk, The Netherlands

Hydrotherapy is increasingly incorporated in the postoperative care of dogs with thoracolumbar intervertebral disc extrusion (IVDE). Although there are no evidence-based guidelines on when to start hydrotherapy, early initiation could theoretically be associated with an increased risk of postoperative complications.
Eighty-three dogs commencing hydrotherapy within five days after surgical treatment for thoracolumbar IVDE were retrospectively included. All postoperative complications were recorded during a follow-up period of minimum 30 days. A complication was deemed major if there was a need for hospitalisation, surgery or if the dog died as a direct consequence of the complication. A complication was deemed minor if outpatient medical treatment was sufficient. No ethical approval was necessary for this study.
Hydrotherapy, including swimming and/or underwater treadmill, was started with a mean of 2.7 (1-5) days after surgery. Ten minor and 16 major complications were recorded in 26 dogs. These complications included euthanasia (n=13, due to insufficient neurological improvement n=8), surgical wound inflammation (n=5), diarrhea (n=4), surgical site infection (n=1), further extrusion of the originally operated intervertebral disc (n=1), urinary tract infection (n=1) and dermatitis (n=1). Twenty-four of the recorded complications were considered unlikely to be directly caused by the initiation time of hydrotherapy. The remaining two complications, including surgical site infection and further extrusion of calcified nucleus pulposus, may have been related to early initiation of hydrotherapy.
Starting hydrotherapy within five days after thoracolumbar hemilaminectomy may be associated with an increased risk for complications. The safety and benefits of postoperative early hydrotherapy need to be further investigated.

LONG-TERM FOLLOW-UP OF THE SPINAL SEGMENTAL STABILISATION TECHNIQUE FOR THE SURGICAL TREATMENT OF DORSAL HEMIVERTEBRAE ASSOCIATED WITH KYPHOSIS

D.E. Mavrides[1], M. Charalambous[2], P.M. Freeman[1]

[1] Department of Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge, CB3 0ES, UK
[2] Faculty of Veterinary Medicine, Ghent University, Campus Merelbeke, Salisburylaan 133, 9820 Merelbeke, Belgium

Optimal treatment for myelopathy associated with thoracic congenital vertebral malformation (CVM) in brachycephalic breeds has not yet been established. Published surgical techniques include spinal segmental stabilisation (SSS) surgery. The aim of this study was to report chronic complications (>2 months post-operatively) following SSS in a group of dogs.

Follow-up medical records (2006-2020) of 12 cases that underwent SSS at three university hospitals were retrieved and analysed with a minimum follow-up period of 1 year. The data collected included signalment, duration of clinical signs and neurological examination pre-operatively, imaging results, neurological status immediately post-operatively and at follow-up periods of >12 months including complications.

All dogs showed initial neurological improvement which was sustained in most cases and 7 of these showed chronic complications. Four out of these seven were managed without further surgical intervention although two of these dogs were severely impaired. Most chronic complications were similar in nature with overlapping features, and they were all associated with implants.

This case series demonstrated that the rate of chronic complications associated with SSS was high (58%) but the majority of these did not require revision surgery. Those requiring revision surgery did not deteriorate post-operatively suggesting that long-term improvement does not require the permanent presence of implants. The findings of this study support the continued use of SSS in selected cases of CVM where neurological deficits are relatively mild and there is owner awareness of potential chronic complications.

Ethical submission was obtained for the study.

EVALUATION OF THE EFFECT OF EXTRADURAL ADMINISTRATION OF MORPHINE FOR POSTOPERATIVE ANALGESIA FOLLOWING VENTRAL SLOT SURGERY IN DOGS WITH CERVICAL DISK HERNIATION

F. Tirrito[1,2], F. Cozzi[1], M. D'Angelo[1], C. Bendinelli[1], G. Barbati[1], B. Contiero[3], M. Baccolini[1], M. Armellini[1], M. Bonaldi[1], R. Lombardo[1]

[1] Clinica Neurologica Veterinaria NVA, Milan, Italy
[2] AniCura Istituto Veterinario di Novara, Granozzo con Monticello, Novara, Italy
[3] Department of Veterinary Medicine, Production and Health, University of Padova, Legnaro, Padova, Italy

Intervertebral disk herniation (IVDH) is a common neurological disorder in dogs.
Intraoperative extradural morphine administration reduces postoperative analgesic requirement in dogs following surgery for thoracolumbar IVDH.
The aim of this study was to investigate if intraoperative extradural morphine administration could reduce postoperative analgesic requirement (rescue analgesia) in dogs with surgically treated cervical IVDH.
Thirty dogs with cervical IVDH were prospectively enrolled.
Dogs were randomly selected to receive either intraoperative extradural morphine administration (14 dogs treated with 0.03 mg/kg instilled in an absorbable gelatin sponge placed on the surgical site) or no treatment (16 dogs received saline).
Clinical, neurologic, pre- and postoperative magnetic resonance imaging findings, intraoperative variables were collected. An observer, blinded to the intraoperative treatment, evaluated pain, before and within 24 hours after surgery using the Glasgow composite pain scale-short form (CMPS-SF).
Rescue analgesia was administered if postoperative CMPS-SF score was > 4.
Demographic data were similar between groups. No significant association was identified between intraoperative morphine administration and the need for rescue analgesia ($p > 0.05$).
No adverse effects were recorded.
Preoperative glucocorticoid administration ($p < 0.001$) and preoperative high CMPS-SF scores ($p = 0.04$) were associated with increased chance of requiring rescue analgesia. Preoperative CMPS-SF score > 5 could potentially be used as indicator of greater degree of pain in the postoperative period, with acceptable accuracy (72%), sensitivity 84% and specificity 64%.
In conclusion, cervical, extradural 0.03 mg/kg morphine administration is a safe treatment although it does not reduce postoperative pain in dogs with cervical IVDH.

THE NOCICEPTIVE WITHDRAWAL REFLEX FOR THE EVALUATION OF ANALGESIA IN PIGS UNDERGOING EXTRACORPOREAL MEMBRANE OXYGENATION: A PILOT STUDY

M. Petrucci[1], C. Spadavecchia[2], K. F. Bachmann[3], D. Berger[3], A. Mirra[2], D. Casoni[1]

[1] University of Bern, Faculty of Medicine, Experimental Surgery Facility, Department for BioMedical Research, Bern, Switzerland
[2] University of Bern, Vetsuisse Faculty, Department of Anaesthesia and Pain Therapy, Bern, Switzerland
[3] University of Bern, Inselspital, Department of Anaesthesiology and Pain Medicine and Department of Intensive Care Medicine, Bern, Switzerland

During extracorporeal membrane oxygenation (ECMO), autonomic reactions are not reliable indicators of adequate antinociception. Therefore, alternative methods are required. This study aims at describing nociceptive withdrawal reflex (NWR)[1] thresholds before and after intrathecal analgesia in pigs.

Ten ASA I pigs underwent thoracotomy for setting up veno-arterial ECMO. After standardised sedation, general anaesthesia was induced with propofol and ketamine and maintained with propofol and fentanyl infusion. Intrathecal analgesia ropivacaine 0.75% (0.75 mg kg^{-1}) and morphine (0.1 mg kg^{-1}) was injected via a spinal catheter. NWR thresholds were assessed in the hind-limb before injection (B) and at 40-60 minutes post-injection (PI), end of surgical stimulus, and during ECMO at 180-240, 300-360 and 420-480 minutes PI. Additional ropivacaine (0.75 mg kg^{-1}) was provided if thresholds decreased to B + 20%. Nociceptive flexor response to claw pinching was also tested at each time point. Thresholds were compared with one-way repeated measure ANOVA followed by Hold-Sidak method. Ethical permission: BE 111/18.

Thresholds were 75±35 mA before injection, 111±40 mA at 40-60 minutes PI, 128±28 mA at end of surgical stimulus, 133±29 mA at 180-240, 107±53 mA at 300-360 and 105±64 mA at 420-480 minutes PI. Thresholds were significantly higher at end of surgical stimulus (p=0.043) and 180-240 minutes PI (p=0.019) compared to B. Positive nociceptive flexor responses were found in two animals, at baseline (NWR= 105 mA) and 300-360 minutes PI (NWR=112 mA), respectively. Seven animals needed additional ropivacaine at 341±141 minutes PI.

The NWR allowed quantifying and optimizing intrathecal analgesia in pigs undergoing ECMO.

1. von Dincklage, F., Hackbarth, M., Schneider, M., Baars, J. H. & Rehberg, B. Introduction of a continual RIII reflex threshold tracking algorithm. Brain Res 1260, 24–29 (2009).

TONGUE ATROPHY AS A NEUROLOGICAL SIGN IN HEREDITARY POLYNEUROPATHY IN ALASKAN MALAMUTES

J. Hultman[1], K. H. Jäderlund[1], L. Moe[1], A. Espenes[2], F. S. Skedsmo[1,2]

[1] Department of Companion Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Norway
[2] Department of Preclinical Sciences and Pathology, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Norway

Alaskan malamute polyneuropathy (AMP) is an inherited degenerative neuropathy caused by a mutation in the N-myc downstream-regulated gene 1 (NDRG1). A human polyneuropathy caused by mutations in the same gene is classified as Charcot-Marie-Tooth type 4D (CMT4D). In a subset of CMT4D-affected humans, macroscopic tongue atrophy was briefly reported besides more classical signs of polyneuropathy. Clinical signs in affected dogs are characterized by exercise intolerance, inspiratory stridor, paresis, ataxia and muscle atrophy.

Data on tongue appearance, electromyography (EMG) and histopathology of the tongue and hypoglossal nerve were sampled in a number of Alaskan malamutes homozygote for the NDRG1 mutation. All data were sampled either as part of the standard diagnostic procedures or post mortem and therefore no ethical approval was required.

All affected Alaskan malamutes had an abnormal tongue appearance displayed as wrinkles and grooves on the dorsal surface in addition to clinical signs previously associated with AMP. EMG of the tongue showed spontaneous activity. Histopathology of the tongue muscle and hypoglossal nerve displayed changes resembling those reported from other muscles and nerves, including thinly myelinated nerve fibres, small onion bulbs, myelin folds and angular atrophic myofibres.

NDRG1-associated polyneuropathy may involve degeneration of the hypoglossal nerves with secondary neurogenic tongue atrophy. To date, there are no reports in dogs with inherited peripheral polyneuropathies describing similar macroscopic and histopathologic changes in the tongue. Tongue atrophy should be considered as a potential additional clinical sign in dogs with peripheral polyneuropathies.

Poster Abstracts

THESE PROCEEDINGS FAITHFULLY REPORT ALL ABSTRACTS PROVIDED
BY THE AUTHORS WHO ARE RESPONSIBLE OF THE CONTENT OF THEIR WORKS.

1

SUBEPENDYMAL PSEUDOCYSTS IN A 10-MONTH-OLD POMERANIAN

K. Santifort[1,2] N. Bergknut[2], I. van Soens[2], P. Mandigers[1,3], K. van Schaik-Gerritsen[1], M. Beukers[2], S. Steggerda[4]

[1] Evidensia Small Animal Hospital, Arnhem, The Netherlands
[2] Evidensia Small Animal Hospital 'Hart van Brabant', Waalwijk, The Netherlands
[3] Department of Clinical Sciences of Companion Animals, Utrecht University, The Netherlands
[4] Department of Neonatology, University Medical Center Leiden, The Netherlands

Cystic structures adjacent to lateral ventricles are abundantly reported in human medicine, especially in fetuses and neonates. Several entities are described with partly overlapping terminology such as connatal cysts, coarctation of lateral ventricles, periventricular (pseudo)cysts and subependymal pseudocysts (SPCs).
A 10-months-old male Pomeranian was presented with cervical hyperesthesia and tetraparesis after a trauma. MRI and CT studies revealed atlantoaxial instability, atlanto-occipital overlapping, supraoccipital bone dysplasia and ventriculomegaly. Additionally, two paraventricular cyst-like structures were observed in the rostral area of the lateral ventricles, without visible connection to the ventricular lumen. Signal characteristics were identical to CSF.
In literature, differential etiological diagnoses for intracranial cystic lesions are described: normal variants, developmental cystic lesions, cysts due to perinatal injury, vascular cyst-like structures, hemorrhagic cysts and infectious cysts. The localization of bilaterally symmetrical cyst-like structures ventrolateral to the rostral aspect of the lateral ventricles in this case best fit the description of SPCs in humans. In humans, two types of SPCs are recognized: acquired (post-hemorrhagic) and congenital (germinolytic). Congenital SPCs may have a vascular, infectious, genetic, metabolic or toxic background. They may be an isolated finding in normal neonates, but have also been linked to other neuropathology. The authors only found mention of SPCs in veterinary literature in an article about bovine viral diarrhea virus infected calves. In this case, congenital SPCs were tentatively diagnosed based on MRI findings and not deemed clinically significant. Histopathologic confirmation of the existence of this entity in dogs remains to be documented, as well as its possible relevance.

2

SUSPECTED TROCHLEAR NERVE NEOPLASIA IN A DOG

K. Santifort[1,2], P. Mandigers[1,3], L. Garosi[4]

[1] Evidensia Small Animal Hospital, Arnhem, The Netherlands
[2] Evidensia Small Animal Hospital 'Hart van Brabant', Waalwijk, The Netherlands
[3] Department of Clinical Sciences of Companion Animals, Utrecht University, The Netherlands
[4] VetOracle Teleradiology, Norfolk, United Kingdom

Neoplasia of the trochlear nerve (TNN) is reported infrequently in human medicine. The diagnosis is based on neuroimaging and clinical signs, predominantly diplopia. We report a case of suspected TNN in a dog.
A 13-year-old male Kooikerhondje was presented with acute vestibular signs including a left-sided head tilt, horizontal nystagmus and vestibular ataxia. Hematological and biochemical tests were unremarkable. MRI revealed a T2 hyper-/isointense and contrast-enhancing mass lesion coursing rostrally on the right side from dorsal to the trigeminal nerve roots near the caudal colliculus, adjacent to the mesencephalon, to the cavernous sinus corresponding to the path of the TN. CSF analysis revealed a protein concentration of 31 mg/dL. Outward rotation of the eyeball was inferred based on the fundoscopy finding of lateral deviation of the superior retinal vein. The dog was presumptively diagnosed with idiopathic vestibular disease (left) and a right-sided TNN. Follow-up revealed expected amelioration of vestibular signs. Upon further questioning during the next 6 months of follow-up, the owners reported that the dog does not catch a thrown kibble as he used to (possible sign of diplopia).
TNN (schwannoma) is considered very rare in humans, with less than 40 reported cases since 1976. They are most frequently localized in the ambient cistern (adjacent to the mesencephalon). Human patients with an isolated trochlear nerve mass and deficit have a good prognosis. Serial MRI scans are recommended without specific antitumoral therapy unless they develop signs of brain stem compression. There are no reports of confirmed TNN in dogs.

3

LONG-TERM FOLLOW-UP OF A SPINAL NEPHROBLASTOMA IN A DOG TREATED WITH SURGICAL REMOVAL AND ADJUNCTIVE RADIATION THERAPY

M. Hermans[1], D. Polidoro[1], J. Benoit[3], I. Cornelis[1], T. Rick[2], K. Kromhout[2], B. Van Goethem[1], L. Van Ham[1], and S.F.M. Bhatti[1]

[1] Small Animal Department, Small Animal Teaching Hospital
[2] Department of Medical Imaging and Small Animal Orthopaedics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[3] Radiotherapy Service, Oncovet, Lille, France

Spinal cord nephroblastoma is a neoplasia in dogs, occurring usually between the 10th thoracic and 3rd lumbar spinal cord segments, presenting as an intradural-extramedullary solitary mass. The mass is believed to originate from ectopic metanephric blastemal remnants, trapped between the dura mater and the spinal cord during embryogenesis, which undergo neoplastic transformation. This neoplasm usually affects dogs between 5 months and 4 years of age. The purpose of the present report is to describe successful long-term treatment with surgery and radiation therapy of a spinal nephroblastoma in a 10-month-old American Staffordshire Terrier.
The dog was presented with a progressive, non-painful, thoracolumbar (T3-L3) myelopathy. CT showed an intradural-extramedullary, hyperattenuating mass lesion at the level of T12 with associated compression of the spinal cord. On MRI the mass was iso- to hyperintense on T1- and T2-weighted images and was hyperintense on STIR images. The mass had moderate contrast enhancement. Based on clinical and medical imaging findings a nephroblastoma was suspected. Marginal surgical removal of the mass was performed and after histopathological confirmation of the diagnosis, (external beam) radiation therapy was started. The patient received a total of 5000cGy over 20 fractions of 250cGy each. Thirty-two months post-therapy the neurological examination of the dog is still unremarkable.
In most documented cases conservative or surgical management are given, however, prognosis is poor. To our knowledge only one case has been reported of a dog receiving surgical and radiation therapy without clinical evidence of tumour recurrence for >2.5 years after treatment (Brewer et al., 2011).

Brewer D.M., Cerda-Gonzales S., Dewey C.W., Diep A.N., Van Horne K. And McDonough S.P. (2011). Spinal cord nephroblastoma in dogs: 11 cases (1985-2007). Journal of the American Veterinary Medical Association 238(5), 618-624.

4

HEAD-SHAKING NYSTAGMUS IN TWO DOGS

K. Santifort[1,2] N. Bergknut[2], I. van Soens[2], L. Garosi[3], S. Platt[3,4], L. Lehner[5]

[1] Evidensia Small Animal Hospital, Arnhem, The Netherlands
[2] Evidensia Small Animal Hospital 'Hart van Brabant', Waalwijk, The Netherlands
[3] VetOracle Teleradiology, Norfolk, United Kingdom
[4] University of Georgia, College of Veterinary Medicine, Athens, GA, United States of America
[5] Fuziovet, Budapest, Hungary

Head-shaking nystagmus (HSN) is reported in human scientific literature as a sign of vestibular dysfunction of variable etiology. HSN is a nystagmus induced by oscillation of the head at high frequency in the horizontal plane and is employed as a clinical test by neurotologists. We report the clinical signs and diagnostic findings of two dogs with head-shaking nystagmus, previously unreported in veterinary neurology.
A 4-year-old male neutered miniature Poodle was presented with conjugate horizontal nystagmus to the left occurring 10-20 seconds after vigorous head-shaking. A short head nystagmus was also seen. It reportedly started 4 weeks after enucleation of the left eye. The clinical examination, MRI and CSF analysis were normal. Corticosteroids and broad-spectrum antibiotics were prescribed by the referring veterinarian. Markedly decreased episode frequency was reported thereafter.
A 2-year-old female neutered Shetland Sheepdog was presented with a chronic head tilt and conjugate up-beat vertical nystagmus after head-shaking. The clinical examination, MRI, CSF analysis, BAER test, ERG and caloric tests were normal. The dog was treated with pyridoxine hydrochloride, benfotiamin and cyanocobalamin combination, propentofylline and physiotherapy. During follow-up over a period of 10 months, there was no progression or regression of signs.
The cause of the HSN in these two canine cases remains unknown. A human study reports HSN to occur in 100% of vestibular neuritis cases, 69% of Ménière's disease cases and 22% of benign paroxysmal positional vertigo cases. Links to ocular disorders have been reported. It remains speculative if treatment with corticosteroids would be indicated in these cases.

5

INFLAMMATORY DISEASE AFFECTING THE CENTRAL NERVOUS SYSTEM IN DOGS: A RETROSPECTIVE STUDY IN ENGLAND (2010-2019)

Rita Gonçalves[1], Steven De Decker[2], Gemma Walmsley[1], Sarah Butterfield [2], Thomas W. Maddox[1]

[1] Department of Veterinary Science, Small Animal Teaching Hospital, University of Liverpool, Leahurst, Neston, Cheshire, UK 2Queen Mother Hospital, Royal Veterinary College, University of London, Hatfield, UK.

Inflammatory diseases affecting the central nervous system (CNS) are common, life-threatening conditions in dogs that may be associated with immune-mediated or infectious causes. The relative prevalence of different aetiologies causing CNS inflammatory disease is unknown so our aim was to determine this and identify predictors for infectious versus immune-mediated causes.

A retrospective cohort study was carried out over a 10-year period in 2 referral institutions using multivariable and multinomial logistic regression for risk factor identification.

1205 dogs were included. A total of 17 different diagnoses were identified, with immune-mediated disease (82.2%) considerably more common than infectious conditions (17.8%). The most common immune-mediated conditions were MUO (47.6%) and SRMA (29.3%) and the most common infectious conditions were discospondylitis (6.5%) and tetanus (4.6%). Younger age ($p<0.001$, OR=1.017, CI 1.013-1.022) and shorter duration of the clinical signs before presentation ($p<0.001$, OR=1.009, CI 1.004-1.014) were associated with immune-mediated disease whereas being male ($p=0.001$, OR=1.839, CI 1.296-2.609), progressive clinical signs ($p<0.001$, OR=2.967, CI 1.915-4.597) and identification of a possible trigger ($p<0.001$, OR=4.281, CI 2.84-6.453) were associated with infectious causes. 89.5% of all dogs survived to discharge with no significant difference in short or long-term survival between immune-mediated and infectious conditions.

Our data confirms that immune-mediated disease is more common than infectious conditions as a cause for inflammatory CNS disease in dogs in England, as previously suspected. Risk factors for the most common diagnoses were identified from signalment, history and examination findings to give valuable information that can guide clinicians with their investigations.

6

CORRELATION BETWEEN MAGNETIC RESONANCE IMAGING AND HISTOLOGICAL LESIONS IN A CASE OF MENINGOENCEPHALITISMYELITIS SECONDARY TO NEOSPORA CANINUM INFECTION IN A GREYHOUND

G. Albertini[1], F. Stabile[1], D. Yaffy[2], A. Suárez-Bonnet[2], A. Uriarte[1]

[1] Dep. of Neurology and Neurosurgery, Southfields Veterinary Specialists, United Kingdom,
[2] Pathobiology and Population Sciences, Royal Veterinary College, United Kingdom.

Neospora caninum is a protozoal agent known to occasionally cause meningoencephalitis and/or myelitis in dogs. MRI and histological features of *Neospora caninum* myelitis have been described separately. However, to the authors' knowledge, there is currently no description of correlated MRI and histopathological findings of meningoencephalomyelitis secondary to *Neospora caninum* in dogs.

An 11-year old male neutered raw fed greyhound was presented for a two-week history of progressive non-lateralised, non-painful ambulatory paraparesis deteriorating acutely to non-ambulatory tetraparesis. The neurological examination was consistent with a multifocal CNS disease. MRI revealed multifocal, diffuse, bilateral asymmetrical, intra-axial lesions affecting mainly the cortical grey matter than white matter and hippocampus; focal, bilateral, asymmetrical, ill-defined lesions affecting the caudate nucleus, thalamus, cerebellar nodulus, midbrain and cervical spinal cord. Compared to grey matter/spinal cord parenchyma, the lesions were hyperintense in T2w and T2w FLAIR images, iso to hypointense in T1w images and were mildly to markedly diffusely contrast enhancing. CSF analysis revealed a predominantly eosinophilic pleocytosis. Serology and CSF polymerase chain reaction were positive for *Neospora caninum*. Despite medical treatment, the patient deteriorated and was euthanised. Post-mortem examination revealed no macroscopic changes. Microscopic examination of the brain and spinal cord revealed multifocal, marked, necrotizing, lymphoplasmacytic and histiocytic, meningoencephalitis and myelitis with intralesional round protozoal cysts containing myriad tightly packed 2-3 µm basophilic zoites.

In conclusion, *Neospora caninum* should be considered a differential diagnosis in multifocal CNS disease in elderly patients. Moreover, MR imaging should assess the entire central nervous system to assess accurate extension of the lesions.

7

OWNERS' PERCEPTION OF SEIZURE SENSOR DEVICES IN VETERINARY MEDICINE

J.J. Bongers, R. Gutierrez-Quintana, C.E. Stalin

University of Glasgow, Neurology/neurosurgery service of the School of Veterinary Medicine, Glasgow, UK.

Accurate knowledge of seizure frequency is key to optimising treatment. New methods for detecting seizures are currently investigated in humans, which rely on changes in biomarkers, also called 'seizure sensors devices'. A critical step in development, is understanding user needs and requirements. No information has been published regarding this subject in veterinary medicine.
An online survey was created and consisted of 27 open, closed, and scaled questions divided over two parts: part one focussed on general questions related to signalment and seizure semiology, the second part focussed specifically on the use of seizure sensor devices. Two hundred and thirty-one participants caring for a dog with idiopathic epilepsy, were included in the study. Open questions were coded using descriptive coding by two of the authors independently. Data was analysed using descriptive statistics and binary logistic regression.
Our results showed that nearly all dog owners made changes in their daily life which mainly focussed on intensifying supervision. Most owners felt more confident leaving the house if their dog's seizures could be predicted or monitored in some way. Results of part 2 of the study demonstrated that seizure sensor devices would improve owners' confidence in managing epilepsy. Owners that were already keeping track of their dog's seizures were more likely (4.2 times) to show confidence in seizure sensors devices, highlighting the need for better monitoring systems. Our results indicate there is a market for seizure sensor devices in veterinary medicine and provides suggestions which should be taken into consideration when developing such a device.

Ethical approval was granted by the Ethics Committee of the College of Medical, Veterinary & Life Sciences of the University of Glasgow (ethical approval number 200190049).

The submitting author is a third-year neurology resident.

8

IDIOPATHIC GENERALISED TREMOR SYNDROME IN DOGS

S. Phillipps[1], S. DeDecker[2], R. Gutierrez-Quintana[3], E. Alcoverro[4], S. Gomes[5], R. Goncalves[1]

[1] Institute of Infection, Veterinary and Ecological Sciences, Small Animal Teaching Hospital, University of Liverpool, United Kingdom;
[2] Department of Clinical Sciences and Services, Queen Mother Hospital for Animals, Royal Veterinary College, United Kingdom;
[3] Veterinary Clinical Services, Small Animal Hospital, University of Glasgow, United Kingdom;
[4] ChesterGates Veterinary Specialists, United Kingdom;
[5] Dovecote Veterinary Hospital, United Kingdom.

Idiopathic generalised tremor syndrome (IGTS) causes tremor, and often vestibulocerebellar signs. The condition is poorly understood but believed to have an immune-mediated aetiology. Previous publications are restricted to case reports or lack exclusion of structural causes.
Medical records of 76 dogs diagnosed with IGTS that had undergone magnetic resonance imaging (MRI) of the brain and had metabolic and toxic causes excluded were collected retrospectively. Their clinical signs, diagnostic investigation findings, treatment and outcome are described. Approval by the University of Liverpool Veterinary Research Ethics Committee was granted.
Crossbreeds were affected most commonly (42.1%), followed by West Highland white terriers (14.5%) and cocker spaniels (10.5%). There was a higher proportion of affected females (68.4%) than males. The median age of affected dogs was 17 months, median bodyweight was 9.15kg. All dogs presented with tremors and most experienced concomitant neurological signs. Eighteen were pyrexic and 32 had reported gastrointestinal signs. MRI of the brain was normal in most cases whilst cerebrospinal fluid analysis frequently revealed a mild, commonly mononuclear pleocytosis, and elevated total protein concentration. All animals were treated with prednisolone and 39 also received diazepam. Median follow-up time was 17 months during which time 16 patients experienced relapsing clinical signs. Overall outcome was good, although 10 patients experienced persistent mild clinical signs.
IGTS should be suspected in any dog with a generalised tremor and concurrent neurological signs. Further studies into the aetiology of this condition are recommended, an immune mediated pathology in the spectrum of CNS diseases is expected.

9

IMAGING DIAGNOSIS, SURGICAL RESECTION AND HISTOPATHOLOGICAL FINDINGS OF A CANINE ESTHESIONEUROBLASTOMA

E. Hidalgo Crespo[1], A. Farré Mariné[1], S. Sánchez-Briones[1], M. Pumarola[2], A. Luján Feliu-Pascual[1]

[1] Neurology/Neurosurgery Service of AÚNA Especialidades Veterinarias hospital, Spain. 2Mouse and Comparative Pathology Unit. Department of Animal Medicine and Surgery, Universitat Autònoma de Barcelona, Spain

Olfactory neuroblastoma or esthesioneuroblastoma is a rare malignant intranasal tumour originating from the olfactory neuroepithelium. Neoplastic growth may extend to the paranasal and intracranial cavities. Histopathological description in dogs is scarce, mostly postmortem.

A 10-year-old female spayed mixed breed dog was referred for surgical excision of a mass in the right olfactory bulb detected with low-field MRI two weeks earlier. Right circling, and moderate obtundation localised the lesion to the right telencephalon.

Pre-op CT images revealed an extra-axial, well-defined, hyperattenuating lesion extending from the cribriform plate to the optic chiasm, compressing the right olfactory bulb and frontal lobe. It showed strong enhancement after iohexol IV administration, caused moderate perilesional edema,left midline shift and extended into the nasal cavity through the cribriform plate. Differential diagnoses included meningioma, nasal carcinoma, esthesioneuroblastoma, and primitive neuroectodermal tumour.

Macroscopic resection was complete using a bilateral trans-frontal approach. The defect was covered with a titanium mesh. An immediate post-surgical CT showed no macroscopic tumour. Histopathology revealed an infiltrative neoplastic population with small-to-medium size cells, large nuclei and eosinophilic cytoplasm some of them containing granular material. Stroma was rich in collagen and blood vessels. SYN positivity was observed in 10-30% of the cell population. All these findings were consistent with esthesioneuroblastoma. Gradual neurological improvement was reported during the following 4 weeks.

This report describes the CT, surgical and histopathological findings of a surgically-removed esthesioneuroblastoma, a very infrequent neoplasia, which should be considered a differential diagnosis in dogs with extra-axial rostral cranial fossa tumours.

10

DIFFUSE LUMBAR HYPEROSTOSIS SECONDARY TO ATYPICAL T-CELL MULTICENTRIC LYMPHOMA: CASE REPORT

M Foreman[1], A Belmudes[2], K Guerzoni[3], E Villiers[4], E Scarpante[1]

[1] Dick White Referrals, Department of Neurology and Neurosurgery, UK
[2] Dick White Referrals, Department of Diagnostic Imaging, UK
[3] University of Nottingham School of Veterinary Medicine and Science, Department of Veterinary Pathology, UK
[4] Dick White Referrals, Department of Clinical Pathology, UK

A 4-year-old female spayed Bullmastiff-cross presented with a history of progressive paraparesis, as well as weight loss and polyuria-polydipsia. Neurological examination was consistent with L4-S3 myelopathy. On magnetic resonance imaging (MRI), all vertebrae showed homogenously increased short tau inversion recovery (STIR) signal with strong contrast enhancement. The signal intensity changes were associated with circumferential concentric thickening of the vertebral pedicles, dorsal lamina and vertebral body, leading to marked circumferential narrowing of the vertebral canal along the length of L5 with secondary spinal cord compression.

Lateral radiographs of the vertebral column from T6 to Cd2 showed normal to decreased bone radiopacity of the lumbar vertebrae, and loss of visualisation of the dorsal cortex of the vertebral body from L1 to L6. Moderate new bone formation around the spinous processes of T11 and T12, and the articular facets at the level of T11-12 and T12-13 was noted. Bone biopsy of the new bone around the T12-13 articular facet consisted of mature cartilage and bone, which was disorganised and forming thick trabeculae. Fine needle aspiration of the popliteal lymph nodes showed significant expansion in the proportion of intermediate-sized lymphoid cells, suggestive of a lymphoma. Flow cytometry confirmed a T-cell lymphoma.

The dog was euthanised. Necropsy confirmed the presence of stage V multicentric T-cell lymphoma, as well as diffuse hyperostosis of the vertebral bodies. To our knowledge, this is the first report of presumed paraneoplastic lumbar skeletal hyperostosis.

11

SHORT TERM OUTCOMES OF SURGICALLY TREATED, PARAPLEGIC, NOCICEPTIVE NEGATIVE FRENCH BULLDOGS DIAGNOSED WITH INTERVERTEBRAL DISC EXTRUSION

G.M.C. Jones [1], G.B. Cherubini [2], F.J. Llabres-Diaz [1], A.R. Caine [2], A. De Stefani [1]

[1] Dept for Clinical Science and Services, Royal Veterinary College, United Kingdom
[2] Dick White Referrals, United Kingdom

Intervertebral disc extrusions (IVDE) are a common spinal disorder in dogs, especially within chondrodystrophic breeds. Loss of deep nociception is a well-documented negative prognostic indicator in dogs with IVDE, with approximately only 50% of dogs recovering neurological function after surgery. The objective of this study was to assess the rate of recovery in surgically treated, paraplegic, nociceptive negative French Bulldogs.
A retrospective cohort study was performed on French Bulldogs who presented to two referral hospitals between 2015-2020. Their medical and MRI records were reviewed, with analysis of signalment, clinical examination, location of lesion, complications, short term outcome and quantitative MRI changes including lesion length, extent of spinal cord swelling and severity of spinal cord compression.
Forty-nine French Bulldogs met the inclusion criteria, with 14 (28.6%) showing neurological improvement at the time of discharge. Dogs with L4-S3 lesions had a significantly worse outcome (p=.025) with 3/24 (12.5%) dogs showing neurological improvement, compared to 11/25 (44.0%) of dogs with T3-L3 lesions. Dogs which had the larger cord compression (as measured by having a smaller spinal cord height at the site of maximal compression (p=.001), and a greater severity of this compression compared to the height of the normal spinal cord (p=.022)) had a better clinical outcome.
This study suggests that French Bulldogs with IVDE and absent nociception have a worse short term outcome following surgery compared to previous studies. Based on these findings, further investigations into why French Bulldogs show less neurological improvement compared to other chondrodystrophic dogs are warranted.

12

INTEROBSERVER AGREEMENT BETWEEN COMPUTED TOMOGRAPHY AND RADIOGRAPHY IN DETECTING CALCIFIED DISCS IN A POPULATION OF HEALTHY BRITISH DACHSHUNDS

S. Formoso[1], S. Khan[1], M. Lowrie[2], J. Hughes[1], P. Freeman[1]

[1] Dept. of Small Animal Medicine, Queen's Veterinary School Hospital, University of Cambridge, Cambridge, United Kingdom
[2] Dovecote Veterinary Hospital, Derby, United Kingdom

In dachshunds the number of calcified intervertebral discs seen on radiography at a young age is associated with risk of developing disc herniation in later life, and this has been shown to be heritable. Radiographic screening programs have been implemented in several countries to quantify the number of calcified discs and provide breeding recommendations.
The aim of this retrospective study was to estimate agreement between computed tomography (CT) and radiography in detecting calcified discs in a population of healthy British dachshunds.
13 healthy dogs aged between 2-4 years were included in the study. CT and radiographs of the whole spine were available for each. The spinal radiographs had been previously scored by an independent assessor as part of a screening program. Three different observers with different levels of experience assessed the CT images and reported the number of calcified discs identified for each dog.
There was an almost perfect agreement among the three observers identifying calcified discs on CT images. CT was shown to be 5.9 times more sensitive at identifying disc calcifications than radiography, with the highest difference being in the thoracic and the closest agreement in the cervical region. Overall, 145 calcified discs were identified by CT as opposed to 42 by radiography.
This study demonstrates a significant difference in the ability to identify calcified intervertebral discs in a small population of healthy dachshunds between CT and radiography' and suggests CT may be a more appropriate method for assessing disc calcification for potential future breeding schemes.

13

GENERALIZED STIFF, RIGID GAIT IN A DOG AFFECTED BY HYPOTHYROIDISM

F. Tirrito[1,2], C. Ellena[1], F. Ferri[1], F. Cozzi[2], M. Scuttari[1], A. Pratesi[1]

[1] AniCura Istituto Veterinario di Novara, Granozzo con Monticello, Novara, Italy
[2] Clinica Neurologica Veterinaria NVA, Milan, Italy

Hypothyroidism is among the most frequent endocrinopathies in dogs and neuromuscular signs have been reported in affected cases; the most common neurological signs include cranial neuropathies, laryngeal paralysis and generalized neuromuscular weakness. Skeletal muscles involvement is generally subclinical or associated with signs of polyneuropathy.
We describe the clinical, laboratory and electromyographic findings of myotonic-like myopathy in a dog with hypothyroidism.
A 9 years-old male, Maltese dog was referred for a 2-months subacute and progressive history of abnormal gait characterized by hind limbs ataxia and mild paraparesis that progressively worsened in generalized stiffness, rigidity, short-strided gait of the front limbs and exercise intolerance.
Cranial nerves evaluation, postural reactions and spinal reflexes were normal.
Hematologic analyses, total T4 measurement and TSH stimulation test confirmed a diagnosis of hypothyroidism; the ACTH-stimulation test resulted negative for hyperadrenocorticism.
Computer tomography and magnetic resonance imaging excluded spinal cord involvement.
The electromyography (EMG), performed with the dog unsedated, revealed complex repetitive discharges associated with fibrillation potentials and positive sharp waves. EMG abnormalities were mainly detected in proximal appendicular muscles of the front limbs and in cervical epaxial muscles.
A myotonic-like myopathy secondary to hypothyroidism was suspected and supplementation with Levothyroxine (22 µg/kg/die) was started.
Four weeks later, the dog showed significant improvement of clinical signs; only mild rigidity persisted. The re-test of total T4 revealed the hypothyroidism to be not adequately controlled; Levothyroxine dose was increased and clinical signs almost completely solved. Hypothyroidism should be included as differential diagnosis in dogs with myotonic-like myopathy.

14

CORRELATION OF NARROWED INTERVERTEBRAL DISC SPACE ON SURVEY RADIOGRAPHS WITH DIAGNOSIS OF INTERVERTEBRAL DISC HERNIATIONS

S.H. Khan[1], P. Freeman[1]. Queen's Veterinary School Hospital, Cambridge, United Kingdom

Whilst multiplanar imaging has allowed for greater accuracy in the diagnosis of intervertebral disc disease it is not always accessible due to financial, geographic or global pandemic constraints. Such circumstances lead to a reliance of more readily available imaging modalities.
Data were collected from a single hospital's records of dogs who had undergone both survey radiography and magnetic resonance imaging of the same region of the vertebral column. Radiographs were blinded and reviewed by two authors for the presence of a narrowed intervertebral disc space. A diagnosis of intervertebral disc herniation (IVDH) and the presence of a narrowed intervertebral disc space were compared.
A significant correlation between a narrowed intervertebral disc space and a diagnosis of intervertebral disc herniation and also intervertebral disc extrusion (IVDE) was found ($p<0.001$). Odds ratios and percent relative risk calculated for the likelihood of having a diagnosis of IVDH and IVDE when a narrowed disc space is identified were 7.52 and 119.8%, and 8.7 and 314.3% respectively.
A narrowed intervertebral disc space seen on survey radiography increases the likelihood of IVDH in dogs whose neurological dysfunction localises to the spinal cord and is a useful tool for first opinion practitioners and their clients for whom multiplanar imaging is not a viable option.

15

CLINICAL USE OF A MAGNETIC RESONANCE IMAGING-BASED PATIENT-INDIVIDUAL STEREOTACTIC BRAIN BIOPSY DEVICE FOR BRAIN BIOPSIES IN TWO DOGS

S. Gutmann[1], T. Flegel[1], M. Müller[2], R. Möbius[3], J.-P. Fischer[4], I. Kiefer[1], R. Grunert[2], K. Matiasek[5], D. Winkler[3]

[1] Small Animal Department, Faculty of Veterinary Medicine, Leipzig University, Germany
[2] Fraunhofer Institute for Machine Tools and Forming Technology IWU, Dresden, Germany
[3] Department of Neurosurgery, University Clinic of Leipzig, Faculty of Medicine, Leipzig, Germany
[4] Department of Orthopedics, Trauma and Plastic Surgery, University Clinic of Leipzig, Faculty of Medicine, Leipzig, Germany
[5] Section of Clinical and Comparative Neuropathology, Ludwig-Maximilians-Universität, Munich, Germany

Brain biopsy of intracranial lesions require high accuracy during needle placement. In a previous study, a median target point deviation of 0.83 mm for brain biopsy needle placement using the MRI-based patient-individual stereotactic brain biopsy device was determined. The case report describes the clinical use of this MRI-based 3D-printed brain biopsy frame for sampling forebrain lesions in two dogs.
Both dogs displayed generalized tonic-clonic epileptic seizures due to forebrain lesions. For planning of brain biopsies, dogs were prepared as follows: 1. Placement of three bone anchors with markers at the skull, 2. T2W 1mm MRI scan of the brain, 3. Definition of biopsy trajectories in the MRI datasets. The 3D frame consisting of three legs and a biopsy port was designed and printed by an engineer. Five days later the brain biopsy in general anaesthesia was performed. The legs of the frame were fixed to the bone anchors with specific screws. A minimal-invasive access to the brain was created and the brain biopsy needle was placed along the pre-planned trajectory into the intracranial lesion. Brain biopsy samples (2-3) were taken. The dogs received a control MRI and were under observation until discharging of hospital.
Histopathological examination of brain biopsy samples revealed a gliomatosis cerebri in dog 1 and an oligodendroglioma WHO grade III in dog 2. All brain biopsy samples were diagnostic. No complications during or after brain biopsy were noticed. The dogs were discharged 48 hours after biopsy procedure without deterioration of neurological status.

16

TECHNICAL ACCURACY OF THE REGISTRATION PROCESS WITH A FRAMELESS OPTICAL NEURONAVIGATION SYSTEM

T. Bents[1], T. Flegel[1], R. Möbius[2], T. Siegel[1], S. Gutmann[1]

[1] Small Animal Department, Faculty of Veterinary Medicine, Leipzig University, Leipzig, Germany
[2] Department of Neurosurgery, University Clinic of Leipzig, Faculty of Medicine, Leipzig, Germany

For neurosurgical interventions, such as brain biopsies or removal of brain tumors, advanced neuronavigation systems are becoming increasingly important in small animal medicine. Modern neuronavigation systems create a virtual reality image of the brain allowing the surgeon to track instruments in real time. Optical neuronavigation systems consist of a dual camera system emitting infrared light and reflective markers (spheres) identifying the patient as well as the instruments being used. The matching of the surgical situs into the virtual coordinate system of the preoperatively acquired imaging data sets of the patient is performed via an image-to-patient registration process, which includes a so-called registration error.
The aim of the study was to determine the technical accuracy of the registration process of STORZ frameless optical neuronavigation system by using different marker points (pins or anatomical landmarks) for registration process and to compare the registration error between two observers. For each run of each observer the registration error, the maximum registration error and, weather the run was suitable for operation mode (required preset maximum error of 0.5 mm) were recorded.
This study shows that by using pins a very small registration error can be achieved (median of 0.15 mm in both observers). The anatomical landmarks are considerably more imprecise (median up to 0.72 mm), and most runs were unusable for the operation mode. The differences in the registration accuracy among the examiners are in submillimeter range and therefore not clinically relevant. Further, user experience in handling the device has no influence on registration error.

17

SUPTRATENTORIAL SUBDURAL FLUID ACCUMULATION SECONDARY TO STERILE EFFUSIVE MENINGITIS: CASE REPORT

M. Foreman[1], D. Housley[2], R. Rasotto[3], S. Eminaga[1]

[1] Dick White Referrals, Department of Neurology and Neurosurgery, UK
[2] Dick White Referrals, Department of Diagnostic Imaging, UK
[3] Dick White Referrals, Department of Clinical Pathology, UK

An 8-year-old female spayed Lurcher-cross presented with a five-day history of lethargy, inappetence, pain of unknown origin and vacant staring. The day prior to presentation, the dog had also suffered a transient episode of collapse with opisthotonos. Pre-referral haematology, biochemistry, urinalysis and abdominal ultrasound and radiography were all unremarkable. Spinal magnetic resonance imaging (MRI) from C1 to Cd3 had also been performed and showed mild syringomyelia from mid-C2 to caudal-C4.
Neurological examination on presentation revealed an obtunded mental status and discomfort on cervical ventroflexion but was otherwise unremarkable. MRI of the brain revealed moderate-to-severe subdural fluid accumulation around the entire left cerebral hemisphere containing a T2W hyperintense, T1W hypointense, incompletely FLAIR-suppressing and non-enhancing material. There was severe meningeal thickening and enhancement surrounding this fluid accumulation. There was moderate midline shift to the right, moderate caudal transtentorial. herniation and cerebellar impaction into the foramen magnum. There were also faint areas of poorly-defined T2W hyperintensity in the white matter tracts of the left cerebral hemisphere.
A left rostrotentorial craniectomy and durectomy was performed. A moderate amount of clear fluid was drained from the left subdural space. Surgical blood contamination precluded cytological interpretation. Fluid and meningeal tissue culture was negative, including extended and enrichment culture. Histopathology of the excised dura was consistent with moderate chronic neutrophilic and macrophagic meningitis with no infectious agents identified.
This is a report of supratentorial subdural fluid accumulation causing increased intracranial pressure secondary to sterile effusive meningitis.

18

MYCOBACTERIAL EPIDURAL PYOGRANULOMATOUS STEATITIS IN A CAT

C. Posporis[1,3], J.J. Minguez[1], C.J. Fina[2], A. Herrmann[4], A. Wessmann[1]

[1] Pride Veterinary Centre, Derby, Neurology-Neurosurgery service, Derby, UK
[2] Pride Veterinary Centre, Derby, Diagnostic Imaging Service, Derby, UK
[3] The Ralph Veterinary Referral Centre, Neurology-Neurosurgery service, Marlow, UK
[4] Synlab VPG Histology, UK

A two-year-old male neutered domestic shorthaired cat presented with recent spinal hyperaesthesia followed by a 24-hour progressive non-ambulatory non-painful tetraparesis localising to C1-T2 myelopathy. Physical examination, biochemistry, haematology, thoracic and abdominal imaging were unremarkable. MRI showed a well-defined, crescent-shaped, extra-dural, compressive, T2WI/T1WI/STIR hyperintense contrast-enhancing mass lesion within the dorsal and right lateral vertebral canal from C2 to C3-C4. CSF analysis revealed a mild mononuclear pleocytosis and increased protein concentration. Serology for Feline Corona Virus (FeCoV), Toxoplasma IgM/IgG, Cryptococcus antigen, FIV/FeLV and CSF PCR for Toxoplasma gondii and FeCoV were negative. A C2-C3 hemilaminectomy was performed and the mass was resected. Histopathology showed a marked pyogranulomatous cellulitis with multifocal lymphofollicular hyperplasia. PAS and Ziehl-Neelsen staining were unremarkable. Immunohistochemistry for FeCoV was negative. Mycobacterium spp. PCR from the resected tissue showed positive amplicons and the DNA sequence was most closely related to the genus Mycobacterium. Treatment included a one-week course of anti-inflammatory doses of prednisolone and a 6-month antibiotic therapy consisting of Clarithromycin, pradofloxacin and rifampicin. A rapid and complete recovery was confirmed by re-examination after 2 weeks and no recurrence was reported by the time of writing 31 months later.
This is the first report of mycobacterial epidural steatitis in a cat. It emphasises the relevance of mycobacterium infection as a differential diagnosis in patients diagnosed with a pyogranulomatous epidural steatitis, as well as the importance of PCR analysis and sequencing for the detection of mycobacterial organisms in the affected tissues. A good long-term outcome can be achieved with appropriate therapy.

Ethical permission was not indicated for this case report.
The submitting author is a residency-trained clinician.

19

GLOBAL BRAIN ISCHAEMIA AS A CAUSE OF LATE ONSET SEIZURES IN A DOMESTIC SHORTHAIRED CAT

S. Phillipps, F. Schiborra, A. Nagendran

Institute of Infection, Veterinary and Ecological Sciences, Small Animal Teaching Hospital, University of Liverpool, United Kingdom.

Cerebrovascular accidents (CVA) cause sudden onset of seizures in cats and dogs. Global brain ischaemia (GBI) in veterinary species is an uncommon manifestation of CVA and has been associated with cardiovascular dysfunction secondary to anaesthesia. Late-onset seizures after GBI has not been reported in veterinary species before, but both early and late onset seizures secondary to ischaemia are well recognised in human medicine.
A two-year old female neutered domestic shorthaired cat with a history of blindness since ovariohysterectomy ten months previously was presented for investigation of suspected seizure activity over a three-month duration. Neurological examination confirmed central blindness, a quiet and slightly disorientated mentation, absent bilateral nasal mucosal sensation, wide excursions of the head in either direction and reduced postural reactions in all limbs. Routine haematology and biochemical profiles, thiamine and cobalamin levels were unremarkable. Magnetic resonance imaging (MRI) revealed global brain ischaemia and cortical atrophy. The clinical history and imaging findings were consistent with hypoxia and/or hypoperfusion during the previous anaesthesia. Treatment with phenobarbitone resulted in excellent control of seizures with no further events in a five-month follow-up period and though blind, the cat's owners report a good quality of life.
Anaesthesia accidents can occur during short, 'routine' procedures in apparently clinically healthy animals and may have severe long-term effects for patients. This case suggests that late-onset seizures can occur following ischaemic injury. Phenobarbitone effectively managed seizures in this case.

20

RECOVERY AFTER INADVERTENT INTRAMEDULLARY MICROCHIP IMPLANTATION AT C1-C2 IN A KITTEN - A CASE REPORT

N. Schneider[1], A. Blutke[2], B. Parzefall[1]

[1] Neurology Department of the Small Animal Clinic Oberhaching, Oberhaching, Germany
[2] Institute of Experimental Genetics, Helmholtz Zentrum Muenchen, Neuherberg, Germany

Penetrating spinal cord injuries (PSCI) in humans are associated with severe myelopathies and often have a poor prognosis. The decision between medical and surgical treatment is still discussed controversially, as the outcomes are not significantly different. In veterinary medicine, only a small number of surgically treated PSCI cases in companion animals have been published. Information on medical management however is lacking. Here, we report a case of a peracute paralysis in a 15-week-old male British Shorthair cat following inadvertent microchip implantation into the spinal cord.
Neurological examination revealed a non-ambulatory tetraparesis and left front limb plegia localised to C1-C5 spinal cord segments instantly after microchip placement. Computer tomography (CT) was performed showing a microchip that was diagonally placed within the vertebral canal and spinal cord at the level of C1-C2 vertebrae. Based on the microchip-location and the concern of further iatrogenic spinal cord injury through surgery, medical management was chosen. Despite the impressive extent of the injury and the clinical symptomatology, the patient showed continuous neurological improvement and was ambulatory six days later with controlled urination and defecation. After recovery, six weeks later, a permanent mild-moderate tetraparesis with ataxia remained with a good quality of life. At the age of 13 months, a follow-up CT was performed which showed a relative cranial displacement of the microchip reaching into the foramen magnum.
In conclusion, conservative treatment of PSCI in young cats might be an option for patients where severe surgery-related complications are suspected or owners reject surgery.

No ethical permission was needed for this case report.
The submitting author is a neurology resident in training (N. Schneider)

21

MOVEMENT ANALYSIS BY A DOG WITH LOWER BACK PAIN, TREATED WITH ORTHOMANUAL VETERINARY MEDICINE AND MEASURED WITH THE PRESSURE PLATE

M. Geerts[1], D. Aharon[1]

[1] Clinic for Orthomanual Veterinary Medicine, Noorden, The Netherlands.

Charly, a 2.5 year old crossbreed dog was referred to the clinic with unwillingness to jump into the car. A CT-scan of the lower back was included showing lumbosacral instability. Physical, neurological and orthopaedic examinations showed pain during palpation of the lumbosacral region and lumbosacral instability. Concurrent orthopaedic, neurological or systemic disorders were excluded. Based on the clinical signs, findings during examination and the CT-scan lower back instability was diagnosed.

Lower back pain is a frequently observed problem which occurs mostly in older dogs of large to giant breeds. Initial signs are unwillingness to jump and expressions of pain in the lumbosacral spine region. Numerous diseases can cause lower back pain. Degenerative lumbosacral stenosis (DLSS) is frequently diagnosed. With radiography and/or MRI/CT the cause of lower back pain can be confirmed. Currently several therapy strategies are developed for DLSS with various results. Therapy can consist of cage rest, medication and surgery or a combination of these therapies.

Charly was treated orthomanually with manipulation of the lower back. Her gait was measured objectively with a pressure plate before and immediately after treatment, two weeks after treatment and three months after treatment. Control CT-scan of the lower back was conducted after two months. Within two weeks after treatment she showed a complete clinical recovery and obvious improvement was measured with the pressure plate. Three months after treatment she had improved even more. Orthomanual veterinary medicine may be considered an adjunct modality for the conservative treatment of lower back instability in dogs.

22

CT FINDINGS, SURGICAL RESECTION AND HISTOPATHOLOGY, OF AN INTRACRANIAL PRIMITIVE NEUROECTODERMAL TUMOUR IN A DOG

S. Sánchez Briones[1], A. Farré Mariné[1], E. Hidalgo Crespo[1], M. Pumarola[2], A. Luján Feliu-Pascual[1]

[1] Neurology/Neurosurgery Service of AÚNA Especialidades Veterinarias hospital, Spain
[2] Mouse and Comparative Pathology Unit. Department of Animal Medicine and Surgery, Universitat Autònoma de Barcelona, Spain

Primitive neuroectodermal tumours are embryonal neoplasias derived from neuroepithelial cells capable of differentiating into neuronal, ependymal, and glial cells. These are rare and malignant representing less than 3% of reported primary intracranial neoplasms.

A 12-year-old male neutered mixed-breed dog was referred for excision of an extra-axial mass located in the right frontal lobe detected one week earlier with CT. The dog suffered generalised seizures, and neurolocalization was consistent with a right telencephalic lesion.

The mass was macroscopically excised using a right trans-frontal approach. Immediate post-surgical CT showed no tumour left. Histological analysis revealed a papillar meningioma (WHO grade III). The dog recovered uneventfully from the surgery but two months later, suffered seizures and neurological deterioration. Follow-up CT revealed an extra-axial hypoattenuating mass with mild and homogeneous contrast uptake in the right olfactory lobe but extending into the left side. A second surgery was carried out and the lesion was excised on both sides. Post-surgical CT confirmed complete gross excision. The histological analysis revealed a neoplastic cell population of large and polygonal cells compressing and infiltrating the nervous tissue. A solid growth pattern was predominant but rossetes and pseudorossetes were seen. Histopathology and immunohistochemistry were indicative of a primitive neuroectodermal tumour. Toceranib and Lomustine were initiated. The dog recovered from the second surgery, but a week after the reintervention deteriorated neurologically and was euthanatzed one month later. Post-morten examination was not granted.

In conclusion, this case reports the importance of considering neuroectodermal tumours as a possible differential diagnosis of intracranial neoplasia.

23

UNILATERAL BLINDNESS ASSOCIATED WITH STEROID-RESPONSIVE MENINGITIS ARTERITIS IN A NINE-MONTH-OLD BEAGLE

C. Tang[1], P. Alvarez[1], S. Manning[2], A. Wessmann[1]

[1] Pride Veterinary Centre, Neurology-Neurosurgery service, Derby, UK
[2] Pride Veterinary Centre, Ophthalmology service, Derby, UK

A nine-month-old male entire Beagle presented with acute lethargy, pyrexia (39.9C) and marked cervical and thoracolumbar pain. Cranial nerve examination revealed abnormalities of the left eye characterised by an absent menace response, absent dazzle reflex, absent direct and consensual pupillary light reflexes (PLRs) with re-dilation on a swinging flashlight test indicating a non-visual left eye. Funduscopic examination and electroretinography were unremarkable bilaterally. The findings were consistent with a left retrobulbar optic nerve lesion as part of the multifocal CNS localisation. Complete blood profile showed moderate neutrophilia, monocytosis and markedly elevated C-reactive protein. CSF analysis showed neutrophilic pleocytosis (97% neutrophils, 52 total nucleated cell count/ul). MRI of the brain and optic nerves, thoracic and abdominal imaging, urinalysis including culture, synovial joint fluid analyses, and *Toxoplasma gondii* and *Neospora caninum* serology titres were unremarkable. A diagnosis of steroid-responsive meningitis arteritis (SRMA) with left optic nerve involvement was concluded. The dog responded well to immunosuppressive doses of prednisolone showing only a reduced menace response and reduced PLR in the left eye 4 weeks into the treatment.

SRMA is a systemic immune-mediated disorder, yet blindness has not been reported in affected cases. An extension of the leptomeningeal inflammation into the optic nerve sheaths is hypothesised as the underlying pathophysiology. SRMA should be considered as a cause of blindness in the presence of other clinical signs compatible with this condition. Prognosis of recovery for vision in these cases is unknown but may be extrapolated from previous studies of optic neuritis of unknown origin.

Ethical permission was not indicated for this case report.
The submitting author is a young neurologist in training (neurology intern).

24

PRIMITIVE NEUROECTODERMAL TUMOUR WITH PRESUMED DROP METASTASES IN A DOG

G.I. Popa[1], C. Posporis[1], C. Briola[1], L. Benigni[1], J. Burgess[1], E. Collier[1], E. Scurrell[2], S. Zago[1], H.J. Featherstone[1]

[1] The Ralph Veterinary Referral Centre, Marlow, UK
[2] Cytopath Ltd., UK

A 9-month-old male Cocker Spaniel presented with bilateral blindness. Neuro-ophthalmic assessment revealed bilateral mydriasis and positional jerk rotatory nystagmus. The right eye had ventrolateral strabismus, absent menace response and PLR, and resistance to retropulsion; the left eye had reduced menace response and PLR. General physical examination, routine haematology, biochemistry and electroretinography were unremarkable. MRI showed an extra-axial, broad-based, irregular, T2W/FLAIR heterogeneously hyperintense, T1W hypointense, contrast-enhancing mass in the middle and rostral cranial fossae, optic chiasm/nerves and right retrobulbar space. Additional MRI findings included: mildly contrast-enhancing meningeal lesions surrounding the mesencephalon, pons, and C1 spinal cord; diffuse meningeal contrast enhancement; and T2W/FLAIR hyperintense, T1W hypointense, non-contrast-enhancing lesions at the periphery of the cerebellum, in the hypothalamus, third ventricle, piriform cortex and olfactory bulbs/peduncles. CSF analysis showed mild mixed pleocytosis and protein elevation. Infectious diseases screening (*Toxoplasma gondii* IgG/IgM and *Neospora caninum* serology, CSF *Cryptococcus* sp. and *Toxoplasma gondii* PCR) was negative. Ultrasound-guided FNAB of the retrobulbar lesion revealed a poorly differentiated neoplastic cell population that was highly suggestive of a primary neuroectodermal tumour (PNET). Therapy was initiated with oral prednisolone (0.6 mg/kg SID), doxorubicin (30 mg/m^2 IV) and oclacitinib (0.5 mg/kg BID PO). The patient gradually deteriorated and was euthanased within two months. Histopathological and immunohistochemical examination of the retrobulbar mass confirmed the suspected cytologic diagnosis of a PNET.
To the authors' knowledge, a retrobulbar-intracranial PNET with multifocal meningeal lesions, suggestive of drop metastases, has not been previously reported. PNET should be considered as an uncommon differential diagnosis in young dogs.

Ethical permission was not indicated for this case report.
The first author is an Ophthalmology intern.

25

SPINAL ARACHNOID DIVERTICULUM AND SYRINGOMYELIA IN A CAT WITH CHRONIC LUMBAR VERTEBRAL FRACTURE

C.G. Danciu[1], D. Douralidou[1], L. Benigni[1], A. Danielski[1], C. Posporis[1]

[1] The Ralph Veterinary Referral Centre, Marlow, UK.

A 3-year-old female domestic shorthair cat was presented with a 6-week history of progressive, painful, symmetrical, pelvic limb ataxia and ambulatory paraparesis localising to T3-L3 myelopathy, following a road traffic accident. Referred thoracic radiographs showed an oblique fracture line and new bone formation representing early healing around the caudal endplate of L3, collapsed L3-L4 intervertebral disc space, malalignment of the vertebral canal at L3-L4, and a sacrococcygeal fracture that was managed with tail amputation by the referring veterinary surgeon. CT was performed at 6 weeks post-trauma and demonstrated fusion of the dorso-lateral aspects of the vertebral arch, articular facets, and ventral intervertebral disc space at L3-L4. MRI revealed a very large, severely compressive, dorsal, drop-shaped, T2W/STIR hyperintense, T1W hypointense, FLAIR suppressing, non-contrast-enhancing, intradural-extramedullary lesion at L4, compatible with a spinal arachnoid diverticulum (SAD). From L4 to L6, there was a large, well-demarcated, wedge-shaped, dorsal and ventral, T2W hyperintense, FLAIR incompletely and heterogeneously suppressing, T1W hypointense, non-contrast-enhancing, intra-medullary lesion compatible with syringomyelia and spinal cord interstitial oedema. A Funkquist-B dorsal laminectomy with durotomy and resection of the SAD was performed at L3-L4. One month post-operatively, there was marked improvement of the gait with mild persisting ataxia and no detectable spinal pain.
The findings of a SAD immediately caudal to the vertebral fracture is suggestive of a post-traumatic aetiology. To the authors' knowledge, this is the first report of post-traumatic SAD and syringomyelia in a cat.

Ethical permission was not indicated for this case report.
The first author is a Neurology intern.

26

KEY FEATURE-CASES AS VIRTUAL PATIENTS IN VETERINARY NEUROLOGICAL EDUCATION

S. Reeh[1], C. Kleinsorgen[2], E. Schaper[2], H.A.Volk[1], A. Tipold[1]

[1] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany, Centre for E-Learning, Didactics and Educational Research (ZELDA), University of Veterinary Medicine, Hannover, Germany

Virtual patients (VP) are a common eLearning feature in veterinary medicine. Mostly long cases (LC) including explanations and expert opinions are used. Key Feature-Cases (KF) are short cases, focusing a few critical decision points that are essential for clinical reasoning (CR) to solve a case. Usability, learning success and acceptance were determined and compared between the VP-Formats.
Two elective courses were offered to undergraduate veterinary students, presenting 38 VPs in CASUS®. In eight cases students were able to create illness scripts and finally compare it with the expert response using the CR-Tool as new feature. These cases were compared to eight other cases with similar clinical findings without the CR-Tool. Besides the evaluation of learning analytics (time, success, case scores) an evaluation was performed via LimeSurvey®.
A total of 229 students participated, 199 completed the survey. The average processing time of LCs was 53 min, that of KF-Cases 17 min. 78% of LCs were successfully completed, 73% of the KF-Cases. The average processing time of cases with CR-Tool was 19 min. The success rate was 58.3% vs. 60.3% for cases without CR-Tool. 134 respondents agreed that the casework made them feel better prepared to secure a diagnosis in real patients. Flexibility in learning (n=93) and practical relevance (n=65) were the most frequently listed positive remarks.
KF-Cases are suitable for the majority of students and significantly contribute to strengthen clinical decision-making skills in veterinary neurology. The CR-Tool is useful but requires further adaptation in structure and terminology.

27

A SUSPECTED INTERMEDIATE SYNDROME AND INTUSSUSCEPTION FOLLOWING PROPOXUR TOXICITY IN A DOG

B. Bravaccini[1], P. Rocchi[2], G. Zappa[2], G. Galli[1], M. Menchetti[1]

[1] San Marco Veterinary Clinic and Laboratory, Neurology and Neurosurgery Division, Veggiano (PD), Italy
[2] San Marco Veterinary Clinic and Laboratory, Intensive Care Division, Veggiano (PD), Italy

Carbamates are a class of insecticides that act binding to acetylcholinesterase reversibly. Propoxur is a common carbamate used as insecticide/molluscicide. Clinical signs of carbamates toxicosis are a consequence of overstimulated nicotinic and muscarinic receptors. Rare complications, as a delayed neurological syndrome called Intermediate Syndrome (IS) and intussusception have been described, although they have never been observed in the same dog.
An 8-month-old mixed breed dog was referred because of vomiting, generalized muscle tremors and miosis. Five hours before the presentation, the owners saw the dog eating something during the daily walk. The dog was initially treated with fluids, atropine and midazolam. Complete blood exams showed a marked reduction of cholinesterase activity. Blood toxicology tests, performed using ultraperformance liquid chromatography-tandem mass spectrometry, revealed the presence of Propoxur. Around 24h after the presentation, the dog developed a small intestinal intussusception, which was treated with an enterectomy and an end-to-end anastomosis. 36h after the surgical procedure, after an initial improvement, the dog developed weakness and respiratory difficulties. The neurologic exam showed mental obtundation, severe generalized muscle weakness of neck and limbs with major involvement of the thoracic limbs, reduced flexor reflexes in the four limbs and a short and shallow respiratory pattern, pointing out a suspected IS. The dog's neurologic conditions progressively improved and he was discharged at day 5 from the presentation with only mild impairment of the neck strength. Despite the IS and intussusception are rarely described in carbamates intoxication, the clinician should be aware of their possible and simultaneous occurrence.

28

PAROXYSMAL DYSKINESIA IN TWO POMERANIAN DOGS

G. Galli[1], M. Menchetti[1]

[1] San Marco Veterinary Clinic and Laboratory, Neurology and Neurosurgery Division, Veggiano (PD), Italy

Canine paroxysmal dyskinesia (cPxD) is a subtype of movement disorder. Diagnosis of cPxD is limited to observation of an episode that can last minutes to hours, without consciousness impairment or autonomic signs. The possibility to observe these episodes from owners' videos has allowed a greater recognition of cPxD. The aim of this prospective study is to describe in detail the clinical presentation of cPxD in two Pomeranian dogs.
Dogs were prospectively included if they were presented for episodes of involuntary movements without loss of consciousness. Video footage and a detailed description of the episodes were collected.
The age of clinical onset was 4.5 and 6 years. The episodes were characterized by sudden onset of dystonic movements of one pelvic limb, sometimes involving also the thoracic limbs. The dogs showed a kyphotic posture and walking impairment, preferring to lie down during the episodes. The episodes lasted from 2 to more than 30 minutes and the frequency varied from weekly to more than one daily. Both dogs had gastrointestinal signs, ranging from borborigmi to diarrhoea/vomiting. Both dogs were tested for anti-gliadin and anti-transglutaminase-2 antibodies, which resulted above the reference range in one dog. Both dogs received exclusively a gluten-free diet, with complete resolution of the episodes. Eating different type of food caused a long lasting episode in one dog, of more than one-hour duration.
The phenotypic characteristics of the episodes and the response to the diet should help the clinician to differentiate the cPxD in Pomeranians from focal seizures.

29

PHENOTYPIC CHARACTERIZATION OF PAROXYSMAL DYSKINESIA IN TOY POODLE DOGS

M. Menchetti[1], F. Cozzi[2], A. Gardini[1], F. Tirrito[2,3]

[1] San Marco Veterinary Clinic and Laboratory, Neurology and Neurosurgery Division, Veggiano (PD), Italy
[2] Clinica Neurologica Veterinaria NVA, Milan (MI), Italy
[3] AniCura Istituto Veterinario di Novara, Granozzo con Monticello, Novara (NO), Italy

Canine paroxysmal dyskinesia (cPxD) is a movement disorder in which there are recurrent episodes of abnormal, involuntary movements without changes in consciousness. It has been proposed that cPxDs have been misdiagnosed as focal seizures. The increased popularity of smartphones and the possibility to observe these episodes from owners' videos has allowed a greater recognition of cPxD.
A multicentre retrospective study was conducted, with the aim to describe in detail the clinical presentation of cPxD in toy Poodle dogs. Dogs were included if presented for episodes of involuntary movements without loss of consciousness and if video footage and detailed description of the episodes were available. Supporting information was added prospectively by using a questionnaire directed to the owners.
Eight dogs were included. The mean age of onset was 3.4 years. The episodes were mainly characterized by sudden onset of dystonic movements of >1 limbs, difficulties in walking, kyphosis and head/body tremors/oscillations. All dogs appeared frightened during the episodes. The episodes lasted from 2 to >30 minutes. 5/8 dogs suffered from gastrointestinal symptoms. All dogs but one were tested for anti-gliadin and anti-transglutaminase-2 antibodies, which resulted negative in 4/7. 6/8 dogs received exclusively a gluten-free diet with a clinical resolution or marked reduction of the episodes.
The phenotypic characteristics of the episodes and the response to the diet may help the clinician in differentiating the cPxD from focal seizures in toy Poodles. Further studies are needed to investigate the influence of gluten and to elucidate the possible genetic predisposition.

30

VENTRICULOMEGALY IN CAVALIER KING CHARLES SPANIELS WITH CHIARI-LIKE MALFORMATION: RELATIONSHIP WITH CLINICAL SIGNS AND IMAGING FINDINGS

F. Tirrito[1,2], F. Cozzi[1], S. Corazzo[2], B. Contiero[3], R. Lombardo[1]

[1] Clinica Neurologica Veterinaria NVA, Milan, Italy
[2] AniCura Istituto Veterinario di Novara, Granozzo con Monticello, Novara, Italy
[3] Department of Veterinary Medicine, Production and Health, University of Padova, Legnaro, Padova, Italy

Chiari-like malformation (CM) frequently occurs in Cavalier Kings Charles Spaniels (CKCS).
Ventriculomegaly, secondary to disturbance of cerebrospinal fluid flow at the craniocervical junction, has been reported in CKCS with CM. However, its clinical relevance is unclear.
The aim of the study was to calculate lateral ventricles dimension in CKCS with CM and to investigate the association between ventriculomegaly and signalment, clinical signs, ventricular asymmetry, CM and syringomyelia (SM) grade, medullary kinking index, follow-up, and epileptic seizures.
A retrospective study was performed enrolling forty-three client-owned CKCS with magnetic resonance imaging diagnosis of CM. Initial and follow-up (up to 36 months) clinical status was graded. Images were reviewed to quantify dimension of lateral ventricles, to evaluate ventricular symmetry, CM and SM grade, and medullary kinking index. Cases presenting epileptic seizures were also recorded.
The most common initial clinical signs were scratching and neck pain. Ventriculomegaly was identified in 70% of dogs, CM grade 2 was observed in 77% of cases, ventricular asymmetry and syringomyelia were identified in 54% and 80% of dogs, respectively; median medullary kinking index was 37.77%. Moreover, 28% of dogs presented epileptic seizures.
No significant association was identified between dimension of lateral ventricles and signalment, clinical signs, and imaging findings; no significant association was identified between ventriculomegaly and epilepsy ($p \geq 0.05$).
In conclusion, the prevalence of ventriculomegaly in CKCS with CM is high but this finding does not seem related to the severity of clinical signs, to CM/SM, to medullary kinking index, and to epileptic seizures.

31

PHARMACOKINETIC PROFILE OF 3 DIFFERENT ADMINISTRATION ROUTES OF CANNABIDIOL IN HEALTHY DOGS

D. Polidoro[1], R. Temmerman[2], M. Devreese[2], M. Charalambous[1], L. Van Ham[1], I. Cornelis[1], B.J.G. Broeckx[3], P.J.J. Mandigers[4], A. Fischer[5], S.F.M. Bhatti[1]

[1] Small Animal Department, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium.
[2] Department of Pharmacology, Toxicology and Biochemistry, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[3] Laboratory of Animal Genetics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[4] Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
[5] Centre for Clinical Veterinary Medicine, Ludwig Maximilian University of Munich, Munich, Germany

The study protocol was approved by the Ethical Committee of the Faculty of Veterinary Medicine, Ghent University (EC 2018-42).

In veterinary neurology there is a growing interest in cannabidiol (CBD), although there has been much speculation about its therapeutic value in numerous disorders (e.g. epilepsy, pain relief). The oral bioavailability of CBD is low in humans and dogs and continues to be a main issue in clinical trials. This limitation indicates the necessity to explore alternative delivery routes of CBD. The aim of this study was to determine the pharmacokinetic plasma profile of CBD after a single dose via intranasal (IN) and intrarectal (IR) administration in healthy dogs and compare this to the oral administration route (PO).
Six healthy Beagle dogs were randomly allocated to a 3-way crossover study. Following a two-week wash-out period, each dog underwent the same protocol but receiving CBD through a different administration (IN, IR, PO) route. Blood samples were collected before CBD administration and at fixed timepoints until 60 hours after administration.
The mean $AUC_{(0\text{-}inf)}$/dose after 20mg IN and 100mg PO CBD administration was 3 and 13.7 ng/mL*h, respectively ($p = 0.09$). The maximal plasma CBD concentration after 20mg IN and 100mg PO CBD administration was 1.4 and 2.2 ng/mL, reached at 0.5 and 3.5h (T_{max}), respectively ($p = 0.43$). The plasma CBD concentrations after 100mg IR CBD administration were below the limit of quantification and therefore not pharmacokinetically analyzed.
In conclusion, IN or IR administration of CBD did not increase its bioavailability compared to PO administration.

32

WHAT DO WE KNOW ABOUT DIAGNOSIS AND TREATMENT OF IDIOPATHIC VESTIBULAR SYNDROM IN DOGS AND CATS – DO WE REALLY KNOW WHAT WE ARE DOING?

A.M. Mertens[1,2], H.C. Schenk[1], H.A. Volk[2]

[1] Tierklink Lüneburg, Lüneburg, Germany
[2] Dept. Of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hanover, Germany

Idiopathic vestibular syndrome (IVS) is a diagnosis of exclusion, with unclear aetiology, diagnosis and therapy. The aim of the current study was to better characterize and define IVS, its diagnosis and treatment.
One-hundred-thirteen boarded neurology specialist participated in an online survey. IVS definition differed, but IVS was generally defined (n=103) as an acute to peracute onset 'peripheral' vestibular syndrome. As gold standard for diagnosis of IVS neurological exam (NE), MRI, serum biochemistry (SB), complete blood count (CBC), otoscopy, blood pressure (BP), CSF, T4/TSH were chosen. There were discrepancies choosing the five most important diagnostics: North-America, dogs: NE, MRI, SB, CSF, CBC /cats: NE, SB, MRI, otoscopy, BP; EU, dogs: NE, otoscopy, SB, T4/TSH, MRI, CBC /cats: NE, otoscopy, SB, MRI, BP. UK, dogs: NE, MRI; T4/TSH, SB, otoscopy / cats: NE, MRI, SB, BP, otoscopy, SB and CSF. Interestingly, there was a relative consensus for treatment: IV fluids and antiemetics. Additional mentioned drugs varied: propentofylline (only mentioned in the EU) and betahistine, (mentioned in all regions by single individuals).
Despite IVS being a common presentation in practice, opinions about its definition, diagnosis and treatment differ. To the authors knowledge there has been no controlled study into IVS treatment, only into diagnosis. The current study summarises expert opinion and can provide a basis for future studies into diagnosis and treatment.

33

ATYPICAL PRESENTATION OF MULTIPLE CYSTIC LESIONS IN A BRAIN TUMOUR IN A DOG

C.C. Diogo[1], N. Shihab[1], F. Lourinho[1], R. Fernandes[1], M. Rosati[2], R. Trevail

[1] Neurology department of Southern Counties Veterinary Specialists, United Kingdom
[2] Institute of veterinary Pathology, Ludwig Maximillian University of Munich, Germeany

Choroid plexus papilloma is a primary intracranial tumour usually characterized as a well-defined mass with marked, uniform contrast enhancement on MRI. This report describes an atypical presentation of choroid plexus papilloma.
A 7-year-old male Cocker Spaniel presented with a one-month history of vestibular ataxia and seizures, showing vestibular ataxia, circling to the left, delayed proprioception and absent menace response on the left and rotary nystagmus. A multifocal localisation was suspected.
MRI revealed multiple well-defined cystic-like lesions at the level of the optic chiasm, left cerebellar hemisphere, left caudal midbrain and within the right caudal cranial fossa associated with the subarachnoid space. These lesions were markedly hyperintense on T2W and hypointense on T1W. At the level of the caudal cerebellar peduncle, there was a solid rounded contrast enhancing mass and isointense on T2W, being continuous with the choroid plexus of the fourth ventricle suggesting a choroid plexus tumour with 'drop metastases'.
Histopathology revealed cuboidal cell proliferation arranged in numerous papillae lined by one layer of cuboidal cells giving rise to rosettes and pseudorosettes embedded in fibrovascular stroma. Proliferating cells displayed very mild anisocytosis and anisokaryosis with less than one mitosis per 10hpf, confirming a choroid plexus papilloma WHO grade I at the level of cerebellar flocculus with metastases in the ventral subarachnoid space, third and lateral ventricles. Atypical, multiple cystic lesions associated with choroid plexus papilloma metastases has rarely been discussed. This report highlights the importance of this major differential in the presence of this unusual and striking MRI finding.

34

IS ACUTE POLYRADICULONEURITIS PAINFUL IN DOGS?

L. Van Ham[1], D. Polidoro[1], S. Raes[1], I. Van Soens[2], I. Cornelis[1], S.F.M. Bhatti[1]

[1] Small Animal Department, Small Animal Teaching Hospital, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[2] Department of Clinical Sciences, Small Animal Medicine, Faculty of Veterinary Medicine, Liege University, Liege, Belgium

In humans, Guillain-Barré syndrome is the most frequent acute idiopathic polyneuropathy (AIP). It is characterized by progressive weakness, starting in the legs and ascending to the arms and cranial muscles. Pain is a frequent symptom, manifesting in 72% of the cases, the intensity varying from mild to severe. The highest pain levels occur in the first 2 weeks, at the peak, or near the end of the disease.
Acute polyradiculoneuritis (APRN) is considered to be the canine analog of Guillain-Barré syndrome and the most frequent AIP in dogs. The ventral motor nerve roots in particular are affected. It is characterized by acute paraparesis, rapidly progressing to generalized lower motor neuron tetraparesis/tetraplegia. The dorsal sensory nerve roots are variably affected. Pain is rarely reported and generally accepted to be less pronounced and less frequent than in humans.
Three dogs (2 Maltese and 1 Jack Russell terrier) with clinical, electrodiagnostic and histopathological evidence of APRN, almost continuously flexed/extended one or, more frequently, both hindlimbs, producing a dancing movement. In dog 1, these movements started shortly before typical clinical signs of APRN and continued shortly after these signs recovered. Treatment of dogs 1 and 3 with gabapentin for presumed neuropathic pain resulted in disappearance of these hindlimb movements after a few days of treatment only (dog 2 was not treated).
Further research is necessary to know the prevalence and different kinds and mechanisms of pain in dogs with APRN in order to improve therapies for reduction of pain in both dogs and humans.

35

THE INFLUENCE OF KETAMINE ON THALAMIC METABOLITE CONCENTRATION IN IDIOPATHIC EPILEPTIC DOGS AND THEIR HEALTHY SIBLINGS

M. Wieser[1], K.M. Beckmann[2], N. Zölch[3], A.P.N. Kutter[1], N. Mauri[4], H. Richter[4], R.N. Bektas[1]

[1] University of Zurich, Department of Clinical Diagnostics and Services, Section of Anaesthesiology, Switzerland
[2] University of Zurich, Clinic of Small Animal Surgery, Neurology Department, Switzerland
[3] University of Zurich, Department of Forensic Medicine and Imaging, Institute of Forensic Medicine, Switzerland
[4] University of Zurich, Department of Clinical Diagnostics and Services, Clinic for Diagnostic Imaging, Switzerland

Administration of ketamine in idiopathic epilepsy (IE) is controversial as pre-existing neurotransmitter imbalance in IE dogs are suspected and possible pro-convulsive effects of ketamine are reported. However, it is largely unknown to what extent this pre-existing imbalance affects the dog's response to ketamine. Proton magnetic resonance spectroscopy (MRS) allows non-invasive in vivo measurements of brain metabolites including glutamate/glutamine (GLX) and GABA. The aim of this study was to investigate the effect of low dose ketamine on brain metabolites by MRS in IE dogs compared to healthy control dogs. We hypothesize that ketamine will increase brain GLX concentration in IE and healthy control dogs.

21 IE and 12 unaffected dogs were prospectively enrolled. A standardized anaesthetic protocol was used. 3 Tesla MRS was performed in the thalamus before and 2 minutes after 1 mg kg-1 intravenous ketamine administration. MRS date were analysed using LCModel software.

Paired two-samples Wilcoxon test was used to assess changes induced by ketamine and differences between epileptic and non-epileptic dogs after normality testing. A $p < 0.05$ was considered statistically significant.

The changes induced by ketamine were not significantly different GLX, but for the estimates of GABA to water ratio in IE (0.16 (-0.97 - 1.06) (median (range))) compared to healthy controls dogs (-0.20 (-0.95 – 0.68)). Measuring GABA concentrations using MRS is challenging and results should be interpreted with caution.

Administration of low dose ketamine may result in changes in GABA, but not in GLX concentration in IE dogs compared to healthy control dogs.

36

SUSPECTED FAMILIAL PITUITARY NEOPLASIA IN TWO DOGS

L. Espino[1], N. Miño[1], S. Diequez[2], M.L. Suárez[1], A. Seoane[1]

[1] Departamento de Anatomía, Producción Animal y Ciencias Clínicas Veterinarias. Universidad de Santiago de Compostela. Lugo, Spain
[2] Clínica veterinaria la Mascota, Ourense, Spain

Pituitary tumours represent a high percentage of intracranial neoplasia in dogs and humans. In people, most occur sporadically, but inherited genetic predisposing factors are increasingly recognized. To our knowledge, familial pituitary neoplasia has not been reported in veterinary medicine. We herein report a family of French Bulldogs where two members developed a pituitary neoplasia.

The first dog (mother), a 8-year-old, female neutered French Bulldog was presented to our hospital with complaints of worsening abnormal mentation and behaviour during the last two months. Abnormalities detected on neurological examination were indicative of a forebrain lesion. MRI revealed a large (21x23x26 mm) spheroidal mass in the sellar/parasellar region. A non-functional pituitary macroadenoma was suspected based on MRI characteristics and endocrine functional tests results. Supportive treatment and radiotherapy were established but the dog died during treatment. The owner declined autopsy. Three years later, the second dog (son), a 7-year old, male non neutered French Bulldog, was evaluated with similar clinical signs. A pituitary mass with the same characteristics as described for the first dog was observed on MRI although with a small size (16x16x18 mm). Supportive treatment and radiotherapy were established, and the dog is still alive.

Familial isolated pituitary tumours in humans are a well-known clinical entity and account for 2-3% of pituitary neoplasia. Our report highlights the need for genetic studies to confirm the presence of this hereditary tumour in dogs because, in people, this neoplasia tends to affect young patients, to present as macroadenomas and often is relatively difficult to control.

37

A CASE OF GLOBOID CELL LEUKODYSTROPHY FIRSTLY IDENTIFIED IN RUSSIA IN A 3-MONTH-OLD WEST HIGHLAND WHITE TERRIER (WHWT) PUPPY CONFIRMED BY MRI, HISTOPATHOLOGY, AND A GENETIC TEST

A.S. Subbotin, K.P. Bocharova, K.G. Kopitov, A.A. Litvinova

Veterinary Clinic "Beliy Klik" Moscow, Russia

Globoid cell leukodystrophy (Krabbe disease) is a genetic disorder, caused by mutation in a gene encoding galactosylceramidase resulting in the accumulation of galactosylsphingosine (psychosine) which consequently leads to the loss of myelin, reactive astrocytosis, and formation of globoid cells.

A 3-month-old WHWT male puppy with a 21-day progressive paraparesis of the pelvic limbs and urinary incontinence was presented to the clinic. The neurological examination showed ambulatory paraparesis of the pelvic limbs, reduced patellar reflex, disorientation, aggressive behavior, positional bilateral vertical nystagmus, and signs of headache. Complete blood count and biochemistry, radiography and MRI of the thoracolumbar region were all within normal limits. MRI of the brain showed a bilateral symmetrical hypertensive lesion on T2 weighted images (WI) of the white matter at the level of rhinencephalon, corona radiata, occipital lobes, cerebellum hemisphere, and medulla, as well as decreased signal intensity on T2WI of the thalamus, caudate nucleus, midbrain and pons. The absence of corpus colosseum, reduced cerebellum size was also identified. Due to the overall negative prognosis, the animal was euthanized. Results of sequencing showed point substitution 473A>C within both alleles of GALC gene. The autopsy showed inclusion of globoid cells and macrophage infiltration of the white matter.

To our knowledge, this is the first described globoid cell leukodystrophy case in Russia, confirmed by a pathomorphological evolution and DNA analysis. It means that 473A>C mutation can lead to Krabbe disease independently of geographical origin of an animal. Moreover, some of the mentioned MRI changes have never been described before.

38

DISSEMINATED MYCOBACTERIUM TUBERCULOSIS INFECTION PRESENTED INITIALLY AS MYELITIS IN A DOG

C.Y. Tsai[1], P.W. Liao[2], H.W. Chang[2], C.R. Jeng[2], Y.P. Chang[1,3]

[1] National Taiwan University Veterinary Hospital, National Taiwan University, Taiwan
[2] Institute of Molecular and Comparative Pathobiology, School of Veterinary Medicine, National Taiwan University, Taiwan
[3] Institute of Clinical Veterinary Science, School of Veterinary Medicine, National Taiwan University, Taiwan

A 1-year old male neutered mixed-breed dog presented with 2-month progressive pelvic-limb ataxia, diffuse spinal pain, joint swelling and intermittent fever. MRI of the spine was not performed due to financial issue. CSF analysis revealed mild mononuclear pleocytosis, while synovial fluid analysis revealed neutrophilic pleocytosis. ANA titer was >320. Pathogen screening tests, including CSF and synovial fluid bacterial culture, *Cryptococcus* antigen test, PCR of canine distemper virus, *Babesia, Ehrlichia* and *Toxoplasma* in blood and CSF, were all negative, except positive serum *Ehrlichia* antibody. Initially, the patient was treated with doxycycline for suspected ehrlichial meningomyelitis and arthritis, but with minimal improvement. Treatment was then switched to immunosuppressive dosage of prednisolone, targeting systemic lupus erythematosus or steroid responsive meningitis-arteritis. Clinical signs improved in the first 2 weeks, remained static for 5 weeks, but later deteriorated into tetraparesis, obtundation, hematuria, and sepsis at 12th week following treatment. The patient was euthanized. Post-mortem examination revealed multifocal granulomatous lymphoplasmacytic meningoencephalomyelitis and disseminated pyogranulomatous inflammation in multiple organs, including kidneys and lungs. Intralesional acid fast positive rods were detected and *Mycobacterium tuberculosis* was confirmed by PCR.
This case report demonstrated that neurological symptoms, especially signs suggestive of myelitis, can be the initial presentation for *M. tuberculosis* infection in dogs. In countries with low incidence rates in human, *M. tuberculosis* infection in companion animals is considered rare. Due to the non-specific clinical presentation and the difficulties of cultivating *M. tuberculosis*, achieving the antemortem diagnosis would be challenging unless clinicians were aware of this differential diagnosis.

39

UNCOMMON MANIFESTATION OF A CANINE PHEOCHROMOCYTOMA. A CASE REPORT

A. Knebel[1#*], K. M. Gregor[2,3#], A-K. Haverkamp[2], W. Baumgärtner[2], H.A. Volk[1,3]

[1] Small Animal Clinic, University of Veterinary Medicine, Hannover, Germany;
[2] Department of Pathology, University of Veterinary Medicine, Hannover, Germany;
[3] Center for Systems Neuroscience Hannover (ZSN);
[#] Both authors contributed equally to the manuscript, *ECVN resident

A 9-year-old male neutered Golden Retriever was presented with a history of acute onset deteriorating cervical pain. The dog was normal on general physical and neurological examination. Magnetic Resonance Imaging of the cervical spine revealed a focal, extramedullary, infiltrative, poorly demarcated, heterogeneous mass with moderate contrast enhancement at the level of the left cranial articular process of the axis (C2), leading to an osteolysis and pathological fracture of C2 as well as marked soft tissue trauma. Due to severe findings and the grave prognosis, the dog was euthanized.

At post-mortem examination, the right adrenal gland was severely enlarged as a result of a neoplasm arising from the adrenal medulla. C2 was lytic with surrounding musculature displaying a white, well-demarcated, tough mass lesion. In addition, there were neoplastic growths in and adjacent to the prostate and pulmonary lymph nodes. Based on gross, histologic and immunohistochemical findings, a pheochromocytoma (PCC) originating from the right adrenal gland was diagnosed which metastasized into the cervical vertebral column, prostate and pulmonary lymph nodes. PCCs are endocrine tumors derived from chromaffin cells, that can metastasize and invasively infiltrate into the caudal vena cava. Depending on their potential to produce catecholamines, they can also lead to cardiovascular, respiratory and/or gastrointestinal clinical signs.

In conclusion, this case report highlights the variable manifestation of PCC regarding clinical signs and distribution of metastases. PCC should be considered as a differential diagnosis for cervical pain in elderly patients without other clinical signs for PCC.

40

URINARY NEUROTRANSMITTER ANALYSIS IN CANINE BEHAVIOURAL DISORDERS

T. Schmidt[1], S. Meller[1], R.M.A. Packer[2], S.R. Talbot[3], H.A. Volk[1]

[1] Dept. of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany
[2] Dept. of Clinical Science and Services, Royal Veterinary College, Hatfield, UK
[3] Institute for Laboratory Animal Science, Hannover Medical School, Hannover, Germany

Deviations in the neurotransmitter system are associated with numerous psychiatric disorders and neurological diseases. To evaluate neurotransmitter system function, urinary neurotransmitter screening is regularly used in human medicine, e.g. in patients suffering from mood disorders like anxiety and depression. In veterinary medicine anxiety disorders have a high prevalence in dogs. A non-invasive comprehensive neurotransmitter analysis may enable precise diagnostics of canine behavioural disorders and effective neuromodulatory treatment monitoring. The objective of this study was to establish and validate a non-invasive diagnostic tool where characteristic neurotransmitter deviations served as biomarkers for canine behavioural abnormalities. Urine samples of 100 dogs were analysed, consisting of a group suffering from behaviour-related problems in comparison to age- and breed-matching healthy controls. Quantification of urinary neurotransmitter levels was conducted utilising High-performance liquid chromatography Triple Quadrupole MS/MS technology. The behaviour profile of the dogs was determined using a standardized online questionnaire, composed of previously validated questionnaires (C-BARQ, ADHD-RS, DPQ, CCDR).

Regression analysis revealed a hormonal influence on urinary neurotransmitter excretion. An age-dependent association between gender/castration status and urine neurotransmitter levels was found. No correlation between the neurotransmitter levels and the behaviour profile was found.

The evidence from this study suggests that urinary neurotransmitter levels do not correlate with the canine behaviour profile. However, future trials with wide-ranging behaviour analysis and extended neurotransmitter screening in biological fluids, like blood or cerebral spinal fluid, may validate the neurotransmitter analysis as a valuable diagnostic tool for canine behavioural disorders.

41

HEAD TILT IN PET RABBITS (*ORYCTOLAGUS CUNICULUS*): 33 CASES (2009-2021)

T. Liatis[1], N. Makri[1], J. Richardson[1], T. Nuttall[1], A. Suñol [1]

[1] Hospital for Small Animals, Royal (Dick) School of Veterinary Medicine, University of Edinburgh, Edinburgh, UK

Head tilt has been described as a clinical sign of vestibular disease in rabbits. However, the prevalence of the most common diseases causing this clinical sign is unknown.

A retrospective study was designed aiming to investigate the most common causes and the clinical reasoning of head tilt in pet rabbits. Medical records for pet rabbits in our hospital were reviewed (2009-2021). Inclusion criteria were: head tilt, head Computed Tomography (CT) and *Encephalitozoon cuniculi* (EC) serology (positive: IgM or IgG >1:80).

Thirty-three rabbits (17/33 males; 16/33 females) were included. Lop-eared (20/33) outnumbered upright-eared breeds (13/33). Median age of presentation was 5-year-old. Onset of signs was hyperacute/acute in 26/33 rabbits and subacute/chronic in 7/33. Nine rabbits had a previous history of otitis externa (OE), 9/33 otitis media (OM) and 4/33 EC infection (4/33). Most common presenting complaints included head tilt (29/33), wobbliness (15/33) and dysorexia (14/33). Most common neurological signs included head tilt (33/33), vestibular ataxia (26/33), nystagmus (12/33) and hemifacial tetanus (4/33). EC serology was positive in 23/33 rabbits (2/33 IgM; 22/33 IgG). CT revealed OE in 24/33 patients and OM in 20/33. Diagnoses were co-infection (OM and EC; 23/33), EC-only (11/33), OM-only (6/33), open (4/33). Cultures were positive from 6/8 rabbits with OM, from which isolates were: *Pasteurella canis, P.multocida, P.fluorescens, Pseudomonas aeruginosa, Staphylococcus aureus*.

Head tilt in rabbits is accompanied by other neurological signs and is usually a result co-infection of OM and EC. Paired EC serology and head CT should be considered for head tilt investigations in rabbits.

42

BARKING UP THE WRONG TREE: SIGNS OF BACTERIAL LOWER URINARY TRACT INFECTION IN FIVE DOGS WITH IDIOPATHIC EPILEPSY MISTAKEN AS SIDE EFFECTS OF ANTISEIZURE DRUGS

N. Meyerhoff, T. Schmidt, H.A. Volk

Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Germany

Unspecific clinical signs as polydipsia, polyuria, ataxia and behavioral changes are known side effects of antiseizure drugs (ASD) in dogs and reduce quality of life (QoL) of dogs and their owners. Concurrent diseases like lower urinary tract infections (lowUTI) might be misinterpreted as side effects in dogs receiving ASD therapy.

Five dogs were identified during recruitment for an idiopathic epilepsy (IE) treatment trial with ethical permission. Of these animals (n=38; female n= 17, male n=21); five (13,16%) dogs were diagnosed with lowUTI caused by *E.coli*. Affected dogs were female (intact n=3; neutered n=2), weighting over 20kg.

Therapy was phenobarbitone (PhB; n= 5, >3 months), potassium bromide add-on therapy (n= 2). Reported chronic side effects were: mild ataxia, polyuria/polydipsia, behavioral changes, polyphagia and recent deterioration consisting of restlessness (n=5), apathy (n=4), overgrooming anogenital region (n=2), marked ataxia (n=2), incontinence (n=2), exercise intolerance (n=1) and malodor (n=1). Pyuria, hematuria and bacteriuria were detected in affected dogs. Urine analysis revealed positive nitrite (n=2), proteinuria (n=2) and specific gravity (mean: 1015,6, range: 1002-1022) before antibiotic treatment. *E. coli* (>10^6 CFU/ml) was isolated from cystocentesis samples in all dogs. Amoxicillin-clavulanic acid (13-15mg/kg BID, n=34) therapy improved the condition of all dogs within 24-48 hours. Samples of urine were unremarkable at follow-up.

Clinical signs were misinterpreted for weeks in each dog, reducing QoL, potentially aggravating epilepsy. Further studies are needed if polydipsia and diluted urine in dogs treated with ASDs can increase risk for lowUTI in addition to potential immunosuppressive effect of PhB.

43

SHOULD WE TREAT CANINE DRUG-RESISTANT IDIOPATHIC EPILEPSY WITH ANTIBIOTICS?

L. Ledeganck[1], F. Verdoodt[1,2], M. Hesta[2], I. Cornelis[1], L. Van Ham[1], S.F.M. Bhatti[1]

[1] Small Animal Department, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium
[2] Equine and Companion Animal Nutrition, Department of Morphology, Imaging, Orthopedics, Rehabilitation and Nutrition, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

Despite the administration of anti-seizure drugs (ASDs), 30% of dogs with idiopathic epilepsy (IE) are drug-resistant. Therefore, the search for non-drug treatment alternatives is important. We evaluated the effect of amoxicillin-clavulanic acid on the epileptic seizure frequency and cluster seizures canine drug-resistant IE.

A dog with drug-resistant IE of 7.5 months duration became seizure free during an amoxicillin-clavulanic acid treatment of 4 weeks duration for an infectious mono-arthritis. Based on that observation, 4 other dogs with drug-resistant IE were given amoxicillin-clavulanic acid in order to improve their epileptic seizure control. The mean epileptic seizure frequency of these 5 dogs was 3 seizures/week (range 2-7) with a mean cluster seizure frequency of 1 cluster/week (range 0-2) during 2 months prior to antibiotic administration. The mean duration of antibiotic administration was 32 days (range 21-64 days). During amoxicillin-clavulanic acid administration, 3 dogs showed seizure freedom, 1 dog showed an 80% decrease of both epileptic seizure and epileptic cluster frequency, and 1 dog showed an increase in epileptic seizure and epileptic cluster frequency of 54% and 38%, respectively. In the 2-month follow-up period after cessation of antibiotic administration, the mean epileptic seizure and mean cluster frequency increased again to 1.5 seizures/week (range 1-3) and 0.4 clusters/week (range 0-1), respectively.

In these dogs, it was suggested that antibiotic administration generated an altered gut microbiome. This report suggests the presence of a canine gut-brain axis and manipulation of this axis may offer beneficial effects in the epileptic seizure control of dogs with drug-resistant IE.

44

USE OF LEFLUNOMIDE AS A PART OF COMBINED TREATMENT AND AS MONOTHERAPY IN COMPARISON WITH THE STANDARD TREATMENT PROTOCOLS IN ANIMALS WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN (MUO)

A.S. Subbotin, K.P. Bocharova, E.V. Gogua, K.G. Kopitov

Veterinary Clinic “Beliy Klik” Moscow, Russia

MUE is an immune-mediated disease of the central nervous system (CNS) in dogs. The usage of immunosuppressive drugs can improve clinical signs and delay the progression of the disease. Several drugs such as glucocorticosteroids, cytarabine, cyclosporine, and azathioprine are generally used to treat MUO and considered as standard treatment in combination or alone. However, due to the COVID-19 pandemic, the availability of some of these drugs remains limited, suggesting the need for evaluation of alternative medications for treatment MUO, such as leflunomide.
16 dogs with MUO receiving leflunomide with additional immunosuppressive agents have been retrospectively compared with a group of 51 dogs receiving standard treatment. Clinical picture and MRI results consistent with MUO were the inclusion criteria as well as the presence of inflammatory cerebrospinal fluid in some animals. In the leflunomide group treatment started with standard therapy combined with leflunomide in dose 1.1-6.6 mg/kg (mean 3.0 mg/kg). The statistical analysis was performed using the Kaplan-Meier method, log-rank test, and Pearson’s chi-square test. The results didn’t show any statistically significant differences in survival, however the mean survival time in the leflunomide group was 693 days in comparison with 809 days in the control group. Additionally, statistically significant reduction of complications was observed in the leflunomide group which was presented by gastrointestinal disturbances in two patients and pneumonia in one case.
Therefore, leflunomide can be used as an add-on drug for treatment MUO, with a low percentage of adverse reactions. Further investigation is required to evaluate the effectiveness of the drug.

45

CLINICAL USE OF TOCERANIB IN THE TREATMENT OF GLIOMA IN A DOG

R.F. Schamall

Clínica Veterinária Petrópolis - Petrópolis - RJ - Brazil

Gliomas are common CNS tumors affecting dogs, generally presenting a rapid, fatal outcome. Clinical signs are amplified by associated vascular events. Clinical and surgical treatments fail to improve survival. Radiotherapy presents better results, although with high financial costs. Gliomas are fast-growing tumors and, therefore, must induce extensive vascular network, generally by expressing cytokines that promotes extensive neovascularization. Anti-angiogenic drug therapy has been shown to be an interesting alternative in the management of different tumor types, although with variable results. Tyrosine kinase receptors are involved in several important metabolic steps to regulate cell growth and differentiation, and their dysfunctions have already been shown to be an important cause of neoplasia.
We evaluated toceranib (Palladia, Zoetis) as the only treatment for a 13-year-old female Shih-Tzu dog, presenting focal epileptic seizures and subacute onset of behavioral changes. Magnetic resonance imaging (MRI) showed an intra-axial lesion in the right frontoparietal lobe, with moderate perilesional vasogenic edema. Biopsy of the lesion showed results compatible with high-grade astrocytoma. Prednisone and phenobarbital were associated. After 6 months, a follow up MRI showed total regression of the tumoral mass, and normalization of the brain parenchyma, with only one small non-contrast enhanced hyposignal area in T1 remaining in the center of the previous lesion. No adverse clinical and laboratory signs were noted on the dog until the follow-up was lost after one year.
We believe this finding indicates a need for a larger scale study, to better understand the effects of toceranib in the treatment of gliomas in dogs.

46

SUCCESSFUL USE OF INTRAVENOUS HUMAN IMMUNOGLOBULIN FOR TREATMENT OF SUSPECTED ACUTE POLYRADICULONEUROPATHY IN A CAT

D. Sivolapenko[1], P. Amengual-Batle[2], M. Garcia-Arce[1], D. Starybrat[1], K. Marioni-Henry[1]

[1]Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK
[2]Hospital Veterinario Puchol, Neurology Department, Madrid, Spain

A one-year-old male neutered Savannah cat presented for rapidly progressive non-ambulatory tetraparesis. The onset of neurological abnormalities was first noted 24 hours after a vaccine booster, and consisted of cerebellar signs, that lasted 48 hours and spontaneously resolved. Paraparesis was then noted after a week, which progressed, and two days later the cat re-presented and had non-ambulatory tetraparesis with minimal voluntary motor function in all limbs and tail, absent spinal and palpebral reflexes, and difficulty vocalising. An acute polyradiculoneuropathy was suspected. Supportive care and one dose of dexamethasone (0.3 mg/kg IV) were administered, but within 12 hours the clinical signs progressed to tetraplegia and severe hypoventilation with lack of chest excursions. The cat was anaesthetised for mechanical ventilation. After 12 hours, treatment with intravenous human immunoglobulin (IVIg) was attempted via infusion over 6 hours. No adverse reactions were noted. The patient developed aspiration pneumonia later that day and antibiotic treatment was started. Approximately 36 hours since the start of mechanical ventilation, gradual weaning off the ventilator was successfully achieved. Afterwards, the patient demonstrated improved voluntary motor function compared to admission. The following morning, the cat was ambulatory with mild tetraparesis, and able to vocalise normally. At the recheck, 2 weeks later, the physical and neurological examination were normal. The use of IVIg for treatment of Guillain-Barré syndrome in humans and Acute Idiopathic Polyradiculoneuritis in dogs has been described, this is the first case reporting the safe and successful use of IVIg for the treatment of acute polyradiculoneuropathy in a cat.

47

PERACUTE AND SEVERE NECK PAIN ASSOCIATED WITH THICKENING OF THE DORSAL ATLANTO-AXIAL LIGAMENT ON CT IN THREE DOGS

I. Cornelis[1], K. Kromhout[2], E. Stock[2], D. Polidoro[1], L. Van Ham[1], S.F.M. Bhatti[1]

[1] Small Animal Dept., [2]Dept. of Veterinary Medical Imaging and Small Animal Orthopaedics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium.

Traumatic and congenital lesions of the atlanto-axial joint are generally known and thoroughly discussed in veterinary literature. We would like to present three dogs with possibly trauma-induced severe neck pain associated with an abnormal dorsal atlanto-axial ligament (DAL) on CT imaging.

A 3-year-old Border Collie, a 1-year-old Barbet and a 9-month-old Boxer presented with acute and severe neck pain. Acute onset during frisbee playing (Border Collie) and after rolling over (Boxer) were witnessed. Treatment with NSAIDs caused only slight temporary improvement. Severe neck pain was the only abnormality on neurological examination. Complete blood count and serum biochemistry profile were within normal limits in all dogs, except for a moderately increased CRP (30.2, 40.7 and 60.6mg/l; RI <10mg/l). A CT scan of the cervical vertebral column revealed irregular thickening of the DAL in all three dogs and presence of heterogenous contrast enhancement. No spinal cord compression or osseus abnormalities were seen. In all dogs, placement of an external splint caused immediate relief of clinical signs. Complete resolution of clinical signs was obtained after 1-5 months in all dogs. Follow-up CT was performed in one dog (Boxer) after 4 weeks, revealing normalisation of the DAL.

Thickening and possible secondary inflammation of the DAL can be found on CT examination in dogs with peracute and severe neck pain and might be related to hyperflexion/extension of the atlanto-axial joint as is seen in whiplash in people. The condition carries an excellent prognosis after external splinting which can be removed after normalisation of CRP values and eventually CT findings.

48

CALVARIAL IDIOPATHIC HYPEROSTOSIS SYNDROME PRODUCING SKULL PAIN IN A YOUNGPIT BULL TERRIER

A. Bernabé, M. Soler, J.D. García

Dept of Small Animal Medicine and Surgery, University of Murcia, Spain

Calvarial Idiopathic Hyperostosis Syndome (CHS) is a self-limiting bening disease of skull not very reported in veterinary medicine characterized by a proliferative osseous lession of the skull2. In this case we describe a CHS in a young male Pit Bull Terrier producing severe skull pain. A 6-month-old intact male of Pit Bull Terrier presented to the University of Murcia Teaching Hospital for evaluation of a severe swelling of the right side of the head of two weeks of progression. The dog was lethargic and physical examination showed pyrexia, a moderate oculus sinister exophthalmos and lateral globe deviation with severe inflammation and pain of the frontal and occipital bones zone. A complete hematology and biochemistry did not show relevant abnormalities. Computed Tomography (CT) revealed thickening and increased attenuation of the right frontal, parietal and occipital bones. An expansive lesion with heterogeneous attenuation was observed affecting the frontal bones. This lesion presented irregular but well-defined borders that obliterated part of the right frontal sinus, causing slight lateral displacement of the ipsilateral eyeball. A CHS was diagnosed and meloxicam and omperazol was the treatment selected. The clinical signs improved, although suffered a new relapse two weeks later. As CHS has been purported to be associated with bacterial osteomyelitis, a treatment with metronidazole and enrofloxacin was added. The dog improved, although symptoms persisted until the animal was 1 year-old. In summary, the CHS is a shelf-limiting process that it should be treated with non-steroids anti-inflammatory agents and antibiotics until the animals reach skeletal maturity.

49

NORMAL HYPOCRETIN-1 LEVELS IN A DOG WITH SUSPECTED ACQUIRED NARCOLEPSY-CATAPLEXY

M. Pons-Sorolla, C. Maeso, C. Morales-Moliner, M. Pérez-Soteras, P. Montoliu

AniCura Ars Veterinaria, Neurology Department, Spain

Narcolepsy is an infrequent disorder characterized by abnormalities of the sleep-wake cycle and cataplexy, produced by alterations in hypocretin and its receptors. Familial narcolepsy in dogs is caused by mutations in the hypocretin receptor-2 gene, and early onset of signs is observed. Acquired narcolepsy has been associated to loss of hypocretin producing neurons in the hypothalamus, which causes markedly decreased hypocretin-1 levels in CSF.

A 6-year-old male Fox Terrier was referred for an acute onset of collapsing episodes triggered by food or excitement. Episodes consisted of sudden skeletal muscle atonia followed or not by REM sleep, consistent with narcolepsy-cataplexy. Approximately 20-30 daily episodes were reported. Neurological examination was normal except for obtundation, and collapsing episodes occurred every few minutes on consultation. Arterial blood pressure, complete blood analysis, cortisol levels, serum ELISA assay for *Leishmania infantum* and *Ehrlichia ewingii*, echocardiography, electrocardiography during the collapsing episodes, abdominal ultrasound, thoracic radiographs, MRI scan of the head and cerebrospinal fluid (CSF) analysis were unremarkable. CSF hypocretin-1 levels were within normal limits (229,78 pg/mL; ref>110 pg/mL). A presumptive diagnosis of acquired narcolepsy was stablished due to the pathognomonic cataplexy episodes.

Treatment with prednisolone (4 mg/kg followed by tapering dose) and clomipramine resulted in partial response. Clomipramine was substituted for venlafaxine, and marked improvement was achieved.

Acquired adult-onset narcolepsy with normal CSF hypocretin-1 levels has only been reported in one dog with a pituitary macrotumour. The case reported here supports the existence of different pathophysiologic mechanisms, probably targeting different brain localizations, implicated in acquired narcolepsy in dogs.

50

PREVALENCE OF NEUROLOGICAL DISORDERS IN PUG DOGS IN THE UNITED KINGDOM: A SINGLE CENTRE RETROSPECTIVE STUDY - PRELIMINARY ANALYSIS

E. Skovola[1], E. Vettorato[1], G. B. Cherubini[1]

[1] Dick White Referrals, United Kingdom

Due to retrospective descriptive nature of this study ethical approval was not pursued. Informed owner consent to use data for retrospective studies was obtained at the time of hospital admission.

Pug dogs (PDs) are affected by several neurological disorders. This retrospective descriptive study reports their prevalence from a single referral center in the UK.

Medical records of PDs referred to the Neurology-Neurosurgery Department of Dick White Referrals from 2013 to 2020 were retrieved. Signalment, presenting complaint, presence of pain were recorded. Final diagnosis was classified as: encephalopathies, myelopathies or peripheral nervous system (PNS) disease. Descriptive statistical analysis was performed. Data are reported as mean (± standard deviation) or median (95% Confidence Intervals).

A total of 286 records were retrieved and included: 103 PDs were females (66 spayed) and 183 males (66 neutered). The median age was 62 (57 - 65) months; the mean body weight was 8.5 (± 2.2) kg. The most representative clinical complaints were: ambulatory paraparesis (27.6%), seizure-like episodes (20.3%), ataxia (16.4%), spinal pain (10.1%) and vestibular signs (5.6%). Myelopathies were diagnosed in 64.7% of PDs. Encephalopathies and PNS disease in 29.7% and 5.3% of PDs, respectively. Aortic thromboembolism was diagnosed in one case (0.3%). Intervertebral disc extrusion/protrusion (44.3%), spinal arachnoid diverticulum (22.2%) and vertebral malformations (18.9%) were the most prevalent myelopathies. Of encephalopathies, idiopathic epilepsy (44.7%) and meningitis of unknown aetiology (29.4%) were the most represented. Of PNS diseases, otitis (60%) and masticatory muscle myositis (20%) were the most represented.

This is the first study reporting the prevalence of neurological disorders in a large population of PDs in the UK. These results might be useful to guide clinicians in the diagnosis of neurological disorders in this breed.

51

POLYGLUCOSAN BODY NEUROPATHY MEETS INFLAMMATORY DEMYELINATION – A RARE ADULT OVERLAP SYNDROME IN A NEUROMUSCULAR CAT

N. Kolb[1], J.L. Thibaud[2], S. Franzmeier[1], M. Rosati[1], K. Matiasek[1]

[1] Section of Clinical & Comparative Neuropathology, LMU Munich, Germany
[2] Micen Vet, Créteil, France

Immune-mediated polyneuropathy (IMPN) accounts for about 65% of PNS diseases in cats. Most IMPNs present with sudden onset early in life but they may occur throughout lifetime with variable courses and neuromuscular signs. Herein, we describe a case, in which neuromuscular dysfunction was due to IMPN on top of another late-onset neuropathy in a cat.
A 12-year old, male-neutered Domestic Shorthair cat was admitted due to progressive gait abnormalities for 1 year. Neurological examination revealed head tremor, paraparesis and tetraataxia, accentuated in hindlimbs. On electromyography, spontaneous activity was recorded from multiple front and hindlimb muscles. Decreased motor nerve conduction velocity was seen in tibial and peroneal nerves, and muscle action potential was reduced in ulnar nerve upon proximal stimulation. Nerve and muscle biopsies revealed extensive intraaxonal polyglucosan bodies next to chronic-active inflammatory demyelination of large myelinated fibres.
Polyglucosan bodies are a common incidental finding in CNS of geriatric people, dogs and cats. Their occurrence in peripheral axons even at high age is rare and restricted to individual fibres. Widespread abundance and association to progressive neurological dysfunction is a feature of adult-onset polyglucosan body disease (APBD) in people, a rare variant of genetic glycogen storage disorders.
Search of the neuromuscular archive led to one single other case of polyglucosan body neuropathy overlapping with chronic inflammatory demyelinating polyneuropathy (CIDP)-type of IMPN in a 13-year old cat.
The metabolic cause of APBD in cats and whether pure occurrence without inflammation would have manifested clinically is yet unclear as is the efficacy of immunotherapy.

52

SPECIES DIFFERENCES OF BORNAVIRUS ENCEPHALITIS IN BETWEEN HORSES, ALPACAS, SHEEP AND HUMANS

Y. Vollmuth[1], F. Liesche-Starnecker[1], J. Schlegel[1], K. Matiasek[2], M. Rosati[2]

[1] Department of Neuropathology, Institute of Pathology, TU Munich, Germany
[2] Section of Clinical & Comparative Neuropathology, LMU Munich, Germany

Borna disease virus 1 (BoDV-1) causes fatal encephalitis in domestic animal species and humans. Distribution of virus and lesions seems to differ between human and equine patients. There is, however, lack of data on the resemblance to alpacas and sheep. The aim of this study was to provide a topological comparison of BoDV-1 infection in humans and animals to allow conclusions regarding the spreading of the inflammation and infection route.
6 BD-affected human autopsy cases, 5 horses, 4 sheep and 4 alpacas were investigated for expression of BoDV-1 antigen (Bo18), CD45, CD3, CD20, and CD68/Iba1 as well as for presence of BoDV-1 RNA. Immune cell density was calculated via image analysis
In all animals virus antigen and RNA were concentrated on the limbic system, while, in humans, distribution was far more widespread involving basal nuclei and insular cortex, followed by medulla oblongata, mesencephalon and occipital cortex. Lymphocytic infiltration here was most prominent in occipital lobe and striatum compared to hippocampus and brain stem in animals.
The different distribution of BoDV-1 lesions in animals compared to humans might reflect different infection routes and provide new information about the chain of events leading to encephalitis.

53

A COMPARATIVE STUDY INTO INTERVERTEBRAL DISC DISEASE IN ENGLISH COCKER SPANIELS, FRENCH BULLDOGS AND DACHSHUNDS

J. Abouzeid[1], N. J. Grapes[2], P. Freeman[1]

[1] The Queens Veterinary School Hospital, University of Cambridge
[2] The Queen Mother Hospital for Animals, the Royal Veterinary College

This study aims to describe the anatomical distribution and clinical features of intervertebral disc extrusions (IVDE) in English Cocker Spaniels (ECS), Dachshunds and French Bulldogs (FBD) and compare the relative risk for them to experience cervical extrusions.

A retrospective, multicentre study was designed and a total of 951 dogs were included: 474 dachshunds, 332 FBS and 145 ECS with IVDEs.

The imaging data bases at two referral hospitals were searched for dogs of the desired breeds which experienced IVDE between January 2015 to December 2020. IVDE location, signalment, clinical signs and neurological examination findings were recorded. IVDE locations were classified as cervical (C1/2-C5/6), cervicothoracic (C6/7-T2/3), thoracolumbar (T9/10-L3/4) or lumbosacral (L4/5-L7/S1).

The results showed ECS distribution for cervical, cervicothoracic, thoracolumbar and lumbosacral were 24%, 3%, 52% and 21% respectively. Dachshunds showed a distribution of 3%, 1%, 92% and 3%. FBD showed a distribution of 33%, 0%, 54% and 12%. The median age of extrusion presentation was higher in the ECS (8 years) vs Dachshunds and FBD (5 years and 3 years old respectively). ECS were more likely to experience IVDEs between C1-T2 than Dachshunds (OR 9.90; 95% CI 5.39-18.16) but less likely than FBDs (OR 0.73; 95% CI 0.48-1.13). Chi squared showed a significant difference when comparing ECS to Dachshunds ($P<0.001$) but not when comparing ECS and FBDs ($P=0.158$).

In conclusion, cervical extrusions are more common in the FBDs compared to the ECS and Dachshund. ECS are more likely to experience IVDEs at an older median age than FBS and Dachshunds.

54

OLD DOG-NEW TRICKS - SUPECTED MUO IN TWO AUSTRALIAN SHEPHERD DOGS: A CASE SERIES

F.Kajin, H.Volk, N. Meyerhoff, J. Neßler

Dept. of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany

Meningoencephalitis of unknown origin (MUO) is mostly considered a disease of small and terrier breeds aged between approximately three and seven years, with a recent study stating that 25% of MUO cases affect large breeds, with no Australian Shepherds listed until now. In this case study, 2 Australian Shepherds, 10 and 11 years old, were presented with progressive clinical signs of multifocal encephalopathy. Magnetic resonance imaging (MRI) revealed multifocal, intraaxial lesions of the cerebral cortical grey matter in one dog and cerebellar and thalamic grey matter in the other dog respectively. Lesions were hyperintense in T2W and fluid-attenuated inversion recovery sequence with no to mild inhomogeneous contrast enhancement. A diagnosis of MUO was based on diagnostic imaging, cerebrospinal fluid findings, negative regional infectious titres and good response to immunomodulatory therapy. Both dogs had serial MRIs. Follow-up MRI examination after three months showed complete resolution of MRI abnormalities in one dog treated with cytarabine and prednisolone. The other dog showed recurrence of clinical signs 23 months after diagnosis and tapering of prednisolone. Re-MRI showed multifocal de novo lesions. After start of cytarabine and prednisolone treatment, clinical signs improved again. The dog is still alive at the time of writing, the other was lost to follow up 5 months after the diagnosis. In conclusion, MUO should be on the differential list also in elderly patients, which can have good outcomes with immunomodulatory therapy. Further studies are needed to explore if Australian Shepherds are at an increased risk of MUOs at senior age.

Written consent from owners for diagnostic workup of findings was given.

55

EPIDURAL AND SYNOVIAL LIPOMATOSIS IN A 3-YEAR-OLD EURASIAN DOG RECEIVING SUSTAINED STEROID THERAPY

M. Signoret[1], L. Gros[2], R. Dumont[4], C. Dally[3], K. Leboedec[4], L. Cauzinille[1]

[1] Dept. of neurology, CHV Frégis, F-94110 Arcueil, France
[2] Dept. of diagnostic imaging service, CHV Frégis, F-94110 Arcueil, France
[3] LAPVSO, 129 Route de Blagnac, Toulouse, France
[4] Dept. of internal medecine , CHV Frégis, F-94110 Arcueil, France

A 3-year-old male neutered Eurasian dog was presented for evaluation of a several week history of hindlimb paresis, urinary incontinence and loss of appetite. He was treated with immunosuppressive dosages of prednisolone for 2 years for chronic inflammatory enteropathy, and with cyclosporine and leflunomide for 3 months for a suspicion of primary immune-mediated polyarthritis. However, impaired locomotion persisted. Upon presentation, a mild paraparesis was noted. Diffuse pain upon thoraco-lumbar palpation was elicited. CT myelography and MRI revealed an extradural mass extending from T8 to L3 causing dorsal compression and ventral displacement of the spinal cord. Tomographic and MRI findings were consistent with fat. Because of the lack of improvement, the dog was euthanized. Histopathological examination showed tightly packed together mature adipocytes in the ependymal mass and in the tarsal synovial membrane, compatible with lipomatosis. Lipomatous tissue is defined as an overgrowth of non-encapsulated adipose tissue. Some predisposing factors described in humans are reported in this case: long-term steroid treatment, which is the main factor associated with spinal epidural lipomatosis in humans, and possible aberrant handling of fat substrates related to enteritis.

56

VENTRICULOPERITONEAL SHUNTING AND RADIATION THERAPY TREATMENT IN A CAT WITH A SUSPECTED CHOROID PLEXUS TUMOUR AND HYPERTENSIVE HYDROCEPHALUS

E. Mahon*, A. Eiras-Diaz+, S. Mason", F. Stabile*, A. Uriarte*

Department of Neurology and neurosurgery*, Internal medicine+, Radiation therapy"
Southfields Veterinary Specialists, United Kingdom

Radiation therapy (RT) is an established treatment choice for inoperable intracranial tumours in cats. Ventriculoperitoneal shunts (VPS) placement has been described for the treatment of hydrocephalus secondary to intraventricular tumours in dogs. To the best of the authors knowledge, this is the first report of successful VPS placement and subsequent RT treatment in a cat with a suspected choroid plexus tumour causing hypertensive obstructive hydrocephalus.
A 14-year-old male DSH was presented for a history of behavioural changes and urinary incontinence. The neurological examination was consistent with a right forebrain lesion and suspected raised intracranial pressure (ICP). Brain MRI revealed an intraventricular multilobulated well-defined T2W-hyperintense and T1W-hypointense, markedly contrast enhancing mass lesion within the dorsal aspect of the third ventricle, causing hypertensive obstructive hydrocephalus. A VPS was placed within the left lateral ventricle, followed by a RT course of 45-Gray total dose in 18 daily fractions. At the time of writing, 6-months post-RT and 4-months after cessation of prednisolone treatment, the patient remained neurologically normal. 6-months post-RT follow-up CT revealed mild reduction in the mass size and resolution of the hydrocephalus.
Raised ICP causes severe clinical signs, can lead to brain ischaemia and herniation and significantly increases anaesthetic risk during RT treatment. VPS placement in cats with hypertensive obstructive hydrocephalus may allow immediate resolution of neurological signs due to raised ICP, and therefore a safer RT treatment.

57

MULTIPLE ISCHEMIC LACUNAR INFARCT IN THREE EURASIER WITH SUSPECTED PRIMARY HYPERLIPIDAEMIA

G.Brunati [1], C. Cantile[2], A. Tomba[3], B. Lombardo[1],G. Abbiati[1], E. Bersan[1]

[1] Unità Operativa di Neurologia e Neurochirurgia, Malpensa Veterinary Clinic, Samarate, IT
[2] Dept Veterinary Science, Veterinary Neuropathology Lab, Pisa University, IT
[3] NORAD Diagnostic Imaging Service, Samarate, IT

Primary hyperlipidaemia (PH) is rare in dogs, a genetic disorder has been suspected in Miniature Schnauzer; PH has never been reported in Eurasier.
Three Eurasier (2 siblings), median age 19 months (range: 15-22 months), were evaluated for vestibular and forebrain signs. The neurolocalisation was at the central vestibular system (2/3) and forebrain (1/3). MRI found multiple ischemic lacunar infarcts mostly involving thalamus, midbrain and the forebrain (territory of the caudal perforating artery and caudal and medial cerebral arteries). Biochemistry profile revealed severe hypercholesterolaemia (median 926,6 mg/dl; RI: 156-369 mg/dl) and mild hypertriglyceridemia (median 188,33 mg/dl; RI 30-112 mg/dl); the rest of the blood work-up including screening for endocrine disease, urine analysis and CSF was unremarkable.
Two dogs were treated with low-fat diet, omega-3 supplementations and either bezafibrate or artovastatin with a reduction of cholesterol and triglycerides levels and good long-term control of clinical signs.
One dog rapidly deteriorated and died. Post-mortem examination and MRI where performed. Histopathology revealed diffuse atherosclerosis of the cerebral arteries, circle of Willis and basilar artery with thickening of the intima and media caused by deposition of cholesterol-like clefts associated to areas of ischemic necrosis, reflecting the MRI changes.
The increased risks for atherosclerosis and subsequently cerebrovascular accidents in patients affected by severe hypercholesterolaemia is well documented in human medical literature and less common in animals.
In these cases, no predisposing diseases were found and therefore hyperlipidaemia was thought to be primary. In light of the close genetic background of these dogs, a hereditary disorder was postulated but further research is required.

58

GENERALIZED IDIOPATHIC POLYMYOSITIS MIMICKING MASTICATORY MUSCLE MYOSITIS IN A DOG

T. Troupel, N. Van Caenegem, C. Drougard, N. Blanchard-Gutton, S. Blot

Ecole nationale vétérinaire d'Alfort, Univ Paris Est Créteil, INSERM, IMRB, Maisons-Alfort, France

Masticatory muscle myositis and generalized idiopathic polymyositis are the most common immune-mediated inflammatory myopathies in dogs. Unlike human medicine, where the diagnosis and classification of inflammatory myopathies have continuously evolved over the last decades with the combination of histopathological and immunohistochemical evaluation and identification of myositis-specific autoantibodies, in dogs, the latter has only been described in masticatory muscle myositis.
We report a dog that presented with subacute spontaneous pain when chewing or eating and exophthalmos, followed by chronic progressive masticatory muscle atrophy and enophthalmos. Creatine kinase activity was drastically increased (8,180 UI/L). Electromyography showed abnormal spontaneous activity in masseter and temporalis muscles only. These findings were tentatively consistent with masticatory muscle myositis. Serological autoantibodies against type 2M myofibers were negative. Histological and immunohistochemical examinations of the temporal muscle showed marked diffuse endomysial mononuclear cellular infiltration, mainly composed by CD8+ cells, with non-necrotic myofiber invasion, signs of regeneration and marked interstitial fibrosis. Strikingly, similar but milder changes were observed in triceps brachii muscle. Serological and/or PCR testing for neosporosis, toxoplasmosis, leishmaniosis and tick-borne diseases were negative. Taking together, these findings led to the diagnosis of generalized idiopathic polymyositis. Immunosuppressive treatment with prednisolone allowed clinical and biochemical remission. Eight weeks after, relapse was diagnosed based on increased creatine kinase activity elevation (1,679 UI/L). Prednisolone treatment was started over with azathioprine as add-on therapy. Both treatments were progressively and alternatively tapered with satisfactory outcomes.
This case highlights the requirement for multiple muscle biopsies and appeals for extended immunohistochemical studies in canine inflammatory myopathies.

59

CANINE PROTOTHECOSIS CAUSING SEVERE VENTRICULITIS IN A DOG

M. Pons-Sorolla[1 3], C. Maeso[1], E. Dominguez[1], M. Pumarola i Batlle[2], P. Montoliu[1]

[1] Anicura Ars Veterinaria, Neurology Department, Spain
[2] Veterinary Faculty, Universitat Autònoma de Barcelona, Spain
[3] Submitting author: Neurology Resident in training

Canine Protothecosis (CP) is an uncommon infectious disease, being *Prototheca zopfii* the most common identified species in dogs. Magnetic resonance imaging (MRI) description of central Nervous System lesions produced by CP in small animals is limited to four case reports and mainly consists of intraparenchymal lesions frequently surrounding the lateral ventricles. Suspected mild ependymitis was observed in one case. The aim of this case report is to describe new MRI features in a dog with histopathological confirmed CP.
A 5-year-old male crossbreed dog was referred due to a 2-months history of lethargy, hyporexia, diarrhea, weight and vision loss, and lumbar pain. Physical examination was unremarkable. Neurological examination was consistent with multifocal neurolocalization involving forebrain and spinal cord. Complete bloodwork, thoracic radiographs and abdominal ultrasound did not reveal abnormalities. MRI of the head showed severe thickening and enhancement of choroid plexuses, meningeal and ependymal contrast enhancement, multifocal intraparenchymal lesions involving caudate nuclei, hippocampus, thalamus, piriform lobes and corpus callosum, consistent with multifocal inflammatory-infectious disease. Cerebrospinal fluid showed marked mixed pleocytosis. PCR for standard infectious agents were negative. Protothecosis was diagnosed by rectal scrapes and subretinal fluid citology.
Despite treatment with itraconazole, prednisolone, and metronidazole, neurological signs progressed and the dog was euthanized two weeks later. Histopathology showed severe pyogranulomatous choroid-ventricle meningoencephalitis secondary to protothecosis.
To our knowledge, this is the first description of severe ventriculitis associated to protothecosis in a dog. CP should be included in the differential diagnosis of ventriculitis visualized on MRI in dogs.

60

DIAGNOSIS AND TREATMENT OF A TYPE IV DERMOID SINUS IN A CAVALIER KING CHARLES SPANIEL IN THE FRONTAL REGION

C.G.Danciu[1], C. Briola[1], V. Volckaert[1], R. Pittaway[2], D. McCready[1], S. Fitzmaurice[1]

[1] The Ralph Veterinary Referral Centre, Marlow, UK
[2] Dick White Referrals, Six Mile Bottom, UK

Congenital neural tube development defects, such as a dermoid sinus/cyst, have been identified in Rhodesian Ridgeback dogs and in several other breeds, mostly located along the dorsal spine but rarely in the cervical and head region.
A 6 years old, male neutered Cavalier King Charles Spaniel was presented with a four years history of an intermittently draining orifice on the midline of the frontal bone of the skull. Neurological examination was normal. Magnetic resonance imaging and a computed tomography scan of the head revealed an extra-axial mass in the midline between the frontal lobes, contacting the meninges and extending rostrally through a defect in the frontal bone. A cerebrospinal fluid analysis showed a mild mononuclear pleocytosis and negative bacterial culture, consistent with a non-infectious inflammatory response. Surgery was performed and the mass was removed via a frontal craniotomy. Histopathology of the mass found stratified squamous and keratinising epithelium with adnexal structures, which was consistent with a diagnosis of a dermoid sinus.
Five months after the surgical treatment a self-limiting discharge was observed at the level of the scar. However, repeat magnetic resonance imaging failed to identify the underlying reason.
This is the first report of a type IV dermoid sinus in the frontal region including advanced imaging illustration of the disease.

Ethical permission was not indicated for this case report.
The first author is a Neurology intern.

61

EPILEPSY OF UNKNOWN ORIGIN IN A MEERKAT: A CASE REPORT

S. Moya[1], N. Delgado[1], A. Sánchez[2], V. Moya[4], S. Ródenas[3]

[1] Dept. of neurology Animal Bluecare Hospital
[2] Serval exotic clinic
[3] Auna Hospital Veterinario Reference
[4] Dept. of Neurology Anicura Valencia Sur

8-month-old male meerkat (Suricata suricatta) is referred to the neurology service of the hospital for tonic-clonic epileptiform seizures for two weeks. The physical examination and neurological was normal. Bloodtest, x-rays and ultrasound did not reveal abnormalities that justified the pa-tient's symptoms.

The neurological location was in the thalamus-cortex. The most likely differential diagnosis was epilepsy of unknown origin or structural epilepsy, with meningoencephalitis of infectious origin being the most likely diagnosis.

Magnetic resonance imaging (MRI) revealed hyperintensity in T2W and FLAIR in both pi-riform lobes, which could be due to a postictal finding. The rest of the brain, brainstem, and brainstem structures were normal.

Cerebrospinal Fluid analysis (CSF) don,t revealed pleocytosis and protein level was normal (23 mg/dl). Laboratory results are PCR negative for distemper, toxoplasma, and neospora.

Anticonvulsant treatment with levetiracetam was used at dose 10mg/kg each 8 hour. After treatment, the patient improves clinically and presents a reduction in seizure frequency At the time of writing this clinical case, the animal is still alive and stable.

To the author’s knowledge this is the first report of epilepsy of unknown origin in a meerkat. Given the limited bibliography of this type of pathologies in this species, we have no precedents of cases. Periodic controls will be carried out, assessing the improvement or not of the patient and they will be described.

62

MYOSITIS OSSIFICANS CIRCUMSCRIPTA IN AN ADULT MALE KANGAROO

E. Hünerfauth[1], V. Molnár[2], M. Rosati[3], F. J. Soebbeler[1], O. Harms[1], R. Hildebrandt[1], M. Ciurkiewicz[4], W. Baumgaertner[4], H. A. Volk[1], A. Tipold[1], J. Nessler[1]

[1] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Foundation, Hannover, Germany
[2] Hannover Adventure Zoo, Germany
[3] Section of Clinical and Comparative Neuropathology, Centre for Clinical Veterinary Medicine, Ludwig-Maximilians-Universität, Munich, Germany
[4] Department for Pathology, University of Veterinary Medicine Foundation, Hannover, Germany

There was no ethical permission obtained for the study.

An adult male 10 years old red kangaroo was presented with an 11-month history of chronic progressive pelvic limb lameness and unwillingness to jump. Clinical signs were partially responsive to meloxicam. Indurations of lumbar epaxial muscles were noted on palpation.
Magnetic resonance imaging of the lumbar region showed two bilateral asymmetric, well circumscribed mass lesions within both lumbar longissimus muscles. The lesions have a patchy to multicystic appearance with hyper-, hypo- and isointense areas in T2 weighted (w) and T1w sequences without contrast enhancement. The described areas had a hypodense center surrounded by a hyperdense rim giving an “eggshell appearance” on computer tomography.
Histopathological analysis of a biopsy revealed proliferation of fibroblasts and degeneration of myofibers with dystrophic mineralization lined by well differentiated bony trabeculae with rare islets of chondrocytes without evidence of inflammation or malignancy, which is consistent with differentiated and organized metaplasia of muscle tissue into bone.
Based on the clinical and histopathological presentation and diagnostic imaging findings, myositis ossificans circumscripta was suspected. This disease is well known in athletes, where chronic-repeated muscular microtrauma due to intensive exercise consequently leads to heterotopic ossification caused by pathological repair mechanisms.
Conservative treatment with stall rest and non-steroidal anti-inflammatory drugs (meloxicam) led to marked amelioration of clinical signs in the kangaroo within weeks, and no deterioration was observed within a year after initial examination.

63

CERVICAL PAIN SECONDARY TO CERVICAL VERTEBRAL VENOUS THROMBOSIS PRESUMED TO BE ASSOCIATED WITH IATROGENIC HYPERADRENOCORTICISM

R. Cavalerie[1], A. Dean[2], F. Jolivet[3], S. Piazza[1]

[1] Neurology and neurosurgery department, Small animal hospital centre Languedocia, France
[2] Internal medicine department, Small animal hospital centre Languedocia, France
[3] Emergency and critical care department, Small animal hospital centre Languedocia, France

A 3.5-year-old neutered mixed-breed dog was presented for an acute-onset of cervical hyperesthesia and reluctance to move for 24 hours. He's been treated for one month with corticosteroid (prednisolone 0.4 mg/kg, q12h, PO) for an immune-mediated polyarthritis presumed type I.
Only strong cervical hyperesthesia was present. A complete blood count detected a stress leukogram pattern. C-reactive protein dosage was within reference interval. A computed tomography scanner of the cervical region highlighted a medullary compressive internal vertebral venous plexus (IVVP) and vertebral veins (VV) distention. It extended from vertebraes C1 to C6 with a filling defect of their lumen, evocative of thrombosis. Causes of a hypercoagulable state were investigated. Coagulation assessment revealed a severe reduction of antithrombin activity with no underlying cause of loss or production defect. An excessive consumption was suspected. By exclusion, hypercoagulable state was suspected to be secondary to iatrogenic hyperadrenocorticism caused by the corticosteroid treatment. Corticosteroid dose was rapidly decreased at that time then tapered off over 1,5 months. An anticoagulant therapy (clopidogrel 1.0 mg/KG, q24h, PO and rivaroxaban, 0,82/kg, q24h, PO) was immediately initiated.
Hemostasis profile, including antithrombin activity, was within reference value after one month. A follow-up computed tomography scan performed at 3 months, showed normal cervical spine with resolution of vessels' abnormalities. Anticoagulant therapy was stopped. The dog is still alive and free of clinical signs at time of writing.
This is the first case report of cervical IVVP and VV thrombosis in a dog suspected to be due to iatrogenic hyperadrenocorticism with a complete resolution of lesions after tapering off corticosteroid treatment.

64

CLINICAL PRESENTATION, DIAGNOSTIC FINDINGS AND OUTCOME OF PRESUMED IDIOPATHIC HYPOGLOSSAL MONONEUROPATHY IN A CAT

M. Pérez[1 2], C. Maeso[1], P. Montoliu[1], C. Morales[1]

[1] Anicura Ars Veterinaria, Neurology Department, Spain
[2] Submitting author: Young neurologist in training

Hypoglossal Nerve (HN) dysfunction may cause atrophy, asymmetry, or deviation of the tongue. This dysfunction could be related with caudal medulla lesions, or with neuropathy of the HN. Unilateral hypoglossal mononeuropathy are widely described in human medicine. The purpose of this case report is to describe clinical presentation, diagnostic findings and outcome of a hypoglossal mononeuropathy in a cat.
A four-year old neutered male Norwegian forest cat presented with a one-week history of abnormal movement of the tongue and difficulty in grooming behaviour. Neurological examination revealed deviation of the tongue toward the right side, asymmetry due to atrophy of the left side and ipsilateral muscle fasciculations. Also, ptyalism was detected on the left side. Complete bloodwork including serum total T4, magnetic resonance imaging of the head and cerebrospinal fluid analysis were unremarkable. Electromyography of the tongue showed spontaneous fibrillation potentials and positive sharp waves on the left side of the tongue. The cat was discharged without treatment. On consultation follow-up three weeks later, the cat showed an improvement of the clinical signs with a complete recovery two months after the diagnosis. Due to the lack of abnormal findings and spontaneous resolution, a diagnosis of presumed idiopathic left hypoglossal neuropathy was stablished. No relapses have been reported after 36 months.
The main differential diagnosis of unilateral tongue atrophy in veterinary medicine includes neoplasias (meningioma, peripheral nerve sheath tumour) and atlanto-occipital luxation. In the author's knowledge, this is the first report describing a suspected idiopathic hypoglossal dysfunction in a cat.

65

ULTRASOUND-GUIDED ERECTOR SPINAE INTERFASCIAL PLANE BLOCK FOR SPINAL SURGERY IN THREE CATS

D. N. Alza Salvatierra[1], M. E. Herrera Linares[2], L. Motta[2], M. Martinez[2]

[1] Fitzpatrick Referrals, Godalming, United Kingdom. [2]Northwest Veterinary Specialists, Runcorn, UK

The Erector spinae plane (ESP) block consists of an interfascial injection of local anaesthetic between the erector spinae muscle group and the transverse processes of the thoracic vertebrae. This block targets the dorsal rami of the thoracic spinal nerves to desensitise the cutaneous area near the dorsal midline, the paraspinal muscles, the dorsal vertebral laminae and the facet joints.
The purpose of this case series is to describe the perioperative analgesic effect and complications of ultrasound-guided ESP block with bupivacaine in three cats undergoing spinal surgery.
The surgical procedures performed were hemilaminectomy along with durectomy and excision of the mass in cat 1, hemilaminectomy in cat 2 and minihemilaminectomy in cat 3. The bupivacaine dose used was 1.8-2.5 mg/kg. Eight cardiovascular responses were recorded in this case series, but only one was clearly associated with nociception. Just one cat received intraoperative rescue analgesia. Cat 1 and 2 recorded just one high pain score in the first 24 h postsurgery, and cat 3 recorded three high pain scores. The total amount of methadone given in the 24 h post-surgery was 0,6 mg/kg in cat 1, 0,9 mg/kg in cat 2 and 0,8 mg/kg in cat 3. All three cats suffered mild and transient intraoperative complications (bradycardia, hypotension and apnoea episode of <5min), which were easily addressed. There were no postoperative complications.
To the authors' knowledge, this is the first time that ESP block is reported in cats in the literature. This novel locoregional anaesthesia technique is part of a multimodal analgesia approach for spinal surgery in cats as an alternative to traditional systemic analgesia.

66

ATYPICAL MAGNETIC RESONANCE IMAGING FEATURES OF FIBRINOID LEUKODYSTROPHY (ALEXANDER DISEASE) IN A BEAGLE

H.Vandenberghe[1], K. Baiker[2], G. Vinall[1], G. Nye[1], L. Escauriaza[1], N. Granger[1], L. Reeve[1]

[1] Highcroft Veterinary Referrals, Bristol, United Kingdom
[2] School of Veterinary Medicine and Science, University of Nottingham, United Kingdom

A 3-month-old female entire Beagle presented with a history of progressive ataxia. Neurological examination was consistent with a caudotentorial encephalopathy. The dog presented a wide-base stance, bilateral excursions of the head, four limbs ataxia and hypermetria, abnormal hopping responses on all limbs, absent menace response on both eyes but normal vision and decreased oculocephalic reflexes. Several vestibular episodes with opisthotonus and vertical nystagmus were noted.
Reactive encephalopathies were ruled out. Magnetic resonance imaging (MRI) of the brain showed a markedly abnormal cerebellum with symmetrical hyperintensity on T2W and FLAIR sequences and hypointensity of the cerebellar white matter and loss of definition and swelling of the folia on T1W images. These abnormalities extended to the white matter tracts of the caudal aspect of the brainstem and cervical spinal cord. Periventricular and peri-aqueductal hyperintensities were noted on T2W and FLAIR sequences. This suggested a multifocal, mostly caudotentorial leukoencephalopathy. Cisternal cerebrospinal fluid analysis was unremarkable. Serology for Neosporosis was negative.
The dog deteriorated and was euthanized two months after initial presentation. Histopathological analysis of the brain showed accumulation of Rosenthal fibers in the astrocytes consistent with a diagnosis of fibrinoid leukodystrophy.
We would like to flag fibrinoid leukodystrophy as a possible cause of caudotentorial encephalopathy in puppies. This disease has been reported in dogs with typical MRI features close to type I Alexander disease in people. Caudotentorial neurological deficits combined to predominant caudotentorial distribution of the MRI abnormalities in this case are consistent with the less common type II Alexander disease.

67

INVESTIGATING THE EFFECT OF MEDIUM-CHAIN TRIGLYCERIDES ON TH17 AND REGULATORY T CELLS IN 7 HEALTHY BEAGLES

K. Warzecha[1], P. Can[2], R. Carlson[1], S. Meller[1], A. V. Volk[1], H. A. Volk[1], A. Tipold[1], J. Neßler[1]

[1] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany.
[2] Department of Surgery, Faculty of Veterinary Medicine, University of Ankara, Ankara, Turkey

Medium-chain triglycerides (MCT) enriched diets are used to treat epilepsy and cognitive dysfunction in dogs and humans, however, the exact therapeutic mechanism remains largely unclear. Increased levels of Th17 and a Th17/Treg cell imbalance have been suggested to influence seizure severity, behavioural comorbidities and response to treatment in a subset of patients with epilepsy. In children with intractable epilepsy, a ketogenic diet has been shown to correct a Th17/Treg cell imbalance.
To investigate whether oral supplementation of MCT has an effect on Th17 and Treg cells in clinically healthy dogs, we measured absolute numbers of Th17 and Treg cells in peripheral blood of 7 healthy beagles using multicolor flow cytometry. Blood samples were collected at three different time points: while feeding a commercial hypoallergenic diet, 2 hours after one dose of MCT and after 2 weeks of feeding a diet enriched with MCT (9% of caloric intake). The study was conducted in accordance with the local animal welfare and ethic procedures (Approval number: 33.12-42502-04-20/3352).
Two hours after a single MCT feed, levels of stimulated Th17 cells were elevated, while the absolute number of regulatory T cells decreased. There were no significant changes in the absolute number of Th17 and Treg cells after two weeks of feeding a diet enriched with MCT compared to the measurement before feeding MCT.
In conclusion, where a one-off MCT administration did influence Th17 and Treg cells levels in peripheral blood in healthy dogs, a two week MCT administration had no influence.

68

GREATER SWISS MOUNTAIN DOGS WITH IDIOPATHIC EPILEPSY IN GERMANY-AN INVESTIGATION OF THE PHENOTYPE

T. Ostermann[1], J. Neßler[1], H. Urankar[2], N. Bachmann[2], C. Fechler[2], A. Bathen-Nöthen[3], A. Tipold[1]

[1] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine, Foundation, Hannover, Germany
[2] Swiss Mountain Dog Association of Germany e.V
[3] Private Practice Bathen-Nöthen, Cologne, Germany

Genetic predisposition of idiopathic epilepsy (IE) has been demonstrated in individual breeds. According to the responsible breeding association in Germany, the number of Greater Swiss Mountain Dogs (GS) with seizures is increasing and nearly 3 % of registered dogs suffer from seizures.
In order to describe seizure phenotype and to examine seizure causes, a questionnaire based study was performed. In cooperation with the Swiss Mountain Dog Association of Germany e.V. (SSV e.V) we evaluated 112 questionnaires filled in by owners of GS showing seizures and by their veterinarians between the years 2005 to 2021. Seizure characteristics, clinical and further examinations, treatment, treatment response and pedigree information were collected. IE was classified according to the International Veterinary Epilepsy Task Force consensus proposal.
93 (83.06%) dogs had IE (suspected genetic epilepsy) with confidence level I, II or III, the others had structural epilepsy, reactive seizures or epilepsy of unknown cause. The median age at seizure onset was 29.7 months. The most frequent seizure type were focal seizures evolving into generalized ones (62.37%), often starting with vomiting (n=38), retching (n=19) or salivation (n=19).
Furthermore, cluster seizures (CS) (49.46%) and status epilepticus (SE) (38.71%) were observed in a substantial part of the cases. Forty (43.01%) dogs died during the observation period, 34 (36.56%) have been euthanized (n=19) or died spontaneously (n=15) during CS or SE.
In GS idiopathic epilepsy presents with a severe phenotype with frequently occurring CS and SE. This study could serve as basis for further genetic evaluations.

69

SPIKE-AND-WAVE COMPLEXES AS A FEATURE OF JUVENILE MYOCLONIC EPILEPSY IN A MINIATURE POODLE

A. Czerwik, A. Olszewska, M.J. Schmidt

Department of Veterinary Clinical Sciences, Small Animal Clinic - Neurosurgery, Justus-Liebig-University, Frankfurter Str.114, 35392 Giessen, Germany

Epilepsy is one of the most common neurological disorders in dogs in which epileptic activity can be focal or generalized. Focal epileptic episodes can be mistaken with non-epileptic paroxysmal movement disorders. Differentiation between both disorders can be challenging. Confirmation of the epileptic nature of those events can be only obtained by observing characteristic changes in electroencephalography. The aim of this study was to present the neurological and electroencephalographic diagnostic work-up of unusual myoclonic episodes in a dog.

A 9-month-old female Miniature poodle was presented with a history of progressive recurrent episodes of impaired balance, twitches of the body and head movements with wobbling backwards. The consciousness was difficult to assess but was suspected as impaired. Each episodes lasted few seconds, initially once/twice per week and finally progressed within few weeks to multiple times per day. The was no other clinical signs before and after the episodes.

Clinical and neurological examination was normal. EEG using Nikhon Khoden and magnetic resonance imaging of the brain using Siemens 3Tesla device were performed. Four-hour EEG with video monitoring showed frequent, bilaterally synchronous, generalized 4-5 Hz spike and waves- complexes during the awake state. The dog was treated with levetiracetam, and showed 90% decrease in frequency of the episodes in the follow-up after 8 weeks.

The current case report describes the occurrence of juvenile myoclonic epilepsy diagnosed by electroencephalography which is method of choice for the differentiation of epileptic seizures and movement disorders. Spike-and-wave complexes are typical for this epileptic disorder.

70

OCCIPITO-ATLANTO-AXIAL STABILIZATION IN A YOUNG FRENCH BULLDOG USING 3D PRINTED PATIENT-SPECIFIC DRILL GUIDES AND IMPLANTS

L. Escauriaza[1], H. Vandenberghe[1], B. Oxley[3], L. Reeve.[1], N. Granger[1], J. Rose[2]

[1] Bristol Veterinary Specialists at Highcroft, CVS Referrals, United Kingdom.
[2] LumbryPark Veterinary Specialists, CVS Referrals, United Kingdom.
[3] Vet3D, Cumbria, United Kingdom.

Occipito-atlanto-axial (OAA) malformations in dogs cause both contusive and compressive injuries that lead to varying degrees of cervical spinal cord and brainstem disease.

An 8-month-old male entire French bulldog presented with a progressive history of abnormal posture, with the head held in an extended position, and ataxia of all four limbs with a floating forelimb gait. Neurological examination suggested a painful and C1-C5 myelopathy. MRI and CT revealed an abnormal keyhole-shaped and narrowed foramen magnum, hypoplastic occipital condyles and a malformed atlas. There was compression of the cord from the transverse ligament.

A dorsal surgical approach was chosen to replicate the posterior occipito-cervical fixation system used for humans- which usually relies on a pedicle screw and rod system. A human based system could not be used given the size of the animal. Therefore, bespoke 3D printed contoured titanium rods were made. Screw positions in the occiput, C1 and C2 were planned with a computer-assisted-design software and drilling guides made to allow their insertion. The objective of the design was to lay and rest the metal rods on screws and secure these together with polymethylmethacrylate cement for stabilisation. To promote fusion of the OAA region, bone graft and demineralised bone matrix were combined above the occiput and C1, of which the outer cortex was eroded with a burr. Gradual improvement was observed over the following 4 weeks, with mild residual ataxia and normal head/neck carriage at 6 months follow-up.

This case reports an innovative technique using 3D-printed metallic implants and drilling guides to bridge the OAA region.

71

OTITIS MEDIA/INTERNA WITH OR WITHOUT POLYP IN CATS: DOES MENINGEAL ENHANCEMENT ON POST-CONTRAST MRI AND/OR INFLAMMATORY CSF CHANGE OUR PERSPECTIVES?

G.F. Dutil[1], J. Guevar[1], D. Schweizer[2], P. Roosje[3], F. Kajin[4], H.A. Volk[4], N. J. Grapes[5], S. De Decker[5], R. Gutierrez-Quintana[6], J. Abouzeid[7], P. Freeman[7], K. Faller[8], V.M. Stein[1], A. Maiolini[1]

[1] Division of Clinical Neurology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland
[2] Division of Clinical Radiology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland
[3] Division of Clinical Dermatology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland
[4] Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Germany
[5] Department of Clinical Science & Services, Royal Veterinary College, University of London, Hatfield, United Kingdom
[6] Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, United Kingdom
[7] Division of Clinical Neurology, Cambridge University, Cambridge, United Kingdom
[8] Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Roslin, United Kingdom

Otitis media/interna (OMI) is a frequent aetiology in cats with peripheral vestibular syndrome (PVS) with or without a polyp. Magnetic resonance imaging (MRI) in combination with cerebrospinal fluid (CSF) examination is perceived as the gold standard diagnostic approach. They provide information about meningeal enhancement (MgE) and CSF abnormalities, which suggest concurrent meningitis. However, the relationship between MgE and abnormal CSF in cats with OMI has not yet been investigated.
Study's objectives were to establish the association between MgE and CSF findings, their individual correlation with bacteriology results from affected ear samples, and with clinicians' therapeutic choice in cats with OMI.
MRI and CSF analyses of 58 cats with PVS diagnosed with OMI were retrospectively evaluated. MgE was reported in 26/58 cases of which 7 had an increased total nucleated cell count (TNCC) in CSF; 9/32 cases had abnormal TNCC without MgE. There was no association between bacteriology results (external ear canal or bulla) and MgE or abnormal CSF results. Prednisolone was prescribed in 10/16 cases with increased TNCC. Among the 42 cases with normal TNCC, 15/42 received prednisolone, and 13/42 received NSAIDs. Various antibiotics were prescribed in 53/58 cats. When given, treatment duration was similar regardless of positive bacterial culture (5.58vs4.22 weeks), increased TNCC (6.13vs4.72 weeks) or MgE (5.33vs4.90 weeks).

No association was found between MgE, CSF or bacteriology findings. In addition, CSF results seem to only influence the choice of anti-inflammatory drugs but not the antibiotic therapy length. The latter was not influenced by the bacteriology results or MgE.

72

SPINAL CORD TO VERTEBRAL CANAL AREA RATIOS IN CERVICAL AND THORACOLUMBAR REGIONS OF FRENCH BULLDOGS COMPARED USING COMPUTED TOMOGRAPHY

S. Silva[1], M-A. Genain[1], S. Khan[1], J. Gauton[1], P. Freeman[1]

[1] Department of Veterinary Medicine, University of Cambridge, United Kingdom

It has been widely reported that the spinal cord to vertebral canal area ratio in the thoracolumbar spine is greater than that in the cervical spine i.e. there is more epidural 'space' in the cervical region than the thoracolumbar. This is frequently reported to be the cause of the often more severe neurological deficits observed in dogs with thoracolumbar disc herniations when compared to cervical. To the authors' knowledge, no studies have previously assessed this theory within the same dog.
Computed tomography images of 37 French bulldogs presenting to the Queen's Veterinary School Hospital between 2016 and 2019 were retrospectively reviewed. Exclusion criteria were evidence of vertebral malformations or spinal cord compression at the sites where measurements were obtained, presence of cervico-thoracic or thoracolumbar transitional vertebrae, or of neurological deficits. Images were independently reviewed by two assessors using Horos® DICOM viewer. Area measurements of the spinal cord and vertebral canal were made at the level of the mid-bodies of C5 and L1. Results demonstrated a statistically significant difference between the area ratio in the cervical and the thoracolumbar spine. The area ratio was lower in the thoracolumbar spine when assessed by both observers individually, suggesting the vertebral canal was relatively larger in this region. Although interobserver agreement was generally poor, intraobserver agreement was good.
In conclusion, this study demonstrated that, contrary to previous reports, the epidural space does not appear larger in the cervical region than the thoracolumbar at least in this population of French bulldogs.

73

EUSTACHIAN TUBE FORMATION AND ANGULATION IN DOGS AFFECTED BY PRIMARY SECRETORY OTITIS MEDIA

F. Possiel[1], S. De Decker[2], H.A. Volk[1], A.V. Volk[1]

[1] Department of Small Animal Medicine & Surgery, University of Veterinary Medicine Hannover, Germany
[2] Department of Clinical Science and Services, Royal Veterinary College, London, UK

Primary secretory otitis media (PSOM) is common especially in brachycephalic dogs. Various aetiologies have been discussed, including infectious, inflammatory and morphological causes. However, there remains a lack of data supporting any of the current hypothesis.
The aim of the current study was to elucidate the role of the eustachian tube in PSOM.
Computer tomography images of 72 dogs with or without PSOM were evaluated in the study. Morphological measurements (Eustachian tube length and width) and angulation of the Eustachian tube of 97 control ears were compared to 47 PSOM affected ears. Data are reported as Median with 25-75 percentiles. Groups were compared with a Mann Whitney U-test and a P-value of less than 0.05 was deemed significant. Eustachian width was significant smaller in width in affected cases (1.02 (0.86-1.46)) compared to controls (1.29 (0.71-1.52)), as was angulation wider in affected (42.22 (33.91-44.43)) versus non-affected (35.64 (31.91-40.12)) respectively.
This study demonstrates that Eustachian tube width and angulation might contribute to development of PSOM, which is similar to what has been shown in children. Future studies are needed to explore if the morphological changes have functional consequences and therefore lead to PSOM.

74

PREVALENCE OF DISCOSPONDYLITIS AND ASSOCIATION WITH VERTEBRAL BODY MALFORMATIONS IN SCREW-TAILED BRACHYCEPHALIC DOGS

N. J. Grapes[1], S. Bertram[2], S. De Decker[1]

[1] Clinical Science and Services, Royal Veterinary College, University of London, Hatfield, UK
[2] Cave Veterinary Specialists, George's Farm, Wellington, Somerset, UK

Discospondylitis is characterised by infection, most commonly bacterial, of the intervertebral disc and vertebral body endplates. This retrospective study aimed to report the prevalence of discospondylitis in screw-tailed brachycephalic dogs and to investigate the association of discospondylitis with congenital vertebral body malformations.
The electronic medical database was searched for screw-tailed brachycephalic dogs diagnosed with discospondylitis between June 2010 and 2020. Cases with a confirmed diagnosis on CT or MRI and complete medical records were included. Discospondylitis location, presence of congenital vertebral body malformations and site of maximal kyphosis were recorded.
Discospondylitis was diagnosed in 87 dogs, equating to 0.17% of the total patients presented to the institution during the study window. Of these 8 were French Bulldogs (0.45% of 1779 French Bulldogs presented) and 5 were English Bulldogs (0.63% of 793 English Bulldogs presented). Discospondylitis was associated with congenital vertebral body malformations in 6 French (75%) and 3 English Bulldogs (60%) respectively, and with the location of maximal kyphosis in 4 French (50%) and 3 English Bulldogs (60%) respectively. Discospondylitis was associated with butterfly vertebrae (n=5), dorsal hemivertebra (n=2), ventral wedge-shape (n=1) and L7 transitional vertebra (n=1). No statistical difference was evident between discospondylitis location in brachycephalic and non-brachycephalic breeds (p= 0.360).
The prevalence of discospondylitis was 2.6 times higher in French Bulldogs and 3.7 times higher in English Bulldogs, compared with the general population. Although congenital vertebral body malformations are commonly interpreted as incidental diagnostic findings, they were frequently found to be associated with discospondylitis.

75

TETHERED CORD SYNDROME RESULTING IN PERINEAL PAIN IN A MIXED BREED DOG: DIAGNOSIS, SURGICAL TREATMENT AND POSTOPERATIVE OUTCOME

E. Parsley[1], A. McElroy[2]. P. Klinge[2]

[1] Department of Clinical Sciences, Cummings School of Veterinary Medicine, North Grafton, MA. [2] Department of Neurosurgery, Rhode Island Hospital, Providence, RI.

Tethered cord syndrome (TCS) is a diverse clinical entity characterized by clinical signs caused by excessive tension on the spinal cord. This tension can result from a caudodorsally displaced, thickened or inelastic filum terminale. It can occur in conjunction with other spinal malformations or as a sole malformation. The reported cases in veterinary medicine highlight clinicals signs of lower motor neuron signs in the pelvic limbs and urinary incontinence. In humans with TCS, pain is a primary symptom, typically localized to the lower back, perineum and lower extremities suspected secondary to muscle spasms, which have not been described in veterinary species.
A 1.5yo female spayed mix breed dog presented with a several month history of suspected back pain, characterized by random yelping. A source of pain could not be identified on examination. An MRI was performed, which identified a caudodorsally displaced filum terminale and reduced dynamic movement of the conus medullary consistent with TCS. A L6-7 dorsal laminectomy and intradural filum release was performed. Intraoperatively, severe muscle tremors were seen during paraspinal muscle dissection, which resolved with diazepam. Postoperatively, the patient's pain worsened despite standard pain management, with pain localized to the perineum. Diazepam was restarted to treat suspected perineal muscle spasms, resulting in marked improvement in the clinical signs of pain. Six months postoperatively, diazepam was fully tapered and the patient has remained clinically normal with no recurrence of clinical signs. This case highlights the possibility of perineal pain secondary to muscle spasms in dogs with TCS.

76

CERVICAL DISC DISEASE IN WHIPPETS: RESULTS OF AN ONLINE SURVEY INVOLVING ITALIAN OWNERS AND BREEDERS

D. Dell'Apa[1], E. Bianchi[1], L. Auletta[2], L. Buonanno[3], M.P. Pasolini[3]

[1] Dept. Of Veterinary Science, University of Parma, Italy; [2]IBB CNR, Naples, Italy; [3]Dept of Veterinary Medicine and Animal Productions University of Napoli Federico II, Italy

Whippet dog is not usually included among the breeds commonly affected by myelopathies associated with degenerative disc disease. Despite this, the experience of some neurologists is that the occurrence of these conditions, especially cervical disc disease (CDD) often associated with severe neurological deficits, is frequent in this breed.
The aim of the study was to get information about the occurrence of CDD in Whippets and the perception of the problem by owners and breeders
In collaboration with the Italian "Club del Levriero", a questionnaire was sent to Italian owners and breeders of Whippets. The answers were processed using spreadsheets and organized in graphs.
The answers about 278 Whippets were recorded. The occurrence of CDD was 7.9% for all dogs, 13% for dogs between 5-10 years old. Diagnosis was based on physical and neurological examinations associated with imaging techniques: Computed tomography (CT) 40%, Magnetic resonance imaging (MRI) 25%, myelography 35%.
Stress on the back, continuously flexed and extended during the rotary gallop, to store energy and develop a high-velocity gait, may be a possible cause of spine diseases. Limits of the study were the not-specialized public that questionary was destined to and that the owners who experienced the problem were probably prompter to respond.
The occurrence of CDD in the Whippet appeared relatively high if compared with other disorders for which specific screenings are recommended by many international breed clubs. These results should prompt veterinary neurologists to further studies on the diagnostic, therapeutic, and prognostic aspects of CDD in Whippets.

77

SUCCESSFUL PAIN MANAGEMENT AFTER FILUM TERMINALE INTERNUM DE-TETHERING IN 2 CKCS WITH CHIARI-LIKE MALFORMATION

A. Uriarte[1] , A. McElroy[2] , P. Klinge[2]

[1] Neurology Service at Southfields Veterinary Referrals, UK
[2] Rhode Island Hospital, Department of Neurosurgery; The Warren Alpert Medical School of Brown University; Providence, USA

Cavalier King Charles Spaniels (CKCS) are affected by Chiari-like malformation (CM) and syringomyelia (SM) causing neuropathic chronic pain. Severely affected cases fail to respond to medical management and occipital cranioplasty is often recommended. Clinical relapse of neuropathic pain is recorded in a high number of cases treated with this surgical approach.

An association between Chiari I malformation (CM1) and tethered cord syndrome in human patients presenting post failed CM1 surgery is recognised (Milhorat et al., 2009). For these patients, de-tethering of the filum terminale internium may be effective in relieving symptomatology, restoring normal brain stem length, normalizing the position of the cerebellar tonsils, and in some cases, avoiding the need for posterior fossa surgery (Milhorat et al 2009). CKCS have a caudally displaced spinal cord and dural sac when compared with a range of weight-matched breeds (Sparks at al., 2019). Additionally, painful CKCS without SM have been found to have a shorter filum terminale internum (Sparks at al., 2020)

Two CKCS affected with CM had a successful resolution of pain following de-tethering surgery, including a 7-year-old who relapsed after occipital cranioplasty and a 1-year-old with no previous surgery.

The filum terminale internum was sectioned via a dorsal laminectomy without complications and both animals were free of pain, without medication, for 20 and 7 months respectively at the time of writing. Follow up MRI was performed on one dog. De-tethering of the filum terminale internum will remain controversial until definitive treatment guidelines are established in human and veterinary medicine.

Platinum Sponsor

Boehringer Ingelheim

PURINA

Bronze Sponsor

IVC EVIDENSIA
REFERRALS

PURINA Institute

Advancing Science for Pet Health

BRINGING A VOICE TO PURINA SCIENCE

- Partnering With Global Thought Leaders
- Sharing Groundbreaking Research
- Shaping The Nutrition Conversation
- Facilitating The Exchange Of Knowledge

For our latest discoveries in nutrition science,
visit PurinaInstitute.com

PURINA® PRO PLAN®

NC NEUROCARE™

THE NUTRITION THAT'S CHANGING MINDS

*based on declared amount of MCT in the ingredient list

MCT

COGNITIVE FUNCTON

BRAIN FUNCTON

Discover the difference nutrition can make to brain health.
Canine NC NeuroCare™, the latest innovation from PURINA® PRO PLAN®, is a ketogenic diet formulated with 6.5% MCT (medium chain triglycerides) which provides an alternative energy source for the brain.[1,2]
It also contains a specific combination of ingredients proven to help with age-related cognitive decline[3]

Find out more about the science behind NeuroCare™ and how this could support your clinical recommendation by contacting your PURINA representative.

References:
1. Law TH, Davies ES, Pan Y, Zanghi B, Want E, Volk HA. A randomised trial of a medium-chain TAG diet as treatment for dogs with idiopathic epilepsy. Br J Nutr 2015;114:1438-1447.
2. Packer RM, Law TH, Davies E, Zanghi B, Pan Y, Volk HA. Effects of a ketogenic diet on ADHD-like behavior in dogs with idiopathic epilepsy. Epilepsy Behav 2016;55:62-68.
3. Pan Y. E cacy of a Therapeutic Diet on Dogs with Signs of Cognitive Dysfunction Syndrome. 2017. ACVIM Forum (National Harbor, Maryland).

34th ESVN-ECVN Symposium
Mallorca (Spain)
23th-24th September 2022

Spinal cord injury
Taking steps forward