



Oral Research Communications of the 22nd ECVIM-CA Congress

Maastricht, Netherlands, 6th to 8th September 2012

Number	Day	Time	First Author Last Name	Title
ESVC - European Society of Veterinary Cardiology				
CA-O-1	Thursday 6 September	15.10- 15.25	Schober	EFFECTS OF ATENOLOL ON FIVE-YEAR SURVIVAL IN CATS WITH PRECLINICAL HYPERTROPHIC CARDIOMYOPATHY
CA-O-2	Thursday 6 September	15.25- 15.40	Ferasin	PLASMA NT-PRO-BNP AND SERUM TROPONIN-I CONCENTRATIONS IN CATS WITH SYSTOLIC ANTERIOR MOTION OF THE MITRAL VALVE (SAM) NOT ACCOMPANIED BY LEFT VENTRICULAR HYPERTROPHY
CA-O-3	Thursday 6 September	15.40- 15.55		WITHDRAWN
CA-O-4	Thursday 6 September	16.10- 16.25	Dirven	PREVALENCE OF HEART MURMURS AND CONGENITAL HEART DISEASE IN 2935 YOUNG CATS
CA-O-5	Thursday 6 September	15.55- 16.10	Dirven	DYNAMIC LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION IN 13 YOUNG CATS
CA-O-6	Thursday 6 September	16.25- 16.40	Weisse	TRANSATRIAL STENTING FOR LONG-TERM MANAGEMENT OF TUMOR OBSTRUCTION OF THE RIGHT ATRIUM IN 3 DOGS
CA-O-7	Friday 7 September	14.25- 14.40	Vollmar	PATHOLOGICAL FINDINGS IN THE VENTRICULAR MYOCARDIUM OF IRISH WOLFHOUSES WITH CARDIOMYOPATHIES.
CA-O-8	Friday 7 September	14.40- 14.55	Vollmar	ATRIAL PATHOLOGY IN IRISH WOLFHOUSES WITH AND WITHOUT ATRIAL FIBRILLATION
CA-O-9	Friday 7 September	14.55- 15.10	Sosa	ECHOCARDIOGRAPHIC EVALUATION OF MECHANICAL SYNCHRONY IN DOBERMAN PINSCHERS
CA-O-10	Friday 7 September	15.10- 15.25	Szatmári	CHITOSAN (HEMCON) PATCH EFFECTIVELY CONTROLS HEMORRHAGE FROM FEMORAL ARTERIAL PUNCTURE SITE IN DOGS AFTER REMOVAL OF A LARGE-BORE INTRODUCER-SHEATH
CA-O-11	Friday 7 September	15.25- 15.40	Wilkie	SERIAL ECHOCARDIOGRAPHIC FINDINGS IN 63 CATS WITH PRIMARY CARDIOMYOPATHY
CA-O-12	Friday 7 September	15.40- 15.55	Porciello	TRANSESOPHAGEAL ECHOCARDIOGRAPHY AS THE SOLE GUIDANCE FOR OCCLUSION OF PATENT DUCTUS ARTERIOSUS USING THE AMPLATZ® CANINE DUCTAL OCCLUDER IN DOGS: A PRELIMINARY STUDY

CA-O-13	Friday 7 September	16.30- 16.45	Baron Toaldo	ECHOCARDIOGRAPHIC EVALUATION OF LEFT AND RIGHT VENTRICULAR DIASTOLIC DYSFUNCTION IN DOGS WITH MITRAL VALVE DISEASE WITH OR WITHOUT PULMONARY HYPERTENSION
CA-O-14	Friday 7 September	16.45- 17.00	Zois	LEFT VENTRICULAR TWIST AND TWIST RATE IN DOGS WITH MITRAL REGURGITATION ATTRIBUTABLE TO MYXOMATOUS MITRAL VALVE DISEASE
CA-O-15	Friday 7 September	17.00- 17.15	Sottiaux	LEFT VENTRICULAR OUTFLOW TRACT DYNAMIC OBSTRUCTION WITHOUT LEFT VENTRICULAR HYPERTROPHY AND WITH REGRESSING LEFT VENTRICULAR HYPERTROPHY
CA-O-16	Friday 7 September	17.15- 17.30	Hezzell	TREATMENT OF DOGS WITH COMPENSATED DEGENERATIVE MITRAL VALVE DISEASE (DMVD) WITH SPIRONOLACTONE
CA-O-17	Friday 7 September	17.30- 17.45	Gommeren	CARDIAC ULTRASOUND IN CANINE EMERGENCIES WITH A SYSTEMIC INFLAMMATORY RESPONSE SYNDROME
CA-O-18	Friday 7 September	17.45- 18.00	Borgeat	ARTERIAL THROMBOEMBOLISM IN 242 CATS PRESENTING TO FIRST OPINION PRACTICE: 2004 TO 2012
CA-O-19	Saturday 8 September	14.25- 14.40	Santilli	LONG-TERM INTRINSIC RHYTHM EVALUTATION IN DOGS WITH ATRIOVENTRICULAR BLOCK
CA-O-20	Saturday 8 September	14.40- 14.55	Hanås	CHARACTERISTICS OF CARDIAC FUNCTION ASSESSED BY COLOUR TISSUE DOPPLER IMAGING IN HEALTHY DOGS DIFFER BETWEEN LARGE AND SMALL BREEDS
CA-O-21	Saturday 8 September	14.55- 15.10	Funayama	EVALUATION OF C-REACTIVE PROTEIN BEFORE AND AFTER MITRAL VALVE REPAIR IN DOGS WITH MITRAL REGURGITATION
CA-O-22	Saturday 8 September	15.10- 15.25	Ljungvall	SERUM SEROTONIN CONCENTRATION IS ASSOCIATED WITH SEVERITY OF MYXOMATOUS MITRAL VALVE DISEASE IN DOGS

ESCG - European Society of Comparative Gastroenterology

GA-O-1	Thursday 6 September	14.25- 14.40	Schmitz	EXPRESSION OF GENES ASSOCIATED WITH THE INFLAMMASOME IN THE DUODENUM OF DOGS WITH INFLAMMATORY BOWEL DISEASE AND HEALTHY DOGS
GA-O-2	Thursday 6 September	14.40- 14.55	Schmitz	EXPRESSION OF TREFOIL FACTOR GENES IN THE GASTRO-INTESTINAL TRACT OF DOGS WITH INFLAMMATORY BOWEL DISEASE AND HEALTHY DOGS
GA-O-3	Thursday 6 September	14.55- 15.10	Schmitz	EFFECT ON GENE EXPRESSION AND PROTEIN PRODUCTION IN DUODENAL BIOPSIES OF DOGS WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE BY EX-VIVO CULTURE WITH ENTEROCOCCUS FAECIUM
GA-O-4	Thursday 6 September	15.10- 15.25	Suchodolski	CHARACTERIZATION OF FECAL BACTERIAL DYSBIOSIS IN CATS WITH CHRONIC ENTEROPATHIES
GA-O-5	Thursday 6 September	15.25- 15.40	Bojanic	PROSPECT® CAMPYLOBACTER MICROPLATE ASSAY DETECTION OF C. UPSALIENSIS AND C. HELVETICUS IN SPIKED FAECAL SAMPLES
GA-O-6	Thursday 6 September	15.40- 15.55	Kempf	FEASIBILITY OF ESOPHAGEAL HIGH-RESOLUTION MANOMETRY IN AWAKE AND SEDATED HEALTHY DOGS
GA-O-7	Thursday 6 September	15.55- 16.10	Kook	WIRELESS AMBULATORY ESOPHAGEAL PH-MONITORING IN HEALTHY DOGS AND DOGS WITH HISTORICAL AND CLINICAL SIGNS INTERPRETED AS GASTROESOPHAGEAL REFLUX
GA-O-8	Thursday 6 September	16.10- 16.25	Corradini	LABORATORY AND ULTRASONOGRAPHIC MONITORING OF DOGS WITH ACUTE PANCREATITIS

GA-O-9	Thursday 6 September	16.25- 16.40	Mas	A BLINDED RANDOMIZED CONTROLLED FIELD TRIAL TO DETERMINE THE EFFECT OF ENTERIC COATING ON THE EFFICACY OF ENZYME REPLACEMENT FOR CANINE EXOCRINE PANCREATIC INSUFFICIENCY
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ESVNU - European Society of Veterinary Nephrology and Urology

RE-O-1	Thursday 6 September	14.25- 14.40	Weisse	PERCUTANEOUS FLUOROSCOPIC-ASSISTED PERINEAL APPROACH FOR RIGID CYTOSCOPY IN 9 MALE DOGS
RE-O-2	Thursday 6 September	14.40- 14.55	Berent	RENAL SPARING TREATMENT OF IDIOPATHIC RENAL HEMATURIA (IRH): ENDOSCOPIC SCLEROTHERAPY
RE-O-3	Thursday 6 September	14.55- 15.10	Berent	INTRARENAL ENDOSCOPIC NEPHROLITHOTOMY FOR REMOVAL OF COMPLICATED NEPHROLITHIASIS IN 9 DOGS AND 1 CAT
RE-O-4	Thursday 6 September	15.10- 15.25	Geddes	SURVIVAL OF CATS WITH NEWLY DIAGNOSED CHRONIC KIDNEY DISEASE (CKD) IS ASSOCIATED WITH PLASMA FIBROBLAST GROWTH FACTOR 23 (FGF-23) CONCENTRATION
RE-O-5	Thursday 6 September	15.25- 15.40	Paepe	PROSPECTIVE EVALUATION OF RAGDOLL AND CONTROL CATS FOR KIDNEY DISEASE BY ROUTINE LABORATORY PARAMETERS AND ULTRASONOGRAPHY
RE-O-6	Thursday 6 September	15.40- 15.55	Zini	RENAL MORPHOLOGY AND FUNCTION IN CATS WITH DIABETES MELLITUS
RE-O-7	Thursday 6 September	15.55- 16.10	Buono	NON-INVASIVE DIAGNOSTIC EVALUATION INCLUDING QUALITATIVE PROTEINURIA TO DETECT AN EARLY RENAL DAMAGE IN CANINE LEISHMANIASIS
RE-O-8	Thursday 6 September	16.10- 16.25	Steinbach	PLASMA AND URINE NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) IN DOGS WITH ACUTE KIDNEY INJURY (AKI) OR CHRONIC KIDNEY DISEASE (CKD)
RE-O-9	Saturday 8 September	10.00- 10.15	Jacinto	URINE CONCENTRATIONS OF PURINE METABOLITES IN UK CAVALIER KING CHARLES SPANIELS

ESVIM - European Society of Veterinary Internal Medicine / ISCAID - International Society for Companion Animal Infectious Diseases

IM-O-1	Thursday 6 September	14.25- 14.40	Theodorou	EFFICACY OF RIFAMPIN IN THE TREATMENT OF EXPERIMENTAL ACUTE CANINE MONOCYTTIC EHRlichiosis: A PILOT STUDY OF A 3-WEEK REGIMEN
IM-O-2	Thursday 6 September	14.40- 14.55	Leal	ACUTE PHASE PROTEINS: POTENTIAL PREDICTORS OF AN IMMUNE-MODULATION IN NATURAL RETROVIRAL-INFECTED CATS RECEIVING RECOMBINANT INTERFERON-OMEGA THERAPY
IM-O-3	Thursday 6 September	14.55- 15.10	Rosa	CANINE THEILERIOSIS: CLINICAL MANIFESTATIONS
IM-O-4	Thursday 6 September	15.10- 15.25	Proksch	THE EFFICACY OF THE PARAMUNITY INDUCER PIND-ORF IN THE TREATMENT OF CANINE PARVOVIRUS
IM-O-5	Thursday 6 September	15.25- 15.40	Barth	COMPARISON OF DIFFERENT DIAGNOSTIC TOOLS FOR THE DETECTION OF BORRELIA BURGDORFERI ANTIBODIES IN DOGS
IM-O-6	Thursday 6 September	15.40- 15.55	Hazart	MOLECULAR CHARACTERIZATION OF LEPTOSPIRA SEROVARS FROM CLINICALLY ILL DOGS AND COMPARISON WITH THE INFECTING SEROGROUP DETERMINED BY MICROSCOPIC AGGLUTINATION TEST
IM-O-7	Thursday 6 September	15.55- 16.10	Diallo	IMPACT OF TRICHOMONADS ON FECES QUALITY IN PUPPIES IN FRENCH BREEDING KENNELS

IM-O-9	Thursday 6 September	16.25- 16.40	Hazuchova	USEFULNESS OF SERUM ACUTE PHASE PROTEINS (APPS) IN CATS WITH BODY CAVITY EFFUSIONS TO HELP WITH A DIAGNOSIS OF FELINE INFECTIOUS PERITONITIS (FIP)
IM-O-10	Thursday 6 September	16.40- 16.55	Mercuriali	CANINE PROTOTHECOSIS IN THE NORTH OF ITALY: 4 CASES (2009-2011)
IM-O-8	Saturday 8 September	9.45- 10.00	Frank	PROSPECTIVE MEDICAL EVALUATION OF 7 DOGS PRESENTED WITH FLY BITING
IM-O-11	Saturday 8 September	11.20- 11.35	Krafft	CCL2 AS A SERUM BIOMARKER OF IDIOPATHIC PULMONARY FIBROSIS IN DOGS
IM-O-12	Saturday 8 September	11.35- 11.50	Krafft	TRANSFORMING GROWTH FACTOR- BETA 1 AND ITS ACTIVATING PATHWAYS IN CANINE IDIOPATHIC PULMONARY FIBROSIS
IM-O-13	Saturday 8 September	11.50- 12.05	Manens	EFFECT OF BODY WEIGHT LOSS ON PULMONARY FUNCTION ASSESSED BY 6-MINUTE WALK TEST AND ARTERIAL BLOOD GASES IN OBESE DOGS
IM-O-14	Saturday 8 September	12.05- 12.20	Marschner	MULTIPLATE CAN BE USED TO DETECT INCREASED PLATELET REACTIVITY IN DOGS WITH DISEASES KNOWN TO PREDISPOSE FOR HYPERCOAGULABILITY AND THROMBOSIS.
IM-O-15	Saturday 8 September	12.20- 12.35	Dunning	THE USE OF 20% HUMAN SERUM ALBUMIN IN 60 DOGS TREATED FOR HYPOALBUMINAEMIA: A REVIEW OF THE SIDE EFFECTS ENCOUNTERED AND INFLUENCE ON OUTCOME

ESVCN - European Society of Veterinary and Comparative Nutrition

NU-O-1	Friday 7 September	15.25- 15.40	Tvarijonaviciute	DO OBESE DOGS SUFFER FROM METABOLIC SYNDROME?
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ESVCP - European Society of Veterinary Clinical Pathology

CP-O-1	Friday 7 September	9.00- 9.15	Atencia	COMPARISON OF URICULT VET [®] AND SENSICULT [®] DIPSLIDES WITH TRADITIONAL LABORATORY TECHNIQUES FOR DIAGNOSING URINARY TRACT INFECTIONS IN DOGS AND CATS
CP-O-2	Friday 7 September	9.15- 9.30	Pazzi	EVALUATION OF HAEMOSTATIC ABNORMALITIES IN NATURALLY OCCURRING CANINE SPIROCERCOSIS
CP-O-3	Friday 7 September	9.30- 9.45	Burchell	WITHDRAWN

ESVONC - European Society of Veterinary Oncology

ON-O-1	Friday 7 September	14.25- 14.40	Rosa	THE ROLE OF HYPOVITAMINOSIS D IN THE MALIGNANT NEOPLASTIC TRANSFORMATION OF THE SPIROCERCA LUPI-ASSOCIATED OESOPHAGEAL NODULE IN THE DOG
ON-O-2	Friday 7 September	14.40- 14.55	Westberg	ADCD40L GENE THERAPY OF CANINE MALIGNANT MELANOMA
ON-O-3	Friday 7 September	14.55- 15.10	Evans	T-CELL RECEPTOR GENE REARRANGEMENTS FOR CHARACTERISATION OF LYMPHOCYTE CLONALITY IN CATS WITH LOW GRADE ALIMENTARY LYMPHOMA
ON-O-4	Friday 7 September	15.10- 15.25	von Euler	SERUM THYMIDINE KINASE ACTIVITY IN CNICALLY HEALTHY AND DISEASED CATS: A POTENTIAL MARKER FOR LYMPHOMA
ON-O-5	Friday 7 September	15.25- 15.40	Langner	STAGE MIGRATION IN DOGS WITH LYMPHOMA USING SYBRGREEN [®] REAL-TIME POLYMERASE CHAIN REACTION – FIRST RESULTS

ON-O-6 Friday 7 September 15.40-15.55 Holtermann EFFICACY AND TOLERABILITY OF MONOTHERAPY WITH MASITINIB FOR CANINE EPITHELIOTROPIC T-CELL LYMPHOMA AND HISTIOCYTIC SARCOMA

ON-O-7 Friday 7 September 16.30-16.45 Jaarsma ISOLATION AND CHARACTERISATION OF INSULINOMA STEM CELLS

ISFM - International Society of Feline Medicine

FE-O-1 Friday 7 September 14.25-14.40 Chakrabarti URINARY VASCULAR ENDOTHELIAL GROWTH FACTOR AS A PROGNOSTIC MARKER IN FELINE CHRONIC KIDNEY DISEASE

FE-O-2 Friday 7 September 14.40-14.55 Fragkou FELINE "TRIADITIS": A PROSPECTIVE STUDY OF 47 CASES

FE-O-3 Friday 7 September 14.55-15.10 Paris CO-CARRIAGE OF FELINE FAECAL PATHOGENS; RESULTS OF AN 8-WAY REAL TIME PCR PANEL

FE-O-4 Friday 7 September 15.10-15.25 Shibly MICROBIOLOGIC AND CYTOLOGIC COMPOSITION OF BRONCHOALVEOLAR LAVAGE FLUID IN CLINICALLY HEALTHY SHELTER CATS WITH PARTICULAR CONSIDERATION OF MYCOPLASMA SPP.

SCH - European Society of Comparative Hepatology

HE-O-1 Friday 7 September 16.30-16.45 Penning SELF-RENEWAL FACTOR BMI1 IS INVOLVED IN CANINE ADULT HEPATIC PROGENITOR CELL ACTIVATION AND HEPATOCELLULAR CARCINOMAS

HE-O-2 Friday 7 September 16.45-17.00 Gow MAGNETIC ASSISTED CELL SORTING OF HEPATIC NON-PARENCHYMAL CELLS FOR CD133 ENRICHES FOR HEPATIC PROGENITOR CELLS

HE-O-3 Friday 7 September 17.00-17.15 van Sprundel NEW PROGNOSTIC CLASSIFICATION OF PRIMARY HEPATIC TUMOURS IN THE DOG

HE-O-4 Friday 7 September 17.15-17.30 Dyggve ANTI-HISTONE ANTIBODIES IN DOBERMAN HEPATITIS

HE-O-5 Friday 7 September 17.30-17.45 van Steenbeek EXTRAHEPATIC PORTOSYSTEMIC SHUNTS: MAPPING A COMPLEX DISORDER USING DIFFERENT DOG BREEDS

VBPS - Veterinary Blood Pressure Society

BP-O-1 Friday 7 September 11.35-11.50 Gommeren QUALITATIVE BEDSIDE EVALUATION OF THE MICROCIRCULATION VIA SIDESTREAM DARK FIELD IMAGING IN DOGS

BP-O-2 Friday 7 September 11.20-11.35 Allerton SEMIQUANTITATIVE BEDSIDE EVALUATION OF THE MICROCIRCULATION VIA SIDESTREAM DARK FIELD IMAGING IN DOGS

BP-O-3 Friday 7 September 11.50-12.05 Vachon EVALUATION OF OSCILLOMETRIC AND DOPPLER ULTRASONIC DEVICES FOR BLOOD PRESSURE MEASUREMENTS IN ANESTHETISED AND AWAKEN HEALTHY DOGS

BP-O-4 Friday 7 September 12.05-12.20 Gommeren REPEATABILITY AND REPRODUCIBILITY OF TRANSCRANIAL DOPPLER ULTRASONOGRAPHY IN HEALTHY BEAGLE DOGS

BP-O-5 Friday 7 September 12.20-12.35 de Laat INFLUENCE OF SEDATIVES, ANTICONVULSANTS AND A NEGATIVE CHRONOTROPE ON TRANSCRANIAL DOPPLER ULTRASONOGRAPHY

ESVE - European Society of Veterinary Endocrinology

EN-O-1	Friday 7 September	9.45- 10.00	Jensen	PHYSIOLOGY AND DIAGNOSTIC POTENTIAL OF SERUM GHRELIN IN CATS WITH DIABETES MELLITUS AND HYPERSOMATOTROPISM
EN-O-2	Friday 7 September	10.00- 10.15	Zini	HISTOLOGICAL INVESTIGATION OF ENDOCRINE AND EXOCRINE PANCREAS IN CATS WITH DIABETES MELLITUS
EN-O-3	Friday 7 September	10.15- 10.30	Niessen	SERUM TYPE III PROCOLLAGEN PROPEPTIDE: AN ALTERNATIVE MEASURE OF GROWTH HORMONE BIOACTIVITY IN CATS WITH DIABETES MELLITUS AND HYPERSOMATOTROPISM
EN-O-4	Saturday 8 September	14.25- 14.40	Batchelor	THE EFFECT OF SINGLE NUCLEOTIDE POLYMORPHISMS ON CANINE SLC5A1 (SGLT1) PROMOTER FUNCTION, AND THEIR RELEVANCE IN DIABETES MELLITUS AND OBESITY IN DOGS
EN-O-5	Saturday 8 September	14.40- 14.55	Padrutt	COMPARISON OF THE GLP-1 ANALOGUES EXENATIDE SHORT-ACTING, EXENATIDE LONG-ACTING AND THE DPP-4 INHIBITOR SITAGLIPTIN TO INCREASE INSULIN SECRETION IN HEALTHY CATS
EN-O-6	Saturday 8 September	14.55- 15.10	Fracassi	USE OF INSULIN DETEMIR IN DOGS WITH DIABETES MELLITUS
EN-O-7	Saturday 8 September	15.10- 15.25	Ravenek	THE ROLE OF THE CANONICAL WNT-PATHWAY IN THE PATHOGENESIS OF CANINE CORTISOL-SECRETING ADRENOCORTICAL TUMORS
EN-O-8	Saturday 8 September	15.25- 15.40	Arenas	ONCE VS TWICE DAILY TRILOSTANE TREATMENT FOR CANINE PITUITARY-DEPENDENT HYPERADRENOCORTICISM
EN-O-9	Saturday 8 September	15.40- 15.55	Burkhardt	EVALUATION OF BASELINE CORTISOL, ENDOGENOUS ACTH AND CORTISOL TO ACTH RATIO TO MONITOR TRILOSTANE THERAPY IN DOGS WITH PITUITARY-DEPENDENT HYPERADRENOCORTICISM
EN-O-10	Saturday 8 September	16.30- 16.45	Campos	EFFECT OF RECOMBINANT HUMAN THYROTROPIN ON THE UPTAKE OF RADIOACTIVE IODINE (¹²³ I) IN DOGS WITH THYROID TUMORS
EN-O-11	Saturday 8 September	16.45- 17.00	Boretti	ONCE DAILY TRANSDERMAL METHIMAZOLE APPLICATION IS AN EFFECTIVE TREATMENT OPTION FOR LONG-TERM MANAGEMENT OF FELINE HYPERTHYROIDISM
EN-O-12	Saturday 8 September	17.00- 17.15	Peterson	HYPERTHYROID CATS ON LONG-TERM MEDICAL TREATMENT SHOW A PROGRESSIVE INCREASE IN THE PREVALENCE OF LARGE THYROID TUMORS, INTRATHORACIC THYROID MASSES, AND SUSPECTED THYROID CARCINOMA
EN-O-13	Saturday 8 September	17.15- 17.30	Baumstark	PLASMA RENIN ACTIVITY FOR MONITORING MINERALOCORTICOID SUBSTITUTION IN DOGS WITH PRIMARY HYPOADRENOCORTICISM
EN-O-14	Saturday 8 September	17.30- 17.45	Rick	PATTERNS OF THYROID HORMONES AND THYROID STIMULATING HORMONE (TSH) IN DOGS RECEIVING PHENOBARBITAL TREATMENT
EN-O-15	Saturday 8 September	17.45- 18.00	Salesov	URINARY AND PLASMA CATECHOLAMINE AND METANEPHRINE IN DOGS WITH PHEOCHROMOCYTOMA, HYPERADRENOCORTICISM AND IN HEALTHY DOGS

BP-O-1

QUALITATIVE BEDSIDE EVALUATION OF THE MICROCIRCULATION VIA SIDESTREAM DARK FIELD IMAGING IN DOGS. K. Gommeren¹, F.J.W. Allerton¹, A. Reynaud¹, E. Morin¹, K. Drobotz², D. Peeters², D. Silverstein².
¹University of Liege, LIEGE, Belgium, ²University of Pennsylvania, PENNSYLVANIA, United States of America

Sidestream dark field imaging (SDF) is a technically relatively simple method to visualize the microcirculation. However, current gold-standard, or 'consensus' analysis (CA) of SDF films takes approximately 1 hour per film limiting the application of SDF in a clinical setting, and leading to increased expense due to analysis of low quality films. We developed a subjective point of care scoring system (Bedside evaluation of the microcirculation, BEM) that could provide real-time intervention points and optimize care for the critical patient. The objective of this study is to evaluate whether the BEM-score correctly identifies films of sufficient and insufficient diagnostic quality as defined by CA. Twenty variable-length microcirculation films taken at the level of the canine tooth were selected from a database of films with available CA. Before the study, three observers were trained using an instruction video to evaluate five quality parameters: stability, content, illumination, focus and pressure. The BEM was performed by viewing and scoring each film four times in immediate succession. All five quality parameters were scored (0 perfect, 1 sufficient and 2 insufficient) according to CA analysis. Only the fourth viewing was considered for analysis. BEM quality analysis was only considered sufficient if no parameter was scored insufficient. Repeatability and reproducibility were assessed by assessing all films in a random order three times daily for three days. BEM pass-fail assessment matched CA 85.6% of the time with individual observer agreement of 84.4-87.8%. Agreement of BEM with CA did not change over the study period (84.4%, 87.8% and 84.4% on days 1, 2 and 3 respectively) indicating accurate quality analysis after a single BEM-score of the training video. The mean cumulative BEM quality score (2.51, SD 1.87) was very similar to CA (mean 2.6, SD 1.66). However mean individual BEM-parameter scores differed from CA reflecting differences in observer interpretation. High levels of inter-observer agreement and the strong correlation with CA for pass-fail assessment demonstrate that BEM quality evaluation can produce repeatable and reliable results. Variation in individual parameter scores may reflect systematic erroneous assignment of certain parameters or individual bias towards assessment of certain features. Nevertheless, this did not impact on the overall evaluation of film quality. This study provides a platform to investigate whether rapid semi-quantitative analysis of the microcirculation itself is similarly feasible.

BP-O-2

SEMIQUANTITATIVE BEDSIDE EVALUATION OF THE MICROCIRCULATION VIA SIDESTREAM DARK FIELD IMAGING IN DOGS. F.J.W. Allerton¹, K. Gommeren¹, A. Reynaud¹, E. Morin¹, D. Peeters², K. Drobotz², D. Silverstein².
¹University of Liege, LIEGE, Belgium, ²University of Pennsylvania, PENNSYLVANIA, United States of America

Sidestream dark field imaging (SDF) is a straightforward technique to evaluate microcirculation. However, current 'consensus' analysis (CA) of SDF films is time-consuming, thereby restricting the clinical application of SDF. A subjective bedside scoring system (BEM) is proposed that could rapidly provide a semi-quantitative assessment. We have previously shown that observers could accurately evaluate film quality parameters. The objective of the present study is to assess the correlation of BEM with CA for quantitative microcirculation parameters. Three observers were trained using an instruction video to evaluate four quantity parameters: total vessel density (TVD), capillary vessel density (CVD), perfused vessel density (PVD) and microvascular flow index (MFI). Fifteen variable-length microcirculation films of sufficient quality, taken at the level of the canine tooth, were selected from a database of films with available consensus analysis. Each parameter was scored (1 lowest -

5 highest). The BEM was performed by viewing and scoring each film four times in immediate succession with the final score being considered for analysis. BEM was performed on each film in random order three times daily for three days. CA scores were divided into quintiles for each parameter and mean BEM score were calculated for each. Conversely, for each BEM score, mean CA scores were calculated, per observer or per day. The mean TVD and PVD BEM scores for the 20% quintile were lower than mean BEM scores for other quintiles. Mean BEM score for the 80-100% quintile was the highest mean BEM score for PVD only. Mean CVD, PVD and MFI values for BEM score 1 were lower than mean values for other BEM scores. In parallel, although TVD never received a BEM score of 1, the mean CA value for films with BEM score 2 were lower than for higher BEM scores. The mean TVD and MFI values for BEM score of 5 were higher than mean values for BEM scores 1-4. Similar values were obtained on each individual study day. This study demonstrates that rapid semi-quantitative assessment of the microcirculation using the BEM-score can produce repeatable and reliable results, although significant overlap exists. Further studies are required to evaluate the value of this technique in a clinical setting.

BP-O-3

EVALUATION OF OSCILLOMETRIC AND DOPPLER ULTRASONIC DEVICES FOR BLOOD PRESSURE MEASUREMENTS IN ANESTHETISED AND AWAKEN HEALTHY DOGS. C. Vachon, M.C. Bélanger, S. Cuvelliez, P.M. Burns. School of Veterinary Medicine, University of Mo, SAINT-HYACINTHE, Canada

Objective: Compare two non-invasive blood pressure (NIBP) measurement devices (petMAP and Doppler) with invasive blood pressure (IBP) measurement in normotensive, anesthetised and awakened dogs.

Design: Prospective clinical study

Animals: Ten female dogs aged between 6 to 60 months (average 20.7 months), and weighting 12.8 to 34.2 kg (average 23.4 kg) undergoing a routine spay.

Interventions: Blood pressure measurement

Procedures: After the induction of general anesthesia, a catheter (20G) was placed in the dorsal pedal artery and invasive systolic (SAP_i), diastolic (DAP_i) and mean (MAP_i) arterial blood pressures were obtained. The NIBP cuffs were placed on the ipsilateral front limb. Five consecutive measurements were obtained with each indirect device and considered as a mean measure. The IBP was obtained simultaneously to the five NIBP measurements and also considered as a mean measurement. Measurements on awakened dogs were obtained four hours after surgery. Doppler's systolic (SAP_d) and petMAP's systolic (SAP_o), diastolic (DAP_o) and mean (MAP_o) arterial blood pressure were evaluated and compared to the corresponding IBP using the Bland-Altman analysis. The percentage of paired measurements with a mean difference of ≤ 10 and ≤ 20 mmHg was also evaluated for the SAP_o, DAP_o and MAP_o.

Results: Agreement between IBP and NIBP measurements obtained with the petMAP and the Doppler was assessed with the Bland-Altman analysis. On anesthetised dogs, both indirect devices underestimated all direct blood pressures. The petMAP bias (standard deviation) were -6.1 mmHg (10.4 mmHg), -6.9 mmHg (6.7 mmHg), and -2.9 mmHg (9.3 mmHg) for SAP_o, DAP_o and MAP_o respectively. The Doppler bias was -4.1 mmHg (24.7 mmHg) for SAP_d. On awakened dogs, the petMAP underestimated SAP_i and overestimated DAP_i and MAP_i. The bias were -5.8 mmHg (16.5 mmHg), 4.6 mmHg (7.9 mmHg) and 3.8 mmHg (8.9 mmHg) for SAP_o, DAP_o and MAP_o respectively. The Doppler underestimated the IBP and the bias was -15.1 mmHg (21.6 mmHg). On anesthetised and awakened patients, the percentage of values lying within 10 and 20 mmHg of the IBP was higher (or equal) for the petMAP compared to the Doppler.

Conclusion: Results suggest a better performance of petMAP device to predict the IBP in normotensive-anesthetised and normotensive-awakened dogs.

BP-O-4

REPEATABILITY AND REPRODUCIBILITY OF TRANSCRANIAL DOPPLER ULTRASONOGRAPHY IN HEALTHY BEAGLE DOGS. K. Gommeren¹, W.G.A deLaat¹, S. Denies¹, A-C Merveille¹, S. Gomart¹, F. Allerton¹, D. Peeters¹. ¹University of Liège, Department of equine and companion animal clinical sciences, LIÈGE, Belgium

Intracranial hypertension (ICH) is associated with high morbidity and mortality in canine veterinary medicine, yet remains difficult to clinically diagnose. The lack of an easily feasible and available diagnostic method has prevented clinical studies on the prevalence, cause and treatment of ICH. Recently, transcranial Doppler ultrasonography (TCD) has been reported as a non-invasive diagnostic method in humans. However, only a few preliminary reports on the use of this technique in dogs have been published. This study evaluated the repeatability and reproducibility of TCD of the basilar and left and right cranial, cerebral arteries in healthy Beagle dogs. TCD was performed using a standard ultrasound machine at the level of the basilar artery, and left and right cranial cerebral artery, in six adult Beagle dogs. Systolic, diastolic and average velocity, resistance (RI) and pulsatility indexes (PI) were assessed for each vessel. Repeatability was evaluated by calculating the intra-class correlation coefficient (ICC) between three separate, consecutive measurements in every dog. An ICC was also determined for the reproducibility of these measurements on three consecutive days. During the procedures, ECG, blood pressure and clinical parameters were monitored. Statistical analysis showed a highly significant repeatability of all measured parameters (systolic, diastolic and average velocity, RI and PI) for all blood vessels (N = 162, ICC = 0.89 - 0.99, p < 0.01). Systolic velocity, RI and PI were also significantly reproducible for the basilar artery (N = 36, ICC = 0.80 - 0.90, p < 0.01), and the left and right cranial cerebral arteries (N = 72, ICC = 0.65 - 0.74, p < 0.01). However, no significant correlation was found between basilar and cerebral blood flow velocities. Measurement of PI and RI of the basal and cranial cerebral arteries using TCD appeared to have high intra-operator repeatability and reproducibility. However, measurements performed on the basilar artery had higher between day reproducibility. Since the technical skill required to assess these parameters subjectively appeared to be less complicated at the level of the basilar artery, TCD in a clinical setting is probably advocated at the basal artery. In conclusion, TCD is characterized by high intra-observer repeatability and reproducibility, making this technique a promising tool for the measurement of PI and RI, which have both been reported to be correlated with intracranial pressure.

BP-O-5

INFLUENCE OF SEDATIVES, ANTICONVULSANTS AND A NEGATIVE CHRONOTROPE ON TRANSCRANIAL DOPPLER ULTRASONOGRAPHY. B.W.G.A deLaat¹, K. Gommeren¹, S. Denies¹, A-C Merveille¹, S. Gomart¹, F. Allerton¹, D. Peeters¹. ¹University of Liège, Department of equine and companion animal clinical sciences, LIÈGE, Belgium

Intracranial hypertension (ICH) is associated with high morbidity and mortality in canine veterinary medicine, yet remains difficult to clinically diagnose. Furthermore, many patients suspected to suffer from ICH are treated with sedatives or anticonvulsants. Besides the impact of these molecules on the patients' neurological examination, they variably influence the cardiovascular system. This study evaluated the effect of various sedatives and anticonvulsants on the pulsatility and resistance index (PI) and (RI), as measured by transcranial Doppler ultrasonography (TCD) in healthy Beagle dogs. Additionally, we evaluated the effect of ivabradine, a specific negative chronotrope, on TCD findings.

TCD was performed at the level of the basilar artery in six adult, Beagle dogs. This technique was performed prior to the injection of molecules (V0), and after administration of acepromazine (ACE, 100 µg/kg IV), diazepam (DIA, 0.5 mg/kg IV), medetomidine (MED, 40 µg/kg IM) or ivabradine (IVA, 1 mg/kg IV). A wash-out period of at least 24 hours was respected

between the administration of each drug. During the procedure, ECG, heart rate (HR) and blood pressure (BP) were monitored.

Results were analyzed using Repeated Measures ANOVA. Correlations between the clinical parameters, and PI and RI were investigated using Pearson's correlation. Results were considered significant when p < 0.05.

Significantly lower PI and RI values [(mean PI; 95% CI), (mean RI; 95% CI)] were obtained for MED [(0.75; 0.67 - 0.83), (0.48; 0.46 - 0.50)], compared to V0 [(1.50; 1.18 - 1.83), (0.70; 0.63 - 0.78)], ACE [(1.68; 1.35 - 2.00), (0.71; 0.64 - 0.77)], DIA [(1.49; 1.06 - 2.00), (0.69; 0.60 - 0.79)] and IVA [(1.85; 1.46 - 2.23), (1.85; 1.46 - 2.23)]. PI for dogs after IVA was significantly increased compared to DIA, but did not differ significantly from other groups. HR was significantly lower after MED compared to other groups, and after IVA, compared to V0. BP was significantly lower after ACE than after IVA, MED or on V0. These clinical parameters were not significantly correlated with PI or RI.

DIA and ACE did not significantly influence RI or PI, however MED significantly decreased RI and PI. These findings agree with previous reports describing a decrease in ICP provoked by MED, as PI is positively correlated with ICP. This effect appears to be independent of the effect of MED on HR, since IVA also significantly decreased HR, yet did not significantly affect PI or RI. In conclusion, blood pressure and heart rate did not significantly affect PI and RI.

CA-O-1

EFFECTS OF ATENOLOL ON FIVE-YEAR SURVIVAL IN CATS WITH PRECLINICAL HYPERTROPHIC CARDIOMYOPATHY. K.E.S. Schober¹, J. Zientek¹, X. Li², V. Luis Fuentes¹, D. Bonagura¹. ¹The Ohio State University, COLUMBUS, United States of America, ²Center for Biostatistics at The Ohio State University, COLUMBUS, United States of America

Hypertrophic cardiomyopathy (HCM) is the most commonly diagnosed heart disease in cats with little documentation of the effects of treatment on outcome in cats with preclinical disease. Therefore, this prospective cohort study was undertaken to evaluate the effects of treatment with atenolol on outcome in cats with asymptomatic HCM. We hypothesized that 1) 5-year mortality would be increased in cats with HCM compared to a matched control group of healthy cats, and 2) administration of atenolol would reduce 5-year cardiac mortality in occult feline HCM. Cats were enrolled over a 5-year time period (2003 to 2007) in a prospective, open-label, observational study. Diagnosis of HCM was based on transthoracic echocardiography. Cats were either treated with atenolol (6.25 to 12.5 mg/cat, q12h, PO) or did not receive treatment. Decision to treat was based on owner preference, suggestion by the clinician, and animal compliance with regard to pill administration. Baseline echocardiograms were analyzed, and morbidity and mortality were monitored at 3 and 6 months and thereafter by annual rechecks, and by phone interviews of referring veterinarians and owners over a 5-year time period. Groups were compared by a non-paired t-test, Mann-Whitney rank sum test, chi-square test, or Fisher's exact test. Kaplan-Meier survival curves were constructed and compared using the Log-Rank test with right censoring. Predictors of 5-year survival were identified by best subsets and multivariate logistic regression. 63 cats with occult HCM (42 treated, 21 not treated) and 31 matched healthy control cats were identified. 27 (43%, 14 cardiac death, 13 non-cardiac death) HCM cats and 10 (32%, all non-cardiac death) control cats reached the study endpoint (death). Statistical analyses (HCM vs. control, HCM treated vs. HCM not treated, HCM without obstruction treated [n=16] vs. HCM without obstruction not treated [n=17]) failed to demonstrate a significant difference (P>0.10) in 5-year all cause and cardiac mortality between groups. Regression analysis identified only age and left atrial size at diagnosis as independent predictors of outcome but not treatment with atenolol, severity of hypertrophy, presence of diastolic dysfunction, and presence of dynamic outflow tract obstruction. This study did not demonstrate any beneficial (nor detrimental) effect of treatment with atenolol on 5-year outcome in cats with occult HCM. Controlled studies are needed to validate our findings.

CA-O-2

PLASMA NT-PRO-BNP AND SERUM TROPONIN-I CONCENTRATIONS IN CATS WITH SYSTOLIC ANTERIOR MOTION OF THE MITRAL VALVE (SAM) NOT ACCOMPANIED BY LEFT VENTRICULAR HYPERTROPHY. L.F. Ferasin¹, H.F. Heidi². ¹SVCC LTD, WESTERHAM, United Kingdom, ²O'Gorman Slater Main & Partners, NEWBURY, United Kingdom

Introduction: Systolic anterior motion of the mitral valve (SAM) is a dynamic left ventricular outflow obstruction frequently observed in feline hypertrophic cardiomyopathy (HCM). However, several cases of SAM have also been observed in cats without left ventricular hypertrophy (LVH) and this finding could be interpreted as an early stage of the disease not yet accompanied by LVH. Alternatively, it could be speculated that the dynamic outflow obstruction could cause intraventricular pressure overload sufficient enough to induce LVH at a later stage. This study was conducted to test the hypothesis that SAM can potentially cause myocardial stress and myocardial damage by measuring plasma NTproBNP and serum troponin-I levels in cats with SAM not associated with LVH.

Methods: The study was based on a retrospective analysis of 13 cats who underwent cardiac investigation of a heart murmur, performed by a boarded cardiologist. These cats were diagnosed with SAM not associated with LVH (IVSd and LVFWd < 5.5mm, both on Bmode and Mmode measurements) via colour Doppler echocardiography. Plasma NTproBNP (Cardiopet test, IDEXX Laboratories, Inc.) and serum high sensitivity troponin-I (hscTnI HS, IDEXX Laboratories, Inc) were measured in these patients, as well as serum urea, creatinine and thyroxin concentrations. The association between biomarkers (NTproBNP and HscTnI) concentration and echocardiographic values (myocardial thickness, left atrial dimension and aortic peak velocity) was determined by using the Spearman correlation coefficient (rho).

Results: All cats were euthyroid and did not show evidence of renal disease. Mean HscTnI measurement was not performed in one cat due to an unsuitable sample. Eleven out of 13 cats (85%) showed NTproBNP values above the normal reference limit (100 pmol/l) with a median concentration of 393 pmol/l (\pm 194, range 109-711). Five out of 12 cats (42%) showed HscTnI values above the normal reference limit (0.16 ng/ml) with a median concentration of 0.24 ng/ml (\pm 0.35, range 0.16-0.99). There was a significant positive correlation between aortic peak velocity and NTproBNP (rho=0.657, P=0.0146).

Conclusion: NTproBNP is increased in cats with SAM without LVH, suggesting the presence of myocardial stress, which appears to be proportional to the degree of outflow obstruction derived by the aortic peak velocity. Some of these cats also present a degree of myocardial insult suggested by the increased serum HscTnI. Whether the increased biomarker concentrations are related to SAM-induced pressure overload or to an early stage of primary myocardial disease needs to be evaluated with appropriate longitudinal studies.

**CA-O-3
M-MODE AND DOPPLER ECHOCARDIOGRAPHIC
PARAMETERS IN KITTENS**

Withdrawn.

CA-O-4

PREVALENCE OF HEART MURMURS AND CONGENITAL HEART DISEASE IN 2935 YOUNG CATS. M.J.M. Dirven¹, M.A. Barendse², M.C. vanMook², J.A. Sterenberg², A. vanden Wildenberg². ¹Utrecht University / Dierenkliniek Rijen, UTRECHT, The Netherlands, ²Dierenkliniek Rijen, RIJEN, The Netherlands

Heart murmurs are caused by turbulent blood flow or by vibration of cardiac structures. Turbulent blood flow in young animals may originate from congenital structural heart disease

or from physiological phenomena. The prevalence of heart murmurs and congenital heart disease in the general (i.e. non referral) feline population are unknown. The aims of this prospective study were to determine the prevalence of heart murmurs in young cats and to determine the prevalence of congenital heart disease in young cats with heart murmurs. In total 2935 domestic shorthair cats aged 2 to 6 months underwent a routine physical examination prior to vaccination between May 1st 2009 until March 31st 2012. Cats were from adoption programs run by either Dierenasiel Breda e.o. (2090/2935) or Dierenopvangcentrum Tilburg (845/2935). In cats with murmurs, the murmur was timed, graded and the point of maximum intensity was determined. Subsequently, 2D, M-mode and Doppler transthoracic echocardiography with continuous eeg monitoring was performed. Heart murmurs were detected in 135 animals (4.6%). Congenital heart disease was detected in 47 animals (1.6%), acquired heart disease in 2 animals (0.06%) and no identifiable heart disease in 86 animals (2.9%) with murmurs. In the 86 animals without heart disease dynamic right ventricular outflow tract obstruction was the cause of the murmur in 2 cases, turbulence within the left ventricle was the cause in 6 cases. In 2 animals with acquired heart disease, pulmonary hypertension associated with *A. abstrusus* was diagnosed. In the 47 cats with congenital heart disease, isolated defects were found in 38 cats, being tricuspid valve dysplasia in 19 cats, dynamic left ventricular outflow tract obstruction associated with mitral valve dysplasia in 13 cats, ventricular septal defects in 3 cats, double chambered right ventricle in 2 cats and pulmonic stenosis in 1 cat. Combination defects were found in 9 cats, being ventricular septal defect and tricuspid valve dysplasia in 3, ventricular septal defects and double chambered right ventricle in 2, ventricular septal defect and atrial septal defect in 1 cat, a ventricular septal defect and pulmonic stenosis in 1 cat and mitral and tricuspid valve dysplasia in 2 cats. In conclusion in this prospective study we found the prevalence of heart murmurs to be 4.6% and the prevalence of congenital heart disease to be 1.6% with atrioventricular valve abnormalities and ventricular septal defects being the most common.

CA-O-5

DYNAMIC LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION IN 13 YOUNG CATS. M.J.M. Dirven¹, M.A. Barendse², M.C. vanMook², J.A. Sterenberg², A. vanden Wildenberg². ¹Utrecht University / Dierenkliniek Rijen, UTRECHT, The Netherlands, ²Dierenkliniek Rijen, RIJEN, The Netherlands

Dynamic left ventricular outflow tract obstruction (DLVOTO) is a common cause of heart murmurs in adult cats. The obstruction is caused by Systolic Anterior Motion (SAM) of the mitral valve. SAM is typically observed in adult cats and humans with hypertrophic cardiomyopathy (HCM). Many studies support the concept that structural deformities of the mitral valves and the papillary muscles could be primary causes of SAM. Congenital malformations of the mitral valve causing SAM and DLVOTO have been observed in dogs and people and are believed to exist in cats, but have not yet been reported. The aim of this study was to report the clinical and echocardiographic findings in young cats with DLVOTO. Thirteen domestic shorthair kittens, between 12-21 weeks of age, presented with a systolic heart murmur between May 1st 2009 until March 31st 2012. All cats underwent a physical examination preceding 2D-, M-mode and Doppler echocardiography. Kittens were from adoption programs run by either Dierenasiel Breda e.o. (n=8/2090) or by Dierenopvangcentrum Tilburg e.o. (n=5/845). Nine kittens were male, four were female. All kittens were asymptomatic. DLVOTO caused by SAM was present in all animals, uninterruptedly in eleven, only at high heart rates in two. Seven cats had normal left ventricular dimensions (nLVD), six cats had concentric left ventricular hypertrophy (cLVH). In five cats papillary muscle abnormalities were noted being an accessory papillary muscle in two and enlarged papillary muscles in three, two of which had cLVH. Twelve animals were reexamined 2-5 months after the initial examination. All animals were still asymptomatic. A heart murmur and DLVOTO could no longer be detected in nine animals, five with initial cLVH and four with initial nLVD. In three animals a heart murmur and DLVOTO were still present. Two of the cats with nLVD developed cLVH. One cat with initial

cLVH continued to have cLVH. Treatment with atenolol was instigated in three cats which continued to have DLVOTO and cLVH. Two cats were reexamined. Treatment with atenolol led to complete reversal of cLVH in both cases.

CA-O-6

TRANSATRIAL STENTING FOR LONG-TERM MANAGEMENT OF TUMOR OBSTRUCTION OF THE RIGHT ATRIUM IN 3 DOGS. C. Weiss¹, A. Berent¹, B. Scansen², R.E. Cober². ¹The Animal Medical Center, NEW YORK, United States of America, ²Ohio State Univ, COLUMBUS, United States of America

Central venous obstruction can have profound systemic effects. Interventional radiology techniques have been used to palliate both malignant and non-malignant causes of vascular obstruction for both intrinsic and extrinsic lesions. Three dogs presented for with large, non-resectable cardiac masses obstructing venous return to the right atrium. Venous return to the heart was severely obstructed leading to congestion with subsequent ascites (2) or head swelling and pleural effusion (1). Due to the extensive nature of the disease, an interventional palliative approach was pursued. Transatrial self-expanding metallic nitinol stents were placed from the CdVC to the CrVC in order to restore venous return to the heart via blood flow through the stent interstices. In all cases, stent placement was successful and resolution of clinical signs achieved. Two dogs required additional stent placement in 14 months and 6 months, respectively, for stent occlusion. In both cases, restenting resulted in ascites resolution or substantial reduction. One dog was euthanized 21 months following initial stent placement for general systemic decline and return of moderate ascites. The second dog remains alive 22 months following initial stent placement on diuretic therapy with moderate ascites present. The third died of undetermined causes 5 1/2 months later. To the authors' knowledge, this is the first report of long-term palliative transatrial stenting for cardiac tumors affecting venous return to the heart. The stents were well tolerated in these canine patients for which surgical options were not possible.

CA-O-7

PATHOLOGICAL FINDINGS IN THE VENTRICULAR MYOCARDIUM OF IRISH WOLFHOUNDS WITH CARDIOMYOPATHIES. A. Vollmar¹, H. Aupperle². ¹Small Animal Veterinary Clinic, BONN, Germany, ²Laboklin, BAD KISSINGEN, Germany

The Irish wolfhound (IW) dog has a high prevalence of heart diseases, particularly dilated cardiomyopathy (DCM) and atrial fibrillation (AF). During a prospective longitudinal study, 1438 Irish wolfhounds were investigated by one veterinary cardiologist (2) between 1990 and 2012. DCM was diagnosed in about 26% of dogs. In 88% of cases, DCM was accompanied by AF. AF without evidence of DCM was diagnosed in 31 dogs (2%). For pathological investigations, hearts of 19 IWs were collected and fixed in 4% buffered formalin. Based on the most recent results from cardiovascular examination, five groups were established: normal hearts (group 1, n=4), DCM with sinus rhythm (group 2; n=2), DCM with AF (group 3; n=6), DCM with AF and congestive heart failure (CHF) (group 4; n=4), AF and left ventricular reverse remodeling (LVRR) due to medical therapy after diagnosis of DCM (group 5; n=3). All hearts were evaluated by one pathologist (1) who was blinded to the clinical diagnosis. Gross inspection included measurements of weight, size, and architecture of left (LV) and right (RV) ventricles. Three sites of each LV, RV, and interventricular septum (IVS) were histologically evaluated, and the extend of myocardial fibrosis, adipocyte infiltration, and angiosclerosis were graded semiquantitatively. IWs with DCM and CHF (group 4) had died significantly younger (5.0±2.0 years) than dogs with normal hearts (7.0±1.9 years) (p=0.05). Concerning gross pathology findings in hearts with clinical DCM diagnosis, LV chambers were dilated in 3/4 cases of group 4, while in groups 3 and 5, the papillary muscles appeared grossly

prominent and not flattened as in group 4. Histopathologically, in control dogs LV and RV myocardium showed no (3/4) or mild (1/4) interstitial collagen deposits, no or single adipocytes, and normal vessels. In contrast, heterogeneous findings were seen in groups 2-5: Most hearts (10/15) showed mild to moderate multifocal myocardial fibrosis and up to moderate diffuse infiltration of adipocytes within the LV myocardium, and mild angiosclerosis, but five hearts were histologically normal. Only in one dog attenuated wavy fibers were seen in the apical region of LV. IVS was normal in 9 out of 15 cases. RV showed mild interstitial fibrosis and mild to moderate adipocytes in most cases (14/19) of all groups. In conclusion, pathological findings in hearts of IWs affected with DCM are different from other breeds. Furthermore, the gross and histological findings are variable and do not correspond to the clinical diagnosis in all cases.

CA-O-8

ATRIAL PATHOLOGY IN IRISH WOLFHOUNDS WITH AND WITHOUT ATRIAL FIBRILLATION. A. Vollmar¹, H. Aupperle². ¹Small Animal Veterinary Clinic, BONN, Germany, ²Laboklin, BAD KISSINGEN, Germany

The Irish wolfhound (IW) dog has a high prevalence of heart diseases, particularly dilated cardiomyopathy (DCM) and atrial fibrillation (AF). During a prospective longitudinal study, 1438 Irish wolfhounds were investigated by one veterinary cardiologist (2) between 1990 and 2012. DCM was diagnosed in about 26% of dogs. In 88% of cases, DCM was accompanied by AF. In addition, AF without evidence of DCM was diagnosed in 31 dogs (2%). For pathological investigations, hearts of 23 IWs were collected and fixed in 4% buffered formalin. Based on the most recent results from cardiovascular examination, three groups were established: DCM with AF (group 1; n=12), AF without evidence of DCM (group 2; n=7), normal hearts (group 3, n=4). Aim of this study was to investigate the histopathological findings in left and right atria of IWs with atrial fibrillation compared to normal hearts of IWs. All hearts were evaluated by one pathologist (1) who was blinded to the clinical diagnosis. Hearts were inspected grossly and two cross sections of each left (LAA) and right (RAA) atrial appendage were embedded in paraffin wax and stained with H&E and picosirius red. Myocardial fibrosis and adipocyte infiltration in both atria were graded semiquantitatively. Mean age ± SD of all dogs at time of death was 6,9 ± 1.7 yrs. The gross and histopathological findings of the left atrial appendage (LAA) were not significantly different among groups, but dogs in both AF groups had RAA dilation (3.6 to 22.0 ml, median 11 ml volume) compared to controls (3.5 to 9.6 ml volume, median 5.34ml). Histopathologically, RAA in control dogs showed small amounts of interstitial collagen and single adipocytes. In contrast, RAA in dogs affected with AF with and without evidence of DCM, had mild to moderate multifocal or diffuse myocardial fibrosis, and diffuse infiltration of adipocytes which was statistically significant different from normal hearts (P=0.005). In general, fibrosis and number of adipocytes were significantly increased in RAA compared to LAA in both groups with AF (P=0.014). Fibrosis and the accumulation of adipocytes within the myocardium are described to result in electrical inhomogeneity predisposing to arrhythmia. On a cellular level, right atrial fibrosis and adipocyte accumulation might be the changes responsible for the development of atrial fibrillation and atrial dilatation in this breed of dogs with an exceptional high prevalence of AF and DCM.

CA-O-9

ECHOCARDIOGRAPHIC EVALUATION OF MECHANICAL SYNCHRONY IN DOBERMAN PINSCHERS. I. Sosa, A. Estrada, B. Pogue, M. Powell, H. Maisenbacher, B. Heatwole, A. Jones. University of Florida, GAINESVILLE, FLORIDA, United States of America

Asynchronous ventricular contraction causes deterioration in cardiac function and reduces the response to medical therapy in

people with heart disease. Various echocardiographic techniques have been used in humans for evaluation of left ventricular (LV) synchronization in order to assess whether cardiac resynchronization therapy (CRT) would be beneficial. Prior studies using tissue Doppler imaging (TDI) derived strain imaging have not detected LV dyssynchronization in Doberman Pinschers with dilated cardiomyopathy (DCM). A newer 2D imaging modality, speckle tracking strain analysis, is more effective in detecting LV dyssynchrony in humans. This technique has not been previously evaluated in Doberman Pinschers with DCM. This study therefore aims to evaluate LV synchrony in Doberman Pinschers with DCM using 2D speckle tracking strain. 52 client-owned Doberman Pinschers were included. Standard echocardiography was used to evaluate systolic function and left ventricular dimension in order to categorize the dogs as normal or abnormal, depending on systolic and diastolic ventricular dimensions, ejection fraction and/or shortening fraction. The operator was blinded to the echocardiographic diagnosis of each dog. Each parameter was measured in triplicate. Radial (RS) and circumferential strain (CS), using right parasternal short axis at the level of the papillary muscles were calculated. Synchrony was assessed by measuring the difference in the QRS onset time-to-peak strain between the septal anterior and posterior left ventricular segments. To evaluate differences between groups a nested effect ANOVA (beat within group) was performed. A $p < 0.005$ was considered significant. Based on the echocardiographic parameters mentioned above, 19/52 dogs were considered normal and 33/52 had DCM. Significant differences were found in the time to peak RS ($P = 0.0009$) between normal dogs and dogs affected with DCM. Mean in time to peak RS was 43.8 ms (± 35.8) in normal dogs and 69.21 ms (± 48.9) in dogs with DCM. Time to peak CS did not exhibit significant differences between groups ($P = 0.62$) and was 55.6 ms (± 49.91) in normal dogs and 60.66 ms (± 63.2) in dogs with DCM. The results of this study show that the delay between the anteroseptal-to-posterior wall peak radial strain is greater in Doberman Pinschers with DCM than in normal dogs. Further studies would be required to evaluate whether there is a difference in synchrony between dogs in occult stage and overt DCM. Ventricular dyssynchrony could negatively affect systolic dysfunction as it does in people, and CRT may therefore be helpful for the treatment of Dobermans with DCM.

CA-O-10
CHITOSAN (HEMCON) PATCH EFFECTIVELY CONTROLS HEMORRHAGE FROM FEMORAL ARTERIAL PUNCTURE SITE IN DOGS AFTER REMOVAL OF A LARGE-BORE INTRODUCER-SHEATH. V. Szatmári. Utrecht University, Faculty of Veterinary Medicine, UTRECHT, The Netherlands

Patent ductus arteriosus is often treated with intra-arterial coil-embolization or implantation of an 'Amplatz Canine Duct-Occluder'. For both procedures an arterial access is necessary. Because of the high risk of developing a fatal hemorrhage from the arterial puncture site after removal of the large-bore introducer sheath upon completing the intervention, cardiologists generally use surgical cut-down with subsequent ligation of the femoral artery instead of percutaneous arterial puncture using Seldinger's technique.

The effect of commercially available chitosan patch has been tested in 10 experimental dogs with the approval of the institute's ethical committee. On the first 4 beagles the committee required a terminal experiment. For the selection of an appropriate introducer-sheath (i.e. smaller than the arterial diameter), the femoral artery was first imaged with ultrasound. Under general anesthesia introducer-sheaths were placed in both femoral arteries using Seldinger's technique. After their removal a chitosan-patch was applied on the wound according to the manufacturer's instructions: 10-minute manual pressure. The dogs were monitored with direct arterial blood pressure measurement, ECG, pulse oxymetry and capnography. All 4 dogs were kept under general anesthesia for several hours and the legs were moved vigorously every 30 minutes to mimic movements of awake animals.

No macroscopic hemorrhage was noticed on the 8 puncture sites and no signs of severe subcutaneous bleeding was suspected

as the blood pressure and heart rate remained stable. After several hours the dogs were euthanized.

After having shown the effective working of chitosan-patch, a permission was granted for survival experiments in 4 beagles. In 2 of these dogs one femoral artery was punctured with an introducer whose thickness exceeded the diameter of the femoral artery. In both dogs an uncontrollable subcutaneous hemorrhage occurred immediately after the 10-minute manual compression time with severe drop of blood pressure and development of tachycardia. Both dogs were euthanized during anesthesia. In another 2 beagles the size of the introducer was smaller than the diameter of the artery (80-100%). No relevant hemorrhage took place in these dogs and they recovered from the procedure without any complications. Similarly good outcome was found in two 9-month-old Boerboels.

From this pilot study we concluded that chitosan-patch can effectively control hemorrhage from a femoral arterial puncture site if the introducer-sheath is thinner than the artery's lumen. Using Seldinger's technique allows a less invasive and quicker cardiac catheterization and preservation of the femoral artery for the leg's blood supply and for repeated intra-arterial interventions.

CA-O-11
SERIAL ECHOCARDIOGRAPHIC FINDINGS IN 63 CATS WITH PRIMARY CARDIOMYOPATHY. L.J. Wilkie, K. Borg-eat, J.R. Payne, D. Connolly, A. Boswood, V. Luis Fuentes. Royal Veterinary College, HERTFORDSHIRE, United Kingdom

Objectives were to examine longitudinal change in echocardiographic left heart chamber dimensions and cardiomyopathy classification in cats with primary myocardial disease. Clinical records from 2004-2012 were reviewed for cats with 2 or more echocardiographic examinations at least 6 months apart and a diagnosis of primary myocardial disease. For each study (2 from each cat), left heart chamber dimensions were measured by a single blinded trained observer in random order, and the cardiomyopathy type was classified according to predefined criteria. Paired comparisons were made using the Wilcoxon signed rank test and Fisher's Exact test. 63 cats met the inclusion criteria. Cardiomyopathy type at entry consisted of hypertrophic cardiomyopathy (HCM, n=60), dilated cardiomyopathy (DCM, n=1), arrhythmogenic right ventricular cardiomyopathy (ARVC, n=1) and 1 normal cat. Overall, median left ventricular (LV) diastolic diameter and median long axis left atrial (LA) diameter both increased ($p=0.007$, 0.001 respectively) whereas LV diastolic wall thickness and LV fractional shortening did not change, but changes in dimensions of $>10\%$ were seen in both directions. Change in cardiomyopathy type was documented in 3 cats: HCM to normal; normal to HCM; HCM to the endomyocardial form of restrictive cardiomyopathy. The inclusion criteria led to a bias towards clinically stable cats with HCM. Despite this, changes in cardiomyopathy phenotype were observed. Either our criteria for the different feline cardiomyopathies should be defined more precisely, or phenotypic expression in cats with cardiomyopathy changes over time.

CA-O-12
TRANSESOPHAGEAL ECHOCARDIOGRAPHY AS THE SOLE GUIDANCE FOR OCCLUSION OF PATENT DUCTUS ARTERIOSUS USING THE AMPLATZ® CANINE DUCTAL OCCLUDER IN DOGS: A PRELIMINARY STUDY. F. Porciello¹, F. Biretoni¹, D. Caivano¹, A. Fruganti¹, M.E. Giorgi¹, M. Rishniw², P. Knafelz³, N.S. Moise⁴. ¹Faculty of Veterinary Medicine, PERUGIA, Italy, ²Veterinary Information Network, DAVIS, United States of America, ³Veterinary Hospital „Gregorio VII,, ROME, Italy, ⁴Faculty of Veterinary Medicine Cornell University, ITHACA, United States of America

Transesophageal echocardiography (TEE) has proven useful in evaluating patent ductus arteriosus (PDA) morphology thereby guiding appropriate device selection. Additionally, TEE, in combination with fluoroscopy, has been used to guide the transcatheter

coil embolization and for deployment of Amplatz Canine Ductal Occluder (ACDO) in dogs. Recently, we described the use of transthoracic echocardiography (TTE) guidance during transcatheter PDA occlusion with ACDO without the use of fluoroscopy, but observed problems of deployment in patients with sub-optimal acoustic windows. However, TEE, can overcome issues of sub-optimal TTE acoustic windows and provides higher image resolution of cardiac and vascular regions. Therefore, we hypothesized that TEE could be used to successfully visualize the vascular structures and interventional devices to safely perform PDA occlusion with ACDO without requiring fluoroscopy. We recruited 5 dogs with patent ductus arteriosus (PDA) for TEE-guided percutaneous ductal occlusion with an ACDO. Dogs were anesthetized, positioned in right lateral recumbency and the right femoral artery was accessed percutaneously (modified Seldinger technique). The TEE probe was advanced to a midesophageal position with minimal force to obtain a long axis 4-chamber view (transverse plane). The probe was then retroflexed and withdrawn to a cranial esophageal position until a cross section of the descending aorta was seen. To visualize PDA to the probe was slightly straightened and turned counterclockwise, and the ultrasonic beam was oriented between 60 and 120 degrees. In all dogs, the guide wire and a long introducer-sheath were guided from the aorta through the PDA into the main pulmonary artery by TEE monitoring. The ACDO was advanced through the introducer-sheath until the flat distal disk was visualized within the main pulmonary artery by TEE monitoring. The distal disk was positioned against the pulmonic ostium and the coupled proximal disk was deployed within the ductal ampulla while being monitored by TEE visualization. The guide wires, long introducer-sheath and ACDO appeared hyperechoic on TEE images and TEE guidance provided images of sufficient quality to clearly monitor the procedures in real-time. Real-time monitoring also allowed for immediate corrections to guide wire, catheter or device positioning. The procedures were successful and without complications in all patients. We have demonstrated that TEE monitoring, like TTE monitoring, can guide every step of transcatheter ACDO embolization procedures without requiring fluoroscopy, thereby avoiding radiation exposure, and provides an alternative to TTE-based guidance, especially when TTE visualization of the PDA is insufficient for safe and timely ACDO deployment.

CA-O-13

ECHOCARDIOGRAPHIC EVALUATION OF LEFT AND RIGHT VENTRICULAR DIASTOLIC DYSFUNCTION IN DOGS WITH MITRAL VALVE DISEASE WITH OR WITHOUT PULMONARY HYPERTENSION. M. Baron Toaldo¹, H. Poser², S. Battaia¹, G. Giulio², B. Contiero², M. Cipone¹, E. Mazzotta², C. Guglielmini². ¹University of Bologna, OZZANO EMILIA, Italy, ²University of Padova, LEGNARO, Italy

Right ventricular (RV) dysfunction occurs in human patients with left-sided cardiac disorders because of the mechanism of ventricular interdependence. Doppler echocardiographic indices of diastolic function of the right ventricle are good prognostic markers during left ventricular (LV) failure secondary to ischemic and dilated cardiomyopathy. The aims of the present study were: to assess LV and RV diastolic function by conventional Doppler and pulsed-wave tissue Doppler imaging (PW-TDI) in dogs with mitral valve disease (MVD), with or without pulmonary hypertension (PH); to test if echocardiographic parameters of LV and RV diastolic dysfunction correlate to the Doppler-estimated pulmonary artery systolic pressure (PASP). 114 dogs were prospectively evaluated, including 86 dogs with MVD. For each dog, a complete echocardiographic evaluation was carried out. Dogs with MVD were divided in 3 groups according to the ACVIM classification of heart failure. Using the cut-off value of tricuspid regurgitation (TR) peak velocity of 2.8 m/s, presence or absence of PH was considered. Standard echocardiographic and mitral and tricuspid Doppler parameters (E wave and A wave), and PW-TDI parameters (systolic wave, Sa; early diastolic wave, e'; late diastolic wave, a'; e'/a' ratio; E/e' ratio) for lateral and septal mitral annulus, and lateral tricuspid annulus were measured. The echocardiographic data were compared by use of ANOVA and multiple contrast *t*-test with Bonferroni correction. The relationship between left-sided echocar-

diographic parameters and RV diastolic parameters was examined by correlation analysis. The correlation of PASP with LV and RV diastolic parameters was examined by multiple linear regression. A value of $P < 0.05$ was considered significant. Dogs were classified as follows: 28 healthy dogs; 36 dogs in class B1; 28 dogs in class B2; 22 dogs in class C and D. No differences were found among groups regarding RV conventional Doppler and PW-TDI parameters. However, a significant, weak correlation was found between some left-sided echocardiographic parameters (left atrial dimension; end diastolic and end systolic volume indexes; peak E wave and A wave velocities and E:A ratio) and some RV PW-TDI parameters. PH was diagnosed in 48 dogs, while 54 dogs were deemed without PH. Dogs with PH had significantly different trans-mitral E and A wave peak velocity and E/e' ratio of lateral and septal mitral annulus. These two latter parameters were also correlated with PASP ($R^2 = 0.241$ and 0.338 , respectively). Our findings highlight the importance of considering ventricular interdependence in dogs with MVD, particularly those with PH.

CA-O-14

LEFT VENTRICULAR TWIST AND TWIST RATE IN DOGS WITH MITRAL REGURGITATION ATTRIBUTABLE TO MYXOMATOUS MITRAL VALVE DISEASE. N.E. Zois¹, N.T. Olsen², S.G. Moesgaard³, C.E. Rasmussen¹, T. Falk¹, J. Högström⁴, H.D. Pedersen³, J.E. Møller⁵, L.H. Olsen⁶. ¹University of Copenhagen, FREDERIKSBERG, Denmark, ²Department of Cardiology, Roskilde Hospital, ROSKILDE, Denmark, ³Novo Nordisk A/S, MAALOEV, Denmark, ⁴Department of Clinical Sciences, Swedish University of Agricultural Sciences, UPPSALA, Sweden, ⁵Department of Cardiology, Copenhagen University Hospital Rigshospitalet, COPENHAGEN, Denmark, ⁶Department of Veterinary Disease Biology, University of Copenhagen, FREDERIKSBERG, Denmark

During the cardiac cycle, the left ventricle (LV) undergo a complex deformation, consisting of overall shortening accompanied by increase in wall thickness and twisting due to the helical orientation of the myocardial fibers. Using speckle tracking echocardiography (STE), the circumferential strain (CS) as well as the twisting motion of the LV, calculated as the net difference between LV apical and basal rotation angles during the cardiac cycle, can be quantified by post-processing 2-dimensional short axis images of the LV. Thus, the aim of this study was to evaluate the global CS and the twisting motion in 101 small-medium sized dogs with varying severity of MR attributable to myxomatous mitral valve disease (MMVD). Using a Vivid-i ultrasound system, all dogs underwent echocardiography including parasternal short axis views at the basal and apical level for offline analysis of rotation, and at the midpapillary muscle level for analysis of global CS, using commercially available software (EchoPAC). Twisting motion during systole (Twist_{SYS}), early (Untwist_{EARLY}) and late (Untwist_{LATE}) diastole were calculated as well as their rates computed as the time derivatives. Furthermore, time to onset of untwist, calculated from start of electromechanical activation until peak Twist_{SYS} was measured. Associations between twist and untwist variables, global CS and conventional echocardiographic indices of MR severity and LV remodeling were examined by multiple linear regression analyses including dog characteristics such as heart rate (HR), sex, breed, body weight and age. Global CS increased with increasing MR ($P < 0.0001$). Untwist_{EARLY} ($P = 0.0004$) and its rate ($P = 0.0008$) also increased with increasing MR, albeit in co-variation with certain baseline dog characteristics. Time to onset of untwist increased with MR ($P = 0.0005$), left atrium to aortic root ratio ($P = 0.0007$) and LV internal diameter in diastole ($P < 0.0001$). In conclusion, Untwist_{EARLY} and global CS gradually increased and the onset of untwist appeared to be delayed with increasing MR severity in small-medium sized dogs with spontaneous MMVD. This hyperdynamic stage with a delay in untwist may represent LV adaptation to loading conditions in MMVD, but might also indicate mid- and subepicardial compensation for an early LV dysfunction, as reflected by delayed onset of relaxation, as timing of contraction-relaxation cross over is the most vulnerable period of myocardial fiber mechanics.

CA-O-15**LEFT VENTRICULAR OUTFLOW TRACT DYNAMIC OBSTRUCTION WITHOUT LEFT VENTRICULAR HYPERTROPHY AND WITH REGRESSING LEFT VENTRICULAR HYPERTROPHY. J Sottiaux. Wey Referrals, SAINT ANDRE DE CORCY, France**

Systolic anterior motion (SAM) of the mitral valve is the mechanical correlate of left ventricular outflow tract dynamic obstruction (LVOTDO) and has been associated with hypertrophic cardiomyopathy (HCM) in most instances. However, SAM without left ventricular hypertrophy or with regressing hypertrophy is increasingly recognised. The echocardiographic studies of 12 cats, diagnosed between 06/2006 and 03/2012, with SAM without HCM (7 cats) or SAM with regressing hypertrophy (5 cats) were reviewed for evaluation of the anatomic and mechanic alteration contributing to LVOTDO. Ventriculo-aortic and aorto-septal malalignment were suggested by the significantly narrower aorto-mitral (AM) and aorto-septal (AS) angle compared to a group of 14 control cats (AS = 120 versus 152 - $p = 0.007$; AM = 14 versus 157 - $p = 0.014$). Other anatomic alterations of the LVOT constituents included false tendon inserted on the septal crest (11/12), basal septal angulation (7/12), apical displacement of the postero-medial or antero-lateral papillary muscle (5/12), bifid/accessory papillary muscle (1/12), aberrant chordal insertion on the septal crest (3/12), severe papillary muscle hypertrophy (3/12), and thickened aortic cusps with sub-aortic ancillary echoes (5/12). Mechanisms of LVOTDO included obstructive mitral septal leaflet (2/12), protrusion of a displaced papillary muscle (2/12), impingement of an angulated basal septum into the LVOT (7/12), and mechanical LVOT narrowing from hypertrophic papillary muscle (1/12). Basal septal impingement into the LVOT was associated with apical ballooning (5/7) without obvious apical akinesis. Out of 7 cats with LVOTDO without hypertrophy, 4 had follow-up studies; only 1 cat responded positively to atenolol treatment. All the cats with initial hypertrophy had reverse remodelling and normalised aortic ejection velocities within 1 month to 11 month after atenolol treatment initiation; 1 cat developed aortic regurgitation. These data indicate that SAM is not exclusively related to HCM and may be a cause, not a complication, of left ventricular hypertrophy.

CA-O-16**TREATMENT OF DOGS WITH COMPENSATED DEGENERATIVE MITRAL VALVE DISEASE (DMVD) WITH SPIRONOLACTONE. M.J. Hezzell, A. Boswood, J. Elliott. The Royal Veterinary College, HATFIELD, United Kingdom**

Therapies that delay the onset of congestive heart failure (CHF) in dogs with DMVD at risk of disease progression would be clinically beneficial. Increases in LA/Ao, LVEDDN and serum NT-proBNP and cTnI concentrations are associated with decreased survival times. Activation of the renin-angiotensin-aldosterone system is implicated in cardiac remodeling in canine DMVD. We hypothesised that administration of spironolactone to dogs with compensated DMVD demonstrating the above risk factors would reduce the rate of cardiac remodeling associated with progressive DMVD. Dogs with ACVIM class B DMVD were recruited to a randomized, blinded, placebo-controlled pilot study. No dogs were receiving medications for cardiac disease. All dogs demonstrated at least one of the following risk factors: echocardiographic evidence of cardiomegaly, NT-proBNP > 550 pmol/L, cTnI > 0.025 ng/mL. No dogs had evidence of other cardiac disease or renal disease, hypoadrenocorticism, hyperkalaemia, or hyponatraemia. Dogs were randomized to receive spironolactone (2mg/kg orally) or placebo SID for 6 months. Comparisons between groups were made using Mann-Whitney tests. Repeated measures linear models were constructed to compare the rate of change of variables over time. Significance was set at $P < 0.05$. Data were analysed based on the intention to treat. Twenty dogs of varying breeds were enrolled. Ten dogs demonstrated 3 risk factors, 7 dogs 2 risk factors and 3 dogs 1 risk

factor. Ten dogs received placebo; age range 6.3-11.7 years (mean \pm SD, 9.0 ± 1.7 years), body weight range 4.5-17.0 kg (10.9 ± 3.9 kg), LA/Ao range 1.06-1.64 (1.28 ± 0.20), LVEDDN range 1.61-2.11 (1.82 ± 0.19), NT-proBNP (median [interquartile range]) 620.5 pmol/L [488.5, 932.8] and cTnI 0.030 ng/mL [0.018, 0.063]. Ten dogs received spironolactone; age range 6-13 years (9.7 ± 2.1 years), body weight range 1.8-23.3 kg (11.4 ± 6.2 kg), LA/Ao range 1.22-1.90 (1.45 ± 0.21), LVEDDN range 1.16-2.56 (1.96 ± 0.39), NT-proBNP 1741.0 pmol/L [1200.3, 2952.0] and cTnI 0.060 ng/mL [0.028, 0.113]. One dog in this group died suddenly, 1 progressed to CHF and 2 received suboptimal spironolactone dosage. NT-proBNP was significantly higher in the spironolactone group at baseline. ($P = 0.010$). NT-proBNP ($P = 0.002$), LA/Ao ($P = 0.002$) and LVEDDN ($P = 0.001$) increased over time in the placebo, but not in the spironolactone group. The rates of change of NT-proBNP ($P = 0.059$), LA/Ao ($P = 0.062$) and LVEDDN ($P = 0.072$) approached, but did not reach, significant differences between groups. In conclusion, treatment with spironolactone might slow the rate of increase in cardiac size in dogs with ACVIM class B DMVD showing risk factors for poor outcome. Decreasing the rate of increase in cardiac size might delay the onset of CHF. Further studies are warranted to investigate these hypotheses.

CA-O-17**CARDIAC ULTRASOUND IN CANINE EMERGENCIES WITH A SYSTEMIC INFLAMMATORY RESPONSE SYNDROME. K. Gommeren, I. Desmas, A. Garcia, C. Clercx, K. Mc Entee, D. Peeters. Liège University, LIÈGE, Belgium**

Cardiac dysfunction is a concern in human systemic inflammatory response syndrome (SIRS) patients, where increased cardiac biomarkers and decreased cardiac function have already been described. In a previous canine SIRS study, an increase of cardiac biomarkers (NT-proBNP, cTnI and lactate) and their prognostic value has been established. The present study evaluated the kinetics of basic echocardiographic parameters (Fractional shortening (FS) and left ventricular ejection fraction (LVEF), which both reflect systolic function; and the ratio of the left atrium to the aorta (LA/Ao), which reflects preload) in canine SIRS. Our hypotheses were that (1) FS, LVEF and LA/Ao are altered in canine SIRS and (2) that these parameters carry prognostic information. Dogs with SIRS, without primary cardiac disease, presenting to the emergency service were prospectively included from January until August 2010. Cardiac ultrasonography was performed by two veterinarians in a standardized fashion at initial presentation, after 6 (T6), 12 (T12), 24 (T24), 72 (T72) hours of hospitalization until discharge or death and at a control visit (T1m) over one month after discharge. Dogs were classified according to their underlying disease process: infection, neoplasia, trauma, gastric-dilation and volvulus (GDV), other GI diseases, and miscellaneous diseases. Statistical analysis was performed with SAS. Univariate analysis was used to assess normal distribution. A mixed procedure and a logistic procedure was performed accordingly ($p < 0.05$). Thirty seven dogs (infection, $n = 6$; neoplasia, $n = 4$; trauma, $n = 4$; GDV, $n = 4$; other GI, $n = 4$ and miscellaneous diseases, $n = 15$) were included. Twenty-eight patients survived, while 9 did not (died, $n = 3$; euthanasia for financial reasons, $n = 2$; euthanasia for prognostic reasons, $n = 4$). Eleven dogs had control visits, 12 owners declined a control echocardiography, 2 patients were lost to follow-up and 3 died before control visit. FS and LA/Ao were significantly correlated with survival to discharge, however LVEF was not. Additionally, LVEF and FS did not change significantly during hospitalization; neither compared to T1m. LA/Ao did however increase significantly during hospitalization. LA/Ao at T0 (1.03 ; 0.76 - 1.74) differed significantly from values at T12 (1.12 ; 0.84 - 1.68), T72 (1.20 ; 0.8 - 1.54) and T1m (1.19 ; 1.05 - 1.59). Unexpectedly, surviving dogs had lower FS (35.7%; 19-64) than non-survivors (44.3%; 33-53). LA/Ao was associated with survival and increased rapidly after hospitalization to values similar to T1m, which probably reflects the efficacy of fluid therapy in emergency cases. In this population of canine SIRS patients, no echocardiographic evidence of cardiac dysfunction was demonstrated.

CA-O-18**ARTERIAL THROMBOEMBOLISM IN 242 CATS PRESENTING TO FIRST OPINION PRACTICE: 2004 TO 2012.**

K.A. Borgeat¹, J.A. Wright², O. Garrod³, V. Luis Fuentes¹.
¹Royal Veterinary College, HATFIELD, United Kingdom, ²Zetland Veterinary Group, BRISTOL, United Kingdom, ³Highcroft Veterinary Group, WHITCHURCH, United Kingdom

Reports from first-opinion practice of feline arterial thromboembolism (ATE) are scarce. Our aim was to describe and evaluate the outcome in cats with ATE presenting to three first-opinion clinics. Clinical records of cats presenting with ATE between 2004-2012 were reviewed for history, clinical findings, presence of congestive heart failure (CHF) and outcome. Kaplan-Meier and log rank analysis was performed to evaluate associations with survival. During the study period, 242 cats presented with ATE; an overall feline incidence of 0.26%. Most cats were male (58.5%) and non-pedigree (92.1%). Signs of cardiovascular disease prior to ATE included cardiomyopathy (12%), a heart murmur (23.5%), a gallop sound/arrhythmia (3.3%) and hyperthyroidism (7.1%). Most cats presented within 6 hours of clinical signs (72.6%). Median age at presentation was 12 [1-21] years. Hypothermia (<37°C, $p=0.0004$, unpaired t-test), CHF ($p<0.0001$, Fisher's Exact test), absence of a murmur ($p=0.0121$, Fisher's Exact test) and >1 limb affected ($p<0.0001$, Fisher's Exact test) were associated with death or euthanasia within 24 hours of clinical signs (170 cats); 163 (67.4%) of these cats were euthanased. Absence of CHF ($p=0.0082$, Fisher's Exact test), 1 limb affected ($p=0.0065$, Fisher's Exact test) and treatment with aspirin±clopidogrel ($p=0.0010$, Fisher's Exact test) were associated with survival to discharge (48.5% of cats surviving the first 24 hours). No identified factor was associated with long-term survival after discharge (median survival time 117.5 [6-2614] days). Recurrence of ATE occurred in 46.4% discharged cats. In first opinion practice, different factors influence survival to discharge and long-term survival in cats with ATE.

CA-O-19**LONG-TERM INTRINSIC RHYTHM EVALUATION IN DOGS WITH ATRIOVENTRICULAR BLOCK.** R. Santilli, T. Vezzosi, M. Perego. Clinica Veterinaria Malpensa, GALLARATE, Italy

Atrioventricular block (AVB) is an arrhythmia resulting from conduction abnormalities through the atrioventricular node that leads to severe signs and sudden death. The aim of this study was to evaluate long-term intrinsic rhythm variations in dogs undergone pacemaker (PM) implantation. Ninety-two dogs of different breeds with 3rd degree AVB (3AVB) (59.8%), advanced 2nd degree AVB (2AVB) (14.1%), paroxysmal 3AVB (12%), 2:1 AVB (7.6%) and 3AVB with atrial fibrillation (6.5%) were retrospectively analyzed. Forty-nine (53.3%) were males and 43 (46.7%) females with a mean age of 8.8 ± 3.3 (SD) years and a mean body weight of $26.5 \text{ kg} \pm 12.8$. The intrinsic rhythm was evaluated the day of PM implantation (T0), after 1 day (confidence interval 95% [CI 95%] 1-2) (T1), 33 days (CI 95% 28-35) (T2), 105 days (CI 95% 98-156) (T3), 275 days (CI 95% 221-380) (T4). According to the AVB grade at different controls, the rhythm disturbance was considered advanced, regressed or unchanged. Shapiro-Wilk and Kolmogorov-Smirnov tests were used to test normalcy, F-test to compare means in a generalized linear model and Chi-squared to examine the association between categorical variables and status at each control. Sixty (65.3%) dogs had no intrinsic rhythm changes, 20 (21.7%) had AVB progression and 12 (13%) had AVB regression. Forty-eight cases of 3AVB remained unchanged, while 4 regressed to sinus rhythm, 2 to 2:1 AVB and 1 to advanced 2AVB. Eight advanced second degree AVBs progressed to complete AVB, 2 regressed to sinus rhythm, 1 to 2:1 AVB and 2 remained unchanged. Five paroxysmal 3AVBs progressed to complete AVB, 3 to 2:1 AVB and 3 remained unchanged. Four 2:1 AVBs progressed to complete AVB, 2 regressed to sinus rhythm and 1 remained unchanged. All AVBs with atrial fibrillation remained unchanged. Chi-square test showed that changes of intrinsic rhythm were associated with the type of AVB ($\chi^2 4.5$, $p<0.03$) and the time of controls ($\chi^2 64.4$, $p<0.0001$), while other factors were not statistically significant.

Regression occurred within 30 days while progression occurred at any times. The results showed that the degree of AVB at the moment of PM implantation should not be considered a definitive diagnosis since more than 1/3 of the cases could present progression or regression. Because of their potential progression, PM implantation should be considered as first choice treatment also in cases of low 2AVBs, and further studies are needed to evaluate the cause of transitory high grade AVBs.

CA-O-20**CHARACTERISTICS OF CARDIAC FUNCTION ASSESSED BY COLOUR TISSUE DOPPLER IMAGING IN HEALTHY DOGS DIFFER BETWEEN LARGE AND SMALL BREEDS.**

A. Hanäs¹, C. Carnabuci², A. Tidholm³, I. Ljungvall², J. Häggström², K. Höglund⁴. ¹Strömsholm Referral Animal Hospital, STRÖMSHOLM, Sweden, ²Dept. of Clinical Sciences, Swedish University of Agricultural Sciences, UPPSALA, Sweden, ³Albano Animal Hospital, DANDERYD, Sweden, ⁴Dept Anatomy, Physiol and Biochem, Swedish University of Agricultural Sciences, UPPSALA, Sweden

Tissue Doppler Imaging (TDI) is a complement to conventional echocardiography for assessment of myocardial function. The aims of the study were to investigate breed differences and intraobserver-variability of colour TDI variables in healthy dogs. Fifty-three privately-owned male dogs were prospectively recruited. Dogs were declared healthy by physical examination, blood pressure measurement, ECG, analyses of urine and blood (haematology and biochemistry), and conventional echocardiographic 2D and Doppler examination, as part of the EU-funded Lupa-project. Directly following these extensive examinations, the TDI acquisition was performed by the same experienced echocardiographer using a Philips HD11xe with a S8-3 (small dogs) and S3-1 (large dogs) MHz probe. Cine-loops were acquired from the right short-axis view and radial colour TDI variables at the endocardium and epicardium of the left ventricular free wall were later analysed. Six other healthy dogs were included in a substudy aimed at evaluating the effect of 6 sources of variation using a hierarchical random-effects model. Ten of the 53 examined dogs were excluded due to breathing artifacts and poor quality of the curves, leaving 43 dogs in the study; Labrador retrievers (19), Cavalier King Charles spaniels (19), and Dachshunds (5), with a mean age of 3.4 ± 1.2 years (SD). A P -value < 0.05 was considered significant in the statistical analyses. Kruskal-Wallis one-way analysis of variance showed that Labrador retrievers had significantly higher values for endocardial and epicardial systolic (S) waves, and longer time to peak for both endocardial and epicardial E- and A-waves, compared to the other two breeds. Labrador retrievers also had significantly lower heart rate (HR). Further analysis of the breed differences using multiple regression analysis showed major effects of body weight and HR on endocardial and epicardial S waves, while time to peak, both endocardial and epicardial, for the E- and A-waves, were primarily affected by HR. Dog was the variance component having the major effect on variability of TDI variables. In conclusion, time to peak of both diastolic waves was longer in Labrador retrievers compared to the small-breed dogs. Furthermore, higher S-wave values in Labrador retrievers might indicate a different contractility pattern in large-breed dogs, and warrants further investigation.

CA-O-21**EVALUATION OF C-REACTIVE PROTEIN BEFORE AND AFTER MITRAL VALVE REPAIR IN DOGS WITH MITRAL REGURGITATION.** M. Funayama, T. Mizuno, M. Mizuno, T. Mizukoshi, K. Harada, T. Sawada, M. Endo, J. Takeuchi, A. Shinoda, A. Takahashi, S. Uchida, M. Uechi. Nihon University, KANAGAWA, Japan

Mitral regurgitation (MR) is the most common heart disease in dogs. Dogs with a more advanced stage of this disease are likely to develop pulmonary edema of heart failure. The aim of this study was to evaluate the plasma C-reactive protein (CRP) concentra-

tion in dogs that underwent mitral valve repair for MR. All dogs were operated between October 2006 and October 2010. The dogs were categorized according to the International Small Animal Cardiac Health Council (ISACHC) classification, and physical examination, thoracic radiography, and 2D color flow Doppler echocardiography were performed before and after surgery. The plasma CRP concentration and white blood cell counts were also determined before and after surgery. Cardiogenic pulmonary edema was diagnosed on the basis of clinical examination and thoracic radiography. Overall, 44 dogs (mean body weight, 5.6 ± 3.1 kg and mean age, 9.3 ± 2.2 years) were enrolled; 11 of these dogs had cardiogenic pulmonary edema. The dogs breeds were Chihuahua ($n = 10$), Cavalier King Charles Spaniel ($n = 10$), Maltese ($n = 7$), Yorkshire Terrier ($n = 3$), Shih Tzu ($n = 2$), Miniature Dachshund ($n = 2$), and others ($n = 10$). No significant difference was found for age and body weight. The vertebral heart size and LA/Ao ratio significantly decreased after surgery compared with the preoperative values. Before the operation, CRP concentration and white blood cell counts in ISACHC class IIIb dogs (2.5 ± 2.3 mg/dL and 21288 ± 7656 μ L, respectively) were higher than those in class Ib (0.2 ± 0.3 mg/dL and 11500 ± 1320 μ L, respectively), class II (0.1 ± 0.1 mg/dL and 8822 ± 2243 μ L, respectively), and class IIIa (0.7 ± 1.8 mg/dL and 11731 ± 4620 μ L, respectively) dogs. Additionally, CRP concentration and white blood cell counts in class IIIb dogs significantly decreased after surgery compared with preoperative values. CRP concentration and white blood cell counts in the dogs with cardiogenic pulmonary edema significantly increased compared with those with non-pulmonary edema. Furthermore, cardiogenic pulmonary edema disappeared within 3 months after surgery, and the CRP concentrations and white blood cell counts became normal. In conclusion, CRP concentration increases in dogs with MR and cardiogenic pulmonary edema. It is widely recognized that inflammatory reaction plays a key role in the development of heart failure. Consequently, these data indicate the importance of strict management for pulmonary edema and inflammation.

CA-O-22

SERUM SEROTONIN CONCENTRATION IS ASSOCIATED WITH SEVERITY OF MYXOMATOUS MITRAL VALVE DISEASE IN DOGS. I. Ljungvall¹, K. Höglund², M.A. Oyama³, A. Tidholm⁴, J. Häggström⁵. ¹Dept. of Clinical Sciences, Swedish University of Agricultural Sciences, UPPSALA, Sweden, ²Dept. Anatomy, Physiol and Biochem, Swedish University of Agricultural Sciences, UPPSALA, Sweden, ³Dept. of Clinical Studies, University of Pennsylvania, PHILADELPHIA, United States of America, ⁴Albano Animal Hospital, DANDERYD, Sweden

The neurotransmitter serotonin (5-hydroxytryptamine, 5HT) has recently been suggested to have a role in development of myxomatous mitral valve disease (MMVD) in dogs. The aim of this study was to investigate whether serum 5HT concentration was associated with MMVD severity in dogs, and to assess potential associations between serum 5HT concentrations and dog characteristics, echocardiographic variables, heart rate, systolic blood pressure, and platelet size (mean platelet volume) in the study population. 120 client-owned dogs with naturally acquired MMVD of varying severity were prospectively recruited for the study. Dogs were classified according to MMVD severity (breeds predisposed to early onset of MMVD, but without echocardiographic evidence of the disease, or mild, moderate or severe disease). Serum 5HT concentrations were analyzed using an ELISA assay. Lower serum 5HT concentrations were shown in dogs with severe MMVD, compared with dogs predisposed to MMVD ($P = 0.0025$) and dogs with mild MMVD ($P = 0.0011$). Unilinear and multiple regression analyses showed that serum 5HT concentrations decreased with increasing left atrial to aortic root ratio (LA/Ao), were higher in Cavalier King Charles Spaniel (CKCS) dogs compared to dogs of other breeds, and were higher in female dogs than in male dogs. The LA/Ao was the variable most strongly associated with serum 5HT concentration. In conclusion, the finding of higher serum 5HT concentrations in dogs predisposed to MMVD (CKCS) and dogs with mild MMVD suggests that alterations in 5HT signaling might play a role in progression of early stages of MMVD.

EN-O-1

PHYSIOLOGY AND DIAGNOSTIC POTENTIAL OF SERUM GHRELIN IN CATS WITH DIABETES MELLITUS AND HYPERSOMATOTROPISM. K.B. Jensen, Y. Forcada, B. Glanemann, D.B. Church, S.J.M. Niessen. Royal Veterinary College, HATFIELD, United Kingdom

Hypersomatotropism (HS) can be a common reason for development of diabetes mellitus in the cat. Remission of diabetes can be achieved with an accurate diagnosis of the HS, although diagnosis is hampered by the relative complexity of confirming HS, requiring a combination of insulin growth factor-1 (IGF-1) or feline growth hormone measurement and intracranial imaging. Unfortunately, all three have limitations as diagnostic aid and when evaluating the success of therapy, particularly radiotherapy (RT). Consequently, more precise markers of HS are required. The current study aimed to evaluate physiological behaviour and diagnostic potential of serum ghrelin in feline HS. As ghrelin is an endogenous ligand of the GH secretagogue receptor, it was hypothesised production of ghrelin might be suppressed in HS and subnormal serum levels could be a marker for increased GH activity. Fasted (pre-insulin) serum samples were collected from 20 normal (age matched control), 20 uncomplicated diabetic (DM) and 33 hypersomatotropic diabetic (HSDM) cats. Cats were categorized into the HSDM-group on the basis of elevated IGF-1 (>1000 ng/ml) and demonstration of a pituitary lesion on imaging. In 13 cats additional serum samples were obtained following RT. Cats were categorized into the DM-group on the basis of low IGF-1 (<700 ng/ml) and normal insulin requirements (<1.5 iu/kg). Serum ghrelin was determined using a total ghrelin ELISA system validated for the cat. Data were tested for normality and concentrations compared between groups using unpaired t-tests and a paired t-test for the before and after RT HSDM-groups. Serum total ghrelin was not different between the HSDM (7.9 ng/ml \pm 3.3) and DM-group (6.7 ng/ml \pm 2.3, $p=0.14$). A significant difference was present between the control group (12.9 ng/ml \pm 6.8) and both the HSDM ($p=0.0007$) and the DM-group ($p=0.0004$). Serum ghrelin concentrations in the HSDM cats undergoing RT ($n = 13$) were significantly higher following completion of treatment (6.7 ng/ml \pm 1.9 versus 8.6 ng/ml \pm 2.2, $p=0.006$). The results suggest feline serum total ghrelin is suppressed to similar levels in both the diabetic and diabetic hypersomatotropic state compared to healthy subjects. Consequently, it appears serum ghrelin levels are not helpful in determining the presence of HS in the diabetic cat. However, the results do indicate treatment of HS with RT results in an increase in serum ghrelin, suggesting the presence of an independent inhibitory effect of excess GH on serum ghrelin production. This potential inhibitory effect of GH might render serum ghrelin measurement useful as an additional tool to assess hypersomatotropic remission after RT. Further studies are however indicated.

EN-O-2

HISTOLOGICAL INVESTIGATION OF ENDOCRINE AND EXOCRINE PANCREAS IN CATS WITH DIABETES MELLITUS. E. Zini¹, F. Lunardi², R. Zanetti³, L. Coppola⁴, M. Ackermann⁵, T.A. Lutz⁶, C.E. Reusch¹, L. Cavicchioli³. ¹Clinic for Small Animal Internal Medicine, University of Zurich, ZURICH, Switzerland, ²Department of Diagnostic Medical Sciences and Special Therapies, UNIVERSITY OF PADOVA, Italy, ³Department of Comparative Biomedicine and Food Sciences, University of Padova, PADOVA, Italy, ⁴Department of Animal Medicine, Production and Health, University of Padova, PADOVA, Italy, ⁵Institute of Virology, University of Zurich, ZURICH, Switzerland, ⁶Institute of Veterinary Physiology, University of Zurich, ZURICH, Switzerland

To date only few studies characterized histopathological features of the endocrine and exocrine pancreas in cats with diabetes mellitus. Loss of β -cells is a consistent finding but no detailed data about the presence and types of inflammatory cells are available. We recently observed that hyperglycemia increases neutrophils in the exocrine pancreas. The aims of the present study were to assess whether diabetic cats have pathological evidence of islet inflammation or pancreatitis and to define islet lesions in comparison to a

well-matched control population. Formalin-fixed, paraffin-embedded pancreatic samples were collected from post-mortem examination performed on diabetic and control cats died due to any disease at the Clinic for Small Animal Internal Medicine, University of Zurich (Switzerland) between 1997 and 2009. Control cats were selected to be matched for age, sex, breed and body weight. Sections were routinely stained with hematoxylin-eosin, and double-labeled immunohistochemistry was performed for the following markers: insulin and myeloperoxidase (neutrophils), insulin and CD3 (T-lymphocytes), insulin and CD20 (B-lymphocytes), insulin and PCNA (proliferation marker), and glucagon and Ki-67 (proliferation marker). Light-microscopic cell counting and morphometric analyses were performed manually and with software (Image-J), respectively. Data were analyzed with contingency tables and t-tests. Thirty-seven diabetic cats and 20 controls were included. The mean insulin-positive cross sectional area was approximately 40% lower in diabetic than control cats ($P < 0.01$), that of glucagon was similar. Proliferation of insulin-positive and glucagon-positive cells and the average counts of neutrophils, T- and B-lymphocytes in the islets did not differ between groups. Interestingly, the presence of (T and B) lymphocytes in general tended to be more frequent in diabetic (8/37=21.6%) than control (1/20=5.0%) cats. In the exocrine pancreas, a trend towards increased presence of necrosis and fibrosis was observed in diabetic cats (6/37=16.2% vs. 0/20=0%; $P=0.07$) but inflammatory infiltration did not differ. Proliferation of acinar cells was 3-fold increased in diabetic cats ($P < 0.01$), notably nearby islets (6-fold, $P < 0.001$). The results confirm previous observations that loss of β -cells occurs in diabetic cats. In addition, a subset of diabetic cats shows lymphocytic infiltration of the islets that might have contributed to β -cell loss. Increased necrosis and fibrosis of the exocrine tissue may suggest that the diabetes leads to pancreatitis in some cats. The increased proliferation rate of acinar cells deserves further investigation. In humans this finding has been associated with chronic pancreatitis as well as transdifferentiation into islet cells.

EN-O-3

SERUM TYPE III PROCOLLAGEN PROPEPTIDE: AN ALTERNATIVE MEASURE OF GROWTH HORMONE BIOACTIVITY IN CATS WITH DIABETES MELLITUS AND HYPERSOMATOTROPISM. S.J.M. Niessen, Y. Forcada, D.B. Church. Royal Veterinary College, NORTH MYMMS, United Kingdom

On the basis of a relatively high prevalence of hypersomatotropism (HS) amongst cats with a diagnosis of diabetes mellitus, as well as the possible subtle phenotype of these patients and the significant implications on prognosis and treatment, screening diabetic cats for HS could be advocated. For most veterinarians serum total insulin-like growth factor-1 (IGF-1) assessment represents the most feasible and accessible means of performing screening. However, hepatic IGF-1 production is dependent on presence of sufficient portal insulin, which can be deficient in newly diagnosed diabetic cats, resulting in false negative results. Additionally, elevation of IGF-1 has been reported in non-acromegalic diabetic cats. Alternative or additional diagnostic tests for HS, as well as to evaluate the success of treatment of HS, are therefore desirable. Since feline HS is associated with tissue growth, serum type III procollagen propeptide (PIIP), a peripheral indicator of collagen turnover, was hypothesised to be a useful indicator of active disease or growth hormone bioactivity. Fasted, pre-insulin, serum samples were prospectively collected from 16 uncomplicated diabetic (DM) and 16 hypersomatotrophic diabetic (HSDM) cats. Cats were categorised into the HSDM-group on the basis of elevated IGF-1 (radioimmunoassay, >1000 ng/ml), followed by demonstration of a pituitary lesion on intracranial imaging and into the DM-group on the basis of low IGF-1 (<600 ng/ml) and modest insulin requirements (<1.5 iu/kg). An ELISA system for PIIP was developed for use in the cat. Data were tested for normality and concentrations compared using the Mann Whitney test. Correlation with serum IGF-1 was assessed by calculating a Spearman's correlation coefficient (ρ). Dilutional parallelism using cat serum with high and low PIIP-activity indicated validity of the ELISA system. Intra-assay coefficient of variation calculation proved adequate precision at high and low concentrations (7.3% and 7.8%) and the assay detection limit was found to be

2.7 ng/ml. Median serum PIIP was 24.3 ng/ml (range: <2.7 -44.7) in the HSDM group, versus 4.9 (range: <2.7 -8.0) in the DM group ($p < 0.001$). There was a significant correlation between serum IGF-1 and PIIP ($\rho = 0.60$, $p < 0.001$). In conclusion, serum PIIP can be measured in the cat. Additionally, serum PIIP seems an alternative measure of growth hormone bioactivity in cats, given the significant elevation in concentration in feline HS. Further evaluation of PIIP in cases with HS will help determine the exact added value of evaluating this parameter in the diagnosis of HS, as well as in the assessment of treatment efficacy.

EN-O-4

THE EFFECT OF SINGLE NUCLEOTIDE POLYMORPHISMS ON CANINE SLC5A1 (SGLT1) PROMOTER FUNCTION, AND THEIR RELEVANCE IN DIABETES MELLITUS AND OBESITY IN DOGS. D. Batchelor, A.J. German, S. Shirazi-Beechey. University of Liverpool, NESTON, United Kingdom

Glucose and galactose are transported across the brush border membrane (BBM) of enterocytes by sodium/glucose cotransporter-1 (SGLT1), coded for by *SLC5A1*. SGLT1 is the sole route for intestinal glucose absorption and its level of expression dictates BBM transport capacity for glucose. The relevance of SGLT1 expression in predisposition to diabetes mellitus and obesity was investigated in dogs. The aims were to assess the effect on promoter function of known SNPs in the 5' flanking region of canine *SLC5A1*, and to search for novel SNPs in well defined samples of dogs with varying risk for diabetes or obesity. Caco-2/TC7 cells were shown to express SGLT1 *in vitro*. The 2kbp fragment of canine *SLC5A1* 5' flanking region from -1974 to +25 relative to the transcription start site was cloned from canine genomic DNA, ligated into PGL3 basic plasmids bearing firefly luciferase as a reporter gene, used for transient transfection of Caco-2/TC7 cells, and shown to drive luciferase production significantly above control ($P < 0.001$). To determine the effect of the three known SNPs in this region on promoter function, new promoter/reporter constructs (all possible permutations of these three SNPs) were created using site-directed mutagenesis. These constructs were used for transient transfection of Caco-2/TC7 cells using *Renilla* luciferase as an internal control. No significant differences in promoter function were seen, suggesting that these three SNPs do not have a significant effect on the constitutive transcription of SGLT1 mRNA in dogs. A search for novel SNPs in this region in dogs was made in two breeds predisposed to diabetes mellitus (Samoyed, Cairn Terrier), two breeds that rarely develop diabetes (Boxer, German Shepherd Dog), and two breeds predisposed to obesity (Labrador Retriever, Cocker Spaniel). Genomic DNA from 10 healthy individuals of each of these breeds was obtained from the UK Companion Animals DNA Archive, with kind permission. The *SLC5A1* 5' flanking region was amplified from each individual by high-fidelity PCR using breed-labelled primers, gel purified, mixed in equimolar amounts and sequenced by pyrosequencing (454 sequencing, GS FLX, Roche). The sequence of the *SLC5A1* 5' flanking region in all individuals of all breeds tested was identical. On this evidence, variations in *SLC5A1* promoter sequence between dogs do not influence the pathogenesis of diabetes or obesity in these breeds.

EN-O-5

COMPARISON OF THE GLP-1 ANALOGUES EXENATIDE (SHORT-ACTING), EXENATIDE (LONG-ACTING) AND THE DPP-4 INHIBITOR SITAGLIPTIN TO INCREASE INSULIN SECRETION IN HEALTHY CATS. I. Padrucci¹, E. Zini¹, K. Kaufmann¹, J. Menard², T.A. Lutz³, C.E. Reusch¹. ¹Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zürich, ZÜRICH, Switzerland, ²Department of Small Animals, Vetsuisse Faculty, University of Zürich, ZÜRICH, Switzerland, ³Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zürich, ZÜRICH, Switzerland

Remission of diabetes mellitus may be achieved in up to 50% of cats. For remission to occur, recovery of β -cell function and possi-

bly of β -cell mass is required. A novel class of antidiabetic drugs that act via the incretin system increase β -cell proliferation and glucose-stimulated insulin secretion in rodents. Two strategies of incretin-based therapies, GLP-1 analogues (e.g. exenatide short-acting (ex-SA), exenatide long-acting (ex-LA)), and DPP-4 inhibitors (e.g. sitagliptin), are successfully used in human diabetics. Knowledge about the use of incretins in cats is scarce. It was demonstrated that ex-SA and a DPP-4 inhibitor (NVP-DPP728) increase insulin secretion after intravenous glucose stimulation in healthy cats. The effects of these drugs after meal stimulation and the use of ex-LA have not been explored in cats so far. The aims of the study were to test whether ex-SA (Byetta[®], q12h, SC), ex-LA (Bydureon[®], q5d, SC) and sitagliptin (Januvia[®], q24h, PO) can be safely used in cats, and to identify the most effective drug and dose in a dose-escalation study. Nine healthy cats were used. Ex-SA was given to 3 cats at 0.2, 0.5, 1 and 2 $\mu\text{g}/\text{kg}$ for 5 consecutive days each. Ex-LA was given to 3 other cats at 40, 100, 200 and 400 $\mu\text{g}/\text{kg}$ with single injections each. Sitagliptin was given to 3 cats at 1, 3, 5 and 10 mg/kg for 5 consecutive days each. A washout period of 2 weeks was allowed between doses. On day 5 of each treatment block, a meal response test (MRT) was performed in all cats after a 16 h fast by feeding 50% of daily energy intake with subsequent blood sampling at timepoints 0, 15, 30, 60, 120 and 300 minutes. Insulin and glucose area under the curves (AUC) were calculated for each drug dose. Gastrointestinal side effects of 1 to 3 days duration were observed in 2 cats of each group, irrespective of the dose. Well-being and appetite were otherwise conserved. Ex-SA increased insulin AUC by 320%, 364%, 547% and 198%, respectively, compared to insulin AUC during MRT without drug administration. Ex-LA and sitagliptin increased insulin AUC by 127%, 169%, 178%, 95% and 43%, 101%, 70%, 56%, respectively. AUC for glucose was similar in all cats, irrespective of the drug and dose. We conclude that ex-SA, ex-LA and sitagliptin can be safely used in healthy cats and that ex-SA increases insulin secretion more effectively than ex-LA and sitagliptin.

EN-O-6

USE OF INSULIN DETEMIR IN DOGS WITH DIABETES MELLITUS. F. Fracassi¹, M. Hafner², S. Corradini¹, F. Boretto², N. Sieber-Rückstuhl², C. Reusch². ¹University of Bologna, OZZANO DELL'EMILIA, Italy, ²Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, Zurich University, ZURICH, Switzerland

Insulin detemir is a synthetic long acting insulin analogue designed to maintain basal levels of insulin in humans with diabetes mellitus (DM). Pharmacokinetic studies in dogs indicate that insulin detemir has a greater effect than other types of insulin, requiring a lower dose. The objective of our study was to evaluate its efficacy and the frequency of hypoglycemia in dogs with DM treated with insulin detemir. Eight dogs were included into the study. Median (range) age was 9 years (7-12), 7 were female (2 intact, 5 spayed), and 1 was intact male; median (range) body weight was 8.5kg (3.7-42.0). Dogs with relevant concurrent diseases (e.g. hypothyroidism, hypercortisolism, neoplasia, renal insufficiency) and dogs with prior administration of diabetogenic drugs were excluded. All dogs received insulin detemir BID for at least 6 months, re-evaluations were performed after 1, 2, 4, 12 and 24 weeks and included clinical signs, blood glucose curves (BGC) and fructosamine concentrations. Median (range) insulin dose was 0.12 U/kg (0.07-0.13) BID at admission which was not significantly different after 24 weeks of therapy (0.12 U/kg, range 0.05-0.34). Initially, all dogs had markedly elevated blood glucose (21.9 mmol/l, 20.5-29.6 mmol/l), and elevated fructosamine concentrations (547 $\mu\text{mol}/\text{l}$, 430-702 $\mu\text{mol}/\text{l}$). Mean (\pm SD) glucose concentrations (mmol/l) of the BGC at each re-evaluation were 12.2 \pm 5.1, 15.1 \pm 5.3, 14.0 \pm 6.9, 17.9 \pm 8.3, 14.0 \pm 3.7; median (range) of the glucose nadir values (mmol/l) were 9.4 (2.3-11.9), 10.9 (3.6-18.1), 6.6 (2.7-8.0), 10.3 (3.9-24.8), 6.2 (3.4-12.1) and fructosamine concentrations ($\mu\text{mol}/\text{l}$) were 509 (274-683), 470 (314-749), 445 (379-460), 501 (417-653), 480 (382-571), respectively. Glucose concentrations (mean) were significantly ($p < 0.001$) lower after 24 weeks therapy than before treatment. Hypoglycemia (glucose nadir < 5 mmol/l) was a consistent problem, identified in 5 dogs (23% of the BGC of the 8 dogs). There were 6 episodes (in 4 dogs) of owners reporting

clinical signs (lethargy, weakness, unsteady gait) that could have been caused by hypoglycemia. Based on owner opinion, clinical assessment of the veterinarian and BGC after 6 months of therapy, good control of the disease was obtained in 5 (62%) and moderate control in 3 dogs (38%). According to our preliminary results insulin detemir is effective in controlling hyperglycemia in dogs with DM. It is more potent than other types of insulin which are also used BID and therefore lower doses were used. Nevertheless hypoglycemia was a common finding especially in small dogs. Therefore insulin detemir should be used with great caution and dilution could be considered.

EN-O-7

THE ROLE OF THE CANONICAL WNT-PATHWAY IN THE PATHOGENESIS OF CANINE CORTISOL-SECRETING ADRENOCORTICAL TUMORS. M.J. Ravelek, M.M.J. Kool, J.A. Mol, H.S. Kooistra, S. Galac. Universiteit Utrecht, UTECHT, The Netherlands

Spontaneous hypercortisolism is due to ACTH-independent hypersecretion of cortisol by an adrenocortical tumor (AT) in about 15% of the cases. Although the understanding of growth and hormonal activity of ATs has expanded in recent years, the pivotal factors/acts in the pathogenesis of the AT remain undisclosed. The canonical Wnt-pathway plays a role in cell survival and cell cycle progression and has been shown to be involved in many different tumor types, including human and mouse ATs. Central in this pathway is β -catenin. Cytoplasmic and/or nuclear accumulation of β -catenin has been demonstrated in human cortisol-secreting ATs. This has been partly explained by mutations in exon 3 of β -catenin. In our study, the activation of the canonical Wnt-pathway was investigated in 11 adrenal adenomas and 25 carcinomas of dogs with ACTH-independent hypercortisolism. Fifteen normal canine adrenals served as control tissue. The mRNA expression was measured for Wnt-ligands (Wnt 2, Wnt 3, Wnt 4, Wnt 5a, Wnt 5b variants 1 and 2, Wnt 6, Wnt 7a, Wnt 10b), Wnt-ligand inhibitors (DKK 3, WIF 1, sFRP 1) and for Wnt target genes (cMyc, Axin2 and CyclinD1). In addition, the coding region of the mRNA of β -catenin was sequenced and the localization of β -catenin was evaluated by immunohistochemistry (IHC). The results of expression analysis of Wnt-ligands and Wnt-ligand inhibitors demonstrated a significant downregulation of Wnt 4 and Wnt 5b variants 1 and 2. Wnt target gene cyclin D1 was significantly downregulated in adenomas, while cMyc and Axin 2 mRNA expression did not differ between ATs and normal adrenals. Sequence analysis of β -catenin revealed a mutation in 12/36 of the ATs: 9 silent mutations, most probably single nucleotide polymorphisms (SNPs), 1 neutral mutation (Arginine to Histidine), 1 nonsense mutation resulting in a premature stop codon and 1 deletion of 26 basepairs combined with a neutral mutation. The amino acid change appeared not to be tumor-associated whereas the stop codon was. There were no activating β -catenin mutations. The IHC demonstrated accumulation of β -catenin in the cytoplasm of part of the ATs, while nuclear staining for β -catenin was rarely present. We conclude that the canonical Wnt-pathway is most likely not involved in the pathogenesis of canine cortisol-secreting ATs.

EN-O-8

ONCE VS TWICE DAILY TRILOSTANE TREATMENT FOR CANINE PITUITARY-DEPENDENT HYPERADRENOCORTICISM. C. Arenas¹, C. Melian², M.D. Pérez Alenza¹. ¹Veterinary Teaching Hospital, University Complutense, MADRID, Spain, ²Clínica Veterinaria Atlántico, LAS PALMAS DE GRAN CANARIA, Spain

Trilostane is the treatment of choice for canine pituitary-dependent hyperadrenocorticism (PDH) however there is controversy about the ideal treatment regime. The objective of this study was to evaluate efficacy and safety of SID vs BID trilostane treatment for canine PDH. This prospective randomised study included 32

dogs with PDH, 16 dogs treated with trilostane SID (initial dose 1-6 mg/kg/24 hrs) and 16 with trilostane BID (0.5-3 mg/kg/12 hrs). A history, physical exam, haemogram, biochemical profile, ACTH stimulation test and urinary cortisol to creatinine ratios (UCCR) were performed before treatment, and at one week (SID 8-12 hrs post trilostane; BID 4-6 hrs) and 1, 3, 6 and 12 months after treatment (8-12 hrs post medication). The median (\pm SD) daily dose throughout the study was similar in dogs receiving SID (3.7 ± 2.1 mg/kg/day) or BID (3.8 ± 0.8 mg/kg/day) trilostane. Baseline cortisol concentration (mean \pm SD) before trilostane and at the five re-evaluations in the SID group were 6.9 ± 2.4 , 3.9 ± 2.5 , 4.3 ± 1.9 , 4.4 ± 1.5 , 5.0 ± 2.0 and 2.2 ± 0.7 and in the BID group were 6.4 ± 3.9 μ g/dl, 3.1 ± 1.4 , 3.7 ± 2.1 , 3.6 ± 1.7 , 3.3 ± 1.6 and 2.5 ± 1.5 . Baseline cortisol was significantly higher ($p=0.023$) in the SID group only at six-month evaluation. Post ACTH cortisol concentrations in the SID group were 29.8 ± 13.2 , 10.3 ± 5.6 , 12.1 ± 5.8 , 10.3 ± 2.2 , 8.8 ± 4.9 and 4.2 ± 2.2 and in the BID group were 32.7 ± 12.4 , 8.6 ± 6.8 , 8.6 ± 4.8 , 8.3 ± 4.4 , 8.9 ± 4.9 and 7.6 ± 7.2 . No statistically significant differences were found at any evaluation. UCCR in dogs in the SID group were 480 ± 509 , 241 ± 163 , 306 ± 201 , 224 ± 104 , 186 ± 119 and 107 ± 66.8 and in the BID group 270 ± 278 , 225 ± 172 , 222 ± 178 , 237 ± 108 , 157 ± 62 and 102 ± 11 . Similarly no statistically significant differences were found throughout the study. In each of the five re-evaluation times, clinical signs (polyuria, polydipsia and/or polyphagia) persisted in 73% (11/15), 62% (8/13), 57% (8/14), 58% (7/12) and in 63% (5/8) of dogs in the SID group. Persistence of clinical signs occurred in 46% (6/13), 27% (3/11), 41% (6/15), 25% (4/16) and 0% (0/12) of dogs in the BID group. Mild adverse effects occurred in 10/16 and in 9/16 of the dogs treated with SID and BID trilostane, respectively. Based on this study, we conclude that the results of ACTH stimulation test and UCCR in dogs with PDH treated with both protocols are similar at most re-evaluation times. However, clinical signs resolved in a greater proportion of dogs receiving trilostane BID. Using trilostane twice daily will help to reduce the number of dogs that do not have a good clinical response.

EN-O-9

EVALUATION OF BASELINE CORTISOL, ENDOGENOUS ACTH AND CORTISOL TO ACTH RATIO TO MONITOR TRILOSTANE THERAPY IN DOGS WITH PITUITARY-DEPENDENT HYPERADRENOCORTICISM. W.A. Burkhardt, F. S. Boretta, C. E. Reusch, N. S. Sieber-Ruckstuhl. Clinic for Small Animal Internal Medicine, Vetsuisse Faculty University of Zurich, ZURICH, Switzerland

The effectiveness of trilostane therapy is monitored by regular ACTH stimulation, which is time-consuming and expensive. Therefore, a monitoring system without a stimulation protocol and with less client expense would be preferable. The aim of our study was twofold: firstly, to evaluate, if baseline cortisol, endogenous ACTH (cACTH) or the baseline cortisol to ACTH ratio (cortisol/ACTH ratio) could replace the ACTH stimulation test; secondly, to evaluate, if baseline cortisol provides additional information than post-ACTH cortisol alone or if its measurement could be abandoned. Forty-one trilostane-treated dogs with PDH diagnosed between April 2006 and December 2011 were included in the study. A total of 148 ACTH stimulation tests with baseline, post-ACTH and delta cortisol (post-ACTH cortisol minus baseline cortisol) and 75 cACTH results and cortisol/ACTH ratios were analyzed. Control of adrenal gland function was classified according to the target range of post-ACTH cortisol concentration as: excessive (< 41 nmol/L; group 1), optimal (41-149 nmol/L; group 2), or inadequate (> 149 nmol/L; group 3). In a second step, control of adrenal gland function was reclassified according to baseline cortisol values only and the new classification was compared with the original one. There was a significant correlation between baseline cortisol and post-ACTH cortisol and a significant difference of baseline cortisol between the groups, however, with a large overlap. Reclassification of the adrenal gland function on the basis of baseline cortisol revealed a misclassification in 53/148 (36%) tests. Endogenous ACTH did not correlate with baseline or post-ACTH cortisol and did not differ between the groups. The baseline cortisol:ACTH ratio differed significantly between group 1 and 3 and between group 2 and 3, but again with a large overlap. To determine if measurement of baseline cortisol gives additional information than post-ACTH cortisol alone, the delta

cortisol values were analysed. Delta cortisol correlated significantly with post-ACTH cortisol but not with baseline cortisol and differed significantly between the groups, the overlap however was large. The large overlap using only single values without taking post-ACTH cortisol into consideration leads to an unacceptably low correct differentiation of control of adrenal gland function. Therefore, the ACTH stimulation test and determination of post-ACTH cortisol cannot be replaced by baseline cortisol, endogenous ACTH or the cortisol/ACTH ratio. However, as baseline cortisol concentration does not give additional information than post-ACTH cortisol alone, its determination can be abandoned.

EN-O-10

EFFECT OF RECOMBINANT HUMAN THYROTROPIN ON THE UPTAKE OF RADIOACTIVE IODINE (123I) IN DOGS WITH THYROID TUMORS. M. Campos, K. Peremans, E. Vandermeulen, L. Duchateau, T. Bosmans, I. Polis, S. Daminet. Ghent University, MERELBEKE, Belgium

In humans, recombinant human thyrotropin (rhTSH) enhances radioactive iodine uptake (RAIU) in patients with differentiated thyroid cancer. This property is particularly interesting in dogs because high doses of radioiodine-131 (^{131}I) are used for the treatment of this disease. No studies have been performed in veterinary medicine to optimize ^{131}I treatment of thyroid cancer. The aim of this study was to evaluate the effect of rhTSH on the uptake of ^{123}I in dogs with thyroid tumors. Nine dogs with thyroid neoplasia were included in this prospective cross-over study. Six dogs had unilateral tumors, 1 dog had bilateral tumors and 2 dogs had ectopic tumors. Diagnosis was based on physical examination, cytology, cervical scintigraphy and, when available, histopathology. In 6 dogs ^{123}I was administered for a baseline RAIU determination in week 1. In week 2 (after a wash out period of 2 weeks), these dogs received rhTSH (100 μ g IV) 24h before ^{123}I injection. In 3 patients the order of the protocol was reversed. For each scan, the dogs received 37 MBq (1mCi) of ^{123}I IV and planar scintigraphy was performed 8h and 24h thereafter for tumor RAIU calculation. Blood samples were taken at baseline and at 6, 12, 24 and 48h after rhTSH administration for measurement of serum total thyroxine (TT4) and serum thyrotropin (TSH) concentrations. rhTSH caused no statistical significant change on thyroid tumor RAIU at 8h ($p=0.89$) or at 24h ($p=0.98$). Despite the lack of overall statistical significance, after rhTSH administration the 8h RAIU increased in 5 tumors and the 24h RAIU increased in 4 tumors. When an increased RAIU was observed, ^{123}I uptake with rhTSH ranged 1.2 to 3.8 times baseline uptake. In 3 patients, the post-rhTSH RAIU more than doubled compared to baseline RAIU. The RAIU of 2 thoracic metastases from 2 patients could be calculated. In 1 thoracic metastasis the RAIU doubled after rhTSH; in the other the RAIU decreased after rhTSH. In euthyroid patients, rhTSH induced a significant increase in TT4 concentrations ($p=0.01$), confirming the biological activity of rhTSH. This study suggests that IV administration of 100 μ g rhTSH 24h before ^{123}I has an inconsistent effect on thyroid tumor RAIU, with a marked increase in uptake in some tumors and a decrease in others. Further studies are necessary to determine the best dosage, route and timing of rhTSH to optimize thyroid tumor RAIU. This study was partly funded by the Dutch Animal Cancer Foundation

EN-O-11

ONCE DAILY TRANSDERMAL METHIMAZOLE APPLICATION IS AN EFFECTIVE TREATMENT OPTION FOR LONG-TERM MANAGEMENT OF FELINE HYPERTHYROIDISM. F.S. Boretta¹, N.A. Sieber-Ruckstuhl¹, B.A. Riond², R.E. Hofmann-Lehmann³, C.E. Reusch¹. ¹Clinic for Small Animal Internal Medicine, ZURICH, Switzerland, ²Clinical Laboratory, Vetsuisse Faculty, University of Zurich, ZURICH, Switzerland

Transdermal methimazole has been suggested as an alternative treatment option of hyperthyroid cats. In a previous study

we could show a good clinical effectiveness of a pleuronic lecithin organogel (PLO-) based product on a twice-daily basis. A reduced dose frequency is known to improve owner compliance, however no study has yet evaluated long-term treatment responses after once daily administration. Objectives of the present study were to assess whether once daily administration of transdermal methimazole in its original formulation of (PLO) was an effective alternative to the twice-daily treatment during a follow-up period of up to 18 months and to evaluate T4 courses during a 10-hour period after methimazole application in selected cats. Twenty client-owned cats with newly diagnosed hyperthyroidism and with available follow-up information were included in the study. Methimazole was formulated in PLO-based vehicle and was applied to the pinna of the inner ear at a starting dose of 5mg/cat q 24 hours. Cats were rechecked 1-2 weeks, 3-4 weeks, 1-2 months, 2-3 months, 3-6 months, 6-12 and 12-18 months after starting therapy. Additionally, in 10 cats T4 concentrations were measured every 2 hours after gel application over a 10 hour period 1 week after starting therapy. After 1-2 weeks, clinical improvement was observed in all animals. A change of treatment to oral medication due to erythema of the internal pinna of the ears was necessary in one cat, while none of the other animals showed any side effects during the follow-up period. Significant decreases in T4 concentrations were determined at all rechecks compared to pre-treatment concentrations. Methimazole dosage was increased in 5, decreased in 11 and remained unchanged in 4 cats. Two cats with a decrease in the dose later had to be re-increased, while one cat was changed to q12 hours. There was no significant change in T4 during the 10-hour period and fluctuations corresponded to variations of precision in series. These results are in accordance with those of our previous study using the twice-daily regimen. We could show that once daily administration of transdermal methimazole in its original formulation of PLO is an effective treatment option for long-term management of feline hyperthyroidism. Further, timing of blood sampling after gel application is not important when assessing response to treatment.

EN-O-12

HYPERTHYROIDCATS ON LONG-TERM MEDICAL TREATMENT SHOW A PROGRESSIVE INCREASE IN THE PREVALENCE OF LARGE THYROID TUMORS, INTRA-THORACIC THYROID MASSES, AND SUSPECTED THYROID CARCINOMA. M.E. Peterson¹, M.R. Broome². ¹Animal Endocrine Clinic, NEW YORK, NY, United States of America. ²Advanced Veterinary Medical Imaging, TUSTIN, CA, United States of America

Thyroid scintigraphy provides valuable information regarding both thyroid anatomy and physiology and plays an integral role in the diagnosis, staging, and management of feline thyroid disease. In this study, we performed thyroid imaging on 1,572 consecutive hyperthyroid cats that were referred for radioiodine therapy between January 2009 and December 2011. Scintigraphy was performed as part of our staging protocol in which thyroid volume is estimated for ¹³¹I dose estimation (Vet Radiol Ultrasound 1996;27:141). In each cat, the location of each area of increased radionuclide uptake (IRU) was also recorded (cervical, thoracic inlet, chest). Finally, each scan was evaluated for features suggesting malignancy (multiple, extensive areas of IRU, heterogeneous pattern of IRU with irregular, spiculated margins, extension of tumor through thoracic inlet into the thorax, and metastasis to regional lymph nodes or lung). Of the 1,572 cats, most had been recently diagnosed. In 228 cats, however, the interval between diagnosis and ¹³¹I treatment ranged from >1 to 6.1 years; almost all of these cats had received long-term antithyroid drug treatment. The 1,572 cats were divided into 5 groups based on interval from diagnosis to ¹³¹I treatment: Group 1 (0-1 year), 1,344 cats; Group 2 (>1-2 years), 114 cats; Group 3 (>2-3 years), 62 cats; Group 4 (>3-4 years), 29 cats; and Group 5 (>4-6.1 years), 23 cats.

When the estimated thyroid volumes in the 5 groups of cats were compared, a progressive, significant ($P < 0.001$) increase in median tumor volume occurred: 2.1 cm³ (Group 1); 4.1 cm³ (Group 2); 5.7 cm³ (Group 3); 6.1 cm³ (Group 4); and 7.7 cm³ (Group 5). The prevalence of cats with areas of IRU within the thoracic cavity also increased progressively: 5.1% (Group 1); 7.9% (Group 2); 14.5% (Group 3); 17.2% (Group 4); and 26.1% (Group 5). Finally, the prevalence of suspected thyroid carcinoma (25 of the 1,572 cats) also increased progressively: 0.7% (Group 1); 3.5% (Group 2); 6.5% (Group 3); 10.4% (Group 4); and 21.7% (Group 5). In contrast, no increase in prevalence of ectopic thyroid tissue was found: 2.9% (Group 1); 2.8% (Group 2); 3.2% (Group 3); 6.9% (Group 4); and 4.3% (Group 5). In conclusion, our results indicate that hyperfunctional thyroid tissue continues to grow and enlarge over time. Thyroid carcinoma is extremely rare in cats with recently diagnosed hyperthyroidism, but the prevalence increases dramatically over time, suggesting that transformation from benign disease is common in cats controlled medically.

EN-O-13

PLASMA RENIN ACTIVITY FOR MONITORING MINERALOCORTICOID SUBSTITUTION IN DOGS WITH PRIMARY HYPOADRENOCORTICISM. M.E. Baumstark¹, M.W. Baumstark², N.S. Sieber-Ruckstuhl¹, F.S. Boretz¹, J. Nussberger⁴, C.E. Reusch³. ¹Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, ZURICH, Switzerland, ²University Medical Center, FREIBURG, Germany, ³Vetsuisse Faculty, University of Zurich, ZURICH, Switzerland, ⁴Service d'Angiologie, CHUV-NES, LAUSANNE, Switzerland

Measurement of plasma renin activity (PRA) is considered the gold standard for monitoring mineralocorticoid substitution in humans with primary hypoadrenocorticism (PH). It is the most sensitive parameter to reflect insufficient as well as inappropriate high replacement. In dogs with PH mineralocorticoid substitution is currently monitored mainly by serum potassium and sodium concentrations. The role of PRA for monitoring mineralocorticoid replacement has not been investigated. The aims of the study were to measure and compare PRA in dogs with newly diagnosed PH and dogs with diseases mimicking PH, and to evaluate PRA in dogs with PH treated with different mineralocorticoid substitution regimens. The following groups of dogs were included in the study: 5 dogs with newly diagnosed PH (group 1), 10 dogs that were already treated for PH (group 2), and 10 dogs with diseases mimicking PH (group 3). In group 1 PRA was measured before treatment and 1-3 weeks, 4-6 weeks, and 7-10 weeks after start of therapy. In group 2 PRA was measured at least twice every 1 to 6 months. In group 3 PRA was measured once at initial presentation. Three dogs of group 1 and 7 dogs of group 2 were treated with fludrocortisone (Florinef[®], Bristol-Myers Squibb). Two dogs of group 1 and 3 dogs of group 2 were treated with DOCP (Percorten[®]-V, Novartis). PRA was measured with an enzymatic assay via trapping of angiotensin I in the Service d'Angiologie, CHUV-NES, Lausanne. Results were analysed by means of non-parametric methods ($p < 0.05$). PRA before treatment was significantly higher in group 1 (1.6-36.0 ng/l/h, median 22.5) than in group 3 (0.5-2.8 ng/l/h, median 1.0). Average PRA during therapy ranged from 0.47 to 29 ng/ml/h (median 8). PRA did not decrease significantly in dogs treated with fludrocortisone. PRA of dogs treated with DOCP (0.11-10.61 ng/ml/h, median 5) was significantly lower compared to dogs treated with fludrocortisone (0.47-38.3 ng/ml/h, median 16.5). All dogs treated with DOCP had normal serum sodium and potassium at all re-checks, whereas dogs treated with fludrocortisone had mild to severe electrolyte abnormalities at several occasions. There was a weak correlation between PRA and serum potassium. Measurement of PRA is a promising tool for monitoring mineralocorticoid substitution in dogs with PH. According to our preliminary results DOCP is superior to fludrocortisone for mineralocorticoid replacement.

EN-O-14

PATTERNS OF THYROID HORMONES AND THYROID STIMULATING HORMONE (TSH) IN DOGS RECEIVING PHENOBARBITAL TREATMENT. M. Rick¹, K. Refsal¹, M. Piechotta². ¹Diagnostic Center for Population and Animal Health, LANSING, United States of America, ²University of Veterinary Medicine Hannover, Clinic for Cattle, Endocrinology Lab, HANNOVER, Germany

Phenobarbital is widely used to control epilepsy in dogs. Use of phenobarbital induces hepatic enzyme activity, and may decrease serum total and free thyroxine (tT4 and fT4), with the exact mechanisms and prevalence of this phenomenon being unknown. The aim of the present retrospective study therefore was to investigate how many dogs treated with phenobarbital show a decrease in thyroid hormones and to give insight into potential mechanisms. For this, tT4, fT4, and TSH were measured in 746 canine serum samples submitted for assessment of therapeutic concentrations of phenobarbital. In a smaller subset of dogs, albumin, total protein, and transthyretin (TTR) were also measured at the Diagnostic Center for Population and Animal Health, Michigan, USA. According to thyroid results, dogs were classified as 'non thyroidal illness' (NTI) (tT4 < 11 nmol/L, fT4 ≥ 6 pmol/L, TSH ≤ 0.48 ng/mL); 'equivocal' (E) (tT4 < 11 nmol/L, fT4 < 6 pmol/L, TSH ≤ 0.48 ng/mL); 'hypothyroid' (HT) (pattern of low tT4 and fT4, TSH > 0.48 ng/mL); and 'normal' (N) (tT4 ≥ 11 nmol/L; fT4 ≥ 6 pmol/L and TSH ≤ 0.48 ng/mL). Forty-five dogs were classified as NTI (6.0%), 52 dogs were classified as E (7.0%), 38 were classified as HT (4.7%), and 552 as N (74%); 52 dogs did not fit in any defined category. There was no statistically significant difference in mean phenobarbital concentrations between NTI, E, HT, and N (94.2 ± 35.1, 100.6 ± 43.9, 86.8 ± 29.4, and 84.3 ± 31.9 µmol/L, respectively). Twenty dogs of each group were analyzed for albumin and total protein and compared to healthy dogs that were not receiving phenobarbital. No statistically significant difference was noticed (p>0.05). The attempt to measure TTR concentrations via commercially available ELISA (TSZ ELISA, Framingham, MA, USA) gave us inconsistency performance. In conclusion, 6% of dogs on phenobarbital treatment were classified as NTI. If group E would be included, this value could be as high as 13%. Neither phenobarbital, nor total protein or albumin concentrations had predictive value for thyroid hormone concentrations. This study was able to define the prevalence of the phenomenon that some dogs on phenobarbital therapy have low thyroid hormone concentrations, but did not give insight into the pathogenesis. Ideally, demonstration of hypothyroidism in dogs receiving phenobarbital should include assays of thyroid hormones and TSH.

EN-O-15

URINARY AND PLASMA CATECHOLAMINE AND METANEPHRINE IN DOGS WITH PHEOCHROMOCYTOMA, HYPERADRENOCORTICISM AND IN HEALTHY DOGS. E. Salesov¹, F. Boretti¹, N. Sieber-Ruckstuhl¹, L. Galeandro¹, C. Reusch¹, M. Hersberger². ¹Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zürich, ZÜRICH, Switzerland, ²Institute of Clinical Chemistry, University Hospital of Zürich, University of Zürich, ZÜRICH, Switzerland

Pheochromocytoma (PHEO) is a rare malignant catecholamine-secreting tumor of the adrenal medulla. Catecholamines and metanephrines in plasma and in 24-h urine are approved biomarkers for the detection of the disease in humans, however, the question which of the tests is best is controversial. We previously demonstrated that measurement of urinary catecholamine and metanephrine to creatinine ratios is helpful for the diagnosis of PHEO in dogs and that urinary normetanephrine to creatinine ratio may be the best test to discriminate between PHEO and hypercortisolism (HC). Knowledge on plasma catecholamines and metanephrines in dogs is scarce and no comparison between urinary and plasma parameters has been performed. The objective of the study was to measure urinary and plasma catecholamines and metanephrines in dogs with PHEO, HC and in healthy dogs and to determine the test with the least overlap between the groups. Six dogs with PHEO, 9 dogs with HC (6 with ATH, 3 with PDH) and 10 healthy dogs were included. Urine samples were collected into HCL containing tubes to ensure a pH < 2, blood samples were collected on ice, centrifuged at 4°C and

immediately snap frozen in liquid nitrogen. All samples were stored at -80°C. Urinary epinephrine (U-Epi), norepinephrine (U-Norepi), metanephrine (U-Meta) and normetanephrine (U-Normeta), and plasma epinephrine (P-Epi), norepinephrine (P-Norepi), free and total metanephrine (PF-Meta and PT-Meta) and free and total normetanephrine (PF-Normeta and PT-Meta) were analysed by HPLC. Urinary catecholamines and metanephrines were expressed as ratios to urine creatinine concentrations. Data were analysed by non-parametric tests (P<0,05). Similar to our previous findings U-Epi, U-Norepi, U-Meta and U-Normeta were significantly higher in dogs with PHEO and U-Norepi and U-Normeta were significantly higher in dogs with HC compared to healthy dogs. Comparison between dogs with HC and dogs with PHEO revealed significantly higher U-Meta and U-Normeta in the latter group. U-Normeta was the only parameter with no overlap. In dogs with PHEO P-Norepi, PF-Meta, PT-Meta, PF-Normeta, PT-Normeta were significantly higher and in dogs with HC P-Norepi, PF-Normeta and PT-Normeta were significantly higher than in healthy dogs. Comparison between dogs with HC and dogs with PHEO showed significant higher PF-Meta, PT-Meta, PF-Normeta, PT-Normeta in the PHEO group. Overlap was present with all 4 parameters, but was least with PF-Normeta and PT-Normeta. According to our preliminary results U-Normeta, PF-Normeta and PT-Normeta are valuable parameters for the diagnosis of PHEO, so far U-Normeta has performed better than the plasma parameters.

FE-O-1

URINARY VASCULAR ENDOTHELIAL GROWTH FACTOR AS A PROGNOSTIC MARKER IN FELINE CHRONIC KIDNEY DISEASE. S. Chakrabarti, H.M. Syme, J. Elliott. Royal Veterinary College, LONDON, United Kingdom

Chronic kidney disease (CKD) is common in geriatric cats and hypoxia might contribute to CKD progression. Vascular endothelial growth factor (VEGF) is a marker of hypoxia. The aim of this study was to evaluate urinary VEGF as a prognostic marker in cats with CKD compared with the established progression factors, proteinuria and hyperphosphataemia. Cats were recruited through geriatric clinics held at two first opinion London practices between 1999 and 2010. Diagnosis of CKD was based on concurrent findings of plasma creatinine >2mg/dl and USG <1.035, with persistence of azotaemia for at least 2 weeks. VEGF was measured in urine samples taken from cats at diagnosis of CKD and indexed to creatinine giving VEGF: creatinine ratios (UVC). Survival was compared among low (<0.3µg/g), medium (0.3-0.6µg/g) and high (>0.6µg/g) categories of UVC using the log-rank test. Multivariable binary logistic regression was used to assess whether UVC was associated with an increase in plasma creatinine concentration of at least 25% within 1 year of diagnosis. Cats which did not demonstrate progression but were followed for <1 year were excluded from the study. Cases which developed hyperthyroidism, received ACE inhibitors, had gross haematuria, urinary tract infections, nephrotic syndrome or evidence of bladder neoplasia were also excluded. Survival data are presented as median [95% confidence interval] and other descriptive data are presented as median (25th, 75th percentile). Significance was set at p<0.05. Cats with low UVC (n=49) had survival of 840 [574, 1106] days, while those with medium (n=30) and high UVC (n=10) had survival of 863 [385, 1341] days and 260 [0, 554] days respectively. There was no difference in survival time between cats with low and medium values of UVC (p=0.414), but cats with both low (p<0.001) and medium (p=0.002) UVC had significantly longer survival than cats with high UVC. Plasma creatinine concentration increased by 52(33, 109)% in cats which progressed (n=40) and 6(0, 14)% in cats with stable renal function in the year following diagnosis (n=39). UVC was also associated with progression of azotaemia (p=0.008) independently of UPC and plasma phosphate concentration. The progressive group had UVC of 0.36(0.26, 0.54) µg/g, while the stable group had UVC of 0.26(0.20, 0.38) µg/g. If high UVC indicates renal hypoxia, the results of this study support the hypothesis that hypoxia is associated with progression in cats with CKD. However, further studies evaluating renal hypoxia directly would be required to verify this.

FE-O-2

FELINE 'TRIADITIS': A PROSPECTIVE STUDY OF 47 CASES. F. Fragkou¹, K.K. Adamama-Moraitou¹, T. Poutahidis¹, N. Prassinou¹, P.G. Xenoulis², J.M. Steiner², T. Rallis¹. ¹Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, Greece, THESSALONIKI, Greece, ²Gastrointestinal Laboratory, Texas A&M University, College Station, USA, TEXAS, United States of America

The term 'triaditis' is used to describe concurrent inflammation of the liver, pancreas, and small intestine, although occasionally only two of these organs may participate. The aim of this study was to investigate the frequency of coexistence of different combinations of cholangitis, pancreatitis and/or inflammatory bowel disease in cats, and describe the clinical, clinicopathological, and histopathological findings. Initially 67 cats were included in the study. Thirty-nine cats had a suspicion of 'triaditis' based on clinical signs (depression, anorexia or polyphagia, vomiting, diarrhea, and/or weight loss), while 28 cats clinically healthy, were considered as controls. Each cat on presentation underwent CBC, biochemistry profile, serum total T4, Spec fPL[®] and fTLI blood examinations. Cats diagnosed with intestinal parasitism, infectious disease, neoplasia, and/or hyperthyroidism were excluded from the study. Biopsies from the liver, pancreas and small intestine (duodenum, jejunum, and ileum) were collected from each sick cat during laparotomy as part of the diagnostic investigation. Biopsies from healthy cats were collected during laparotomy for ovariohysterectomy. All owners had signed a consent form and the study protocol was approved by the University's and State's Ethics Committee. Of the 39 sick cats with a suspicion of triaditis, 12 were excluded because of neoplasia or other conditions. Of the 28 clinically healthy cats, 20 had histopathological evidence of inflammation in their liver, pancreas, and/or intestine and were eventually grouped together with the sick cats. Collectively, histopathological evaluation of the biopsies revealed 47 cats (27 with clinical signs and 20 without) with inflammatory lesions in at least one organ. Of those 47 cats, 40 (85.1%) had histopathological evidence of IBD, 30 (63.8%) of cholangitis, and 12 (25.5%) of pancreatitis. Thirteen cats (27.6%) had only IBD, 8 (61.5%) of which were symptomatic. Six (12.7%) cats had only cholangitis, 2 (33.3%) of which were symptomatic. One (2.1%) had only pancreatitis and was symptomatic. Sixteen cats (34%) had concurrent IBD and cholangitis, 6 (37.5%) of which were symptomatic; 3 (6.4%) had IBD in combination with pancreatitis, 2 (66.7%) of which were symptomatic, while 8 (17%) had IBD, cholangitis and pancreatitis and were all symptomatic. Common biochemical findings were increased activities of ALT (11/47), ALP (11/47), and increased total bilirubin (14/47), fTLI (3/47), Spec fPL (12/47) concentrations. The results of our study indicate that different combinations of concurrent inflammation of the liver, pancreas, and intestine do exist in cats. It also appears that these conditions may be subclinical in many cases.

FE-O-3

CO-CARRIAGE OF FELINE FAECAL PATHOGENS; RESULTS OF AN 8-WAY REAL TIME PCR PANEL. J.K. Paris¹, D. Shaw¹, S. Wills², D.A. Gunn-Moore¹. ¹R(D)SVS Small Animal Hospital, EDINBURGH, United Kingdom, ²IDEXX Laboratories, WETHERBY, United Kingdom

Several potential pathogens are found in feline faeces, ranging in significance from incidental to pathogenic. Treatment recommendations are based on accompanying clinical signs. Real Time PCR has enabled rapid screening of small quantities of faeces for potential pathogens, with high sensitivity and specificity. Co-carriage of feline faecal pathogens may reflect a symbiotic relationship or related pathogenesis, in which case identification of common co-carriage patterns may influence treatment decisions and prognosis. The primary objective of this study was to identify co-carriage of selected feline faecal pathogens. Secondary objectives were to evaluate the prevalence of individual pathogens in feline faeces, and their association with pedigree status, and a history of diarrhoea. Results of a commercial 8-way Feline Diarrhoea RealPCR[™] Panel (IDEXX Reference Laboratories, UK) from June 2010 to January 2012 were evaluated. Real Time PCR was performed for

Trichomonas foetus, *Giardiaspp.*, *Cryptosporidium spp.*, *Toxoplasma gondii*, *Salmonellaspp.*, *Clostridium perfringens* enterotoxin A gene, feline coronavirus, and feline panleukopenia virus. Additional data was recorded when available, including age, gender, breed, and history of diarrhoea. Weak or borderline positive results and those from pooled faecal samples were excluded. Associations of the carriage of pairs of pathogens were evaluated with a Chi-squared test, statistical significance set at $p < 0.05$. Results of 1882 PCR panels were evaluated. The prevalence of faecal pathogens was 17.8% (*Trichomonas foetus*), 19.3% (*Giardia*), 24.8% (*Cryptosporidium*), 0.8% (*Toxoplasma gondii*), 0.5% (*Salmonella*), 54.7% (*Clostridium perfringens*), 57.1% (feline coronavirus), and 22.6% (feline panleukopenia virus). *Salmonella* was the only faecal pathogen significantly associated with a history of diarrhoea. Faecal samples from pedigree cats were significantly more likely than DSH to be positive for *Trichomonas foetus*, *Giardia*, *Clostridium perfringens* and feline coronavirus. Significant co-carriage was identified for feline coronavirus with all other pathogens except *Salmonella*. There was significant co-carriage of *Trichomonas foetus* with *Clostridium perfringens* and *Giardia*, and also for *Giardia* with panleukopenia virus, *Cryptosporidium*, and *Clostridium perfringens*. Finally, there was significant co-carriage of *Cryptosporidium* with *Clostridium perfringens*, panleukopenia virus with *Cryptosporidium*, and *Toxoplasma gondii* with *Salmonella*. In conclusion there was a moderate to high prevalence of all feline faecal pathogens tested except *Toxoplasma gondii* and *Salmonella*. Positive PCR results were more likely in pedigree cats, and *Salmonella* was associated with a history of diarrhoea. Significant co-carriage of faecal pathogens was common, possibly reflecting common environmental risk factors, a shared pathogenesis, or a symbiotic relationship.

FE-O-4

MICROBIOLOGIC AND CYTOLOGIC COMPOSITION OF BRONCHOALVEOLAR LAVAGE FLUID IN CLINICALLY HEALTHY SHELTER CATS WITH PARTICULAR CONSIDERATION OF MYCOPLASMA SPP. S. Shibly¹, A. Bilek¹, S. Jordan², I. Schwendenein¹, J. Sparger¹, R.A. Hirt¹. ¹University of Veterinary Medicine Vienna, VIENNA, Austria, ²Animal Shelter, Dechanthof, 2193 WILFERSDORF BEI MISTELBACH, Austria

Mycoplasma spp have been identified as causative pathogen in feline lower airway disease and are not thought to colonize the lower airways of clinically healthy cats. To challenge this hypothesis, 30 domestic shorthair cats aged 1-10 years (median, 4.5 years), without signs of respiratory disease, housed in a shelter, underwent transoral lower airway washing with sterile saline under general anaesthesia. Retrieved bronchoalveolar lavage fluid (BALF) was subjected to microbiological and cytological analysis. During pre-anaesthetic clinical examination, only minor alterations were discovered: tartar in 7, conjunctivitis in 4, flea infestation in 3 and dirty auditory canals in 3 cats. One animal each showed dandruff, corneal ulceration and a heart murmur 2/6. BALF-cultures of 26 animals (86.7%) were positive for *Mycoplasma* spp. 66.7% of examined cats had *Mycoplasma felis* in their BALF (light growth in 11, moderate growth in 4 and heavy growth in 5 animals), 50% *Ureaplasma felinum/cati* (light growth in 8, moderate growth in 7 cases), 23.3% *Mycoplasma gateae* (light growth in 4, moderate growth in 2 and heavy growth in 1 cat) and 3.3% *Mycoplasma felimimum* (light growth in 1 animal). Using aerobic bacterial culture, *Pasteurella multocida* (46.7%), α -haemolytic *Streptococci* (33.3%), haemolytic *E. coli* (3.3%) and *Acinetobacter Iwoffii* (3.3%) were detected, with only 7 samples (23.3%) yielding negative results. Median BALF-total nucleated cell count was 550/ μ l (range, 4-7790) with a median mononucleated cell percentage of 73%, a median neutrophil fraction of 15.5% and a median eosinophil proportion of 1.5%. Only 2 samples were neutrophil-dominated (92.5 and 97.5%), indicating purulent inflammation. Both specimens were positive for *Mycoplasma felis* (1 light growth, 1 heavy growth), and one showed moderate growth of *Pasteurella multocida*. Like all of the animals included in this study, the corresponding cats remained clinically healthy during a 2-week follow-up period. BALF-samples showed neither cytological nor microbiological signs indicative of upper airway contamination. In contrast to earlier studies, we conclude that - at least in cats housed in shel-

ters and subjected to high infection pressure - in addition to bacteria like *Pasteurella* spp, *Streptococcus* spp and *E. coli*, *Mycoplasma* spp can occur in the feline lower airways without causing respiratory signs.

GA-O-1
EXPRESSION OF GENES ASSOCIATED WITH THE INFLAMMASOME IN THE DUODENUM OF DOGS WITH INFLAMMATORY BOWEL DISEASE AND HEALTHY DOGS. S. Schmitz, H. Munt, D. Werling, K. Allenspach. Royal Veterinary College, NORTH MYMMS, HATFIELD, United Kingdom

Inflammasomes are intracellular multi-protein complexes that coordinate the maturation of Interleukin (IL)-1 β and IL-18 in response to pathogens and metabolic danger signals. Both cytokines are vital for the maintenance of the intestinal homeostasis and have been linked to chronic intestinal inflammation in humans. Both IL-1 β and IL-18 are produced as inactive pro-forms and undergo subsequent maturation through cleavage into their active forms by caspase (casp)-1, which is in turn activated by the inflammasome complex. The best characterized inflammasome subtype in human inflammatory bowel disease (IBD) is NLRP3, which seems to be crucial for the regulation of intestinal homeostasis. Defective NLRP3 signaling has been suggested to contribute to IBD. Additionally, IL-1 β , IL-18 and casp-1 are up-regulated on the mRNA and protein level in human IBD. So far, no study has investigated the role of the inflammasome and respective down-stream cytokines in canine IBD. Thus, the goal of the current study was to investigate the expression of inflammasome components in duodenal tissues from dogs with IBD compared to healthy controls. RNA extraction from endoscopic biopsies (IBD group n = 25, control group n = 20) and reverse-transcriptase quantitative PCR was performed in a SYBRGreen-based assay using specific primers for the following canine genes: NLRP3, casp-1, IL-1 β and IL-18. A 10-fold dilution of plasmid controls for each gene was used to assess assay efficiency. Relative quantification of gene expression was performed using three reference genes (GAPDH, SDHA, TBP). Comparison between groups was performed using Mann Whitney U tests (Graph Pad Prism 5). Significance was set at p < 0.05. Eight samples (5 IBD, 3 controls) had to be excluded due to poor cDNA quality (inadequate expression of reference genes). When comparing the remaining samples in both groups, casp-1 (p = 0.001) and NLRP3 (p < 0.001) expression was significantly lower in IBD dogs than controls. In contrast, IL-1 β (p = 0.138) and IL-18 (p = 0.903) expression was not different between groups. Down-regulation of NLRP3 and casp-1 could be part of a negative feedback loop in the pro-inflammatory environment in IBD. Alternatively, this could represent general disturbances in intestinal homeostasis or failure to up-regulate "danger-signaling pathways" in inflammation. Final conclusions might be difficult to draw without matching protein data, as assessing IL-1 β and IL-18 mRNA levels cannot give insight into the ratio of "pro-cytokines" to active cytokines. Thus, investigating IL-1 β and IL-18 protein content of canine IBD tissues is warranted in the future.

GA-O-2
EXPRESSION OF TREFOIL FACTOR GENES IN THE GASTROINTESTINAL TRACT OF DOGS WITH INFLAMMATORY BOWEL DISEASE AND HEALTHY DOGS. S. Schmitz, S. Hill, D. Werling, K. Allenspach. Royal Veterinary College, NORTH MYMMS, HATFIELD, United Kingdom

The trefoil factor family (TFF) comprises a group of small peptides produced in goblet cells, which are crucial for epithelial restitution and maintenance of tight junction function in the gut. In humans with Inflammatory Bowel Disease (IBD), TFF expression is up-regulated, which is thought to represent an unspecific repair mechanism. However, TFFs have also been shown to be involved in the local control of disease in rodent

models and in humans. So far, there has been no study investigating TFF expression in the canine intestine. Thus, the goal of this study was to assess TFF expression in gastrointestinal tissues from dogs with IBD and healthy dogs. RNA was extracted from endoscopic duodenal (IBD n = 22, healthy controls n = 18) and colonic biopsies (IBD n = 12, controls n = 11) and cDNA generated. Quantitative reverse-transcription PCR was performed for canine TFF1 and TFF3 in a SYBRGreen-based assay. A 10-fold dilution of plasmid controls for each gene was used to assess assay efficiency. Relative quantification of gene expression was performed using three reference genes (GAPDH, SDHA, TBP). For statistical analysis, significance was set at p < 0.05. Overall, TFF1 expression was significantly different across groups (Kruskal Wallis p < 0.0001): In control dogs, TFF1 expression was higher in the colon than in the duodenum (Mann Whitney p < 0.0001). When comparing IBD cases to controls, duodenal TFF1 was significantly up-regulated (Mann Whitney p = 0.0001). TFF3 expression was not different across groups (Kruskal Wallis p = 0.056). However, separate analysis of the intestinal location showed significant down-regulation of TFF3 in the colon of IBD dogs compared to controls (t-test p = 0.018). This study demonstrates evidence for dysregulation of TFF gene expression in canine IBD. A lack of TFF1 could contribute to defective epithelial barrier function, causing "leakiness" of tight junctions. This increased intestinal permeability could lead to an increased antigenic load from microbes or food antigens, which could perpetuate faulty immune recognition of microbe-associated molecular patterns, thus leading to increased intestinal inflammation. Up-regulation of TFF3 in the colon could in turn signify a compensatory repair-mechanism in inflammation. Further investigation of TFF gene or protein expression is warranted in canine IBD.

GA-O-3
EFFECT ON GENE EXPRESSION AND PROTEIN PRODUCTION IN DUODENAL BIOPSIES OF DOGS WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE BY EX-VIVO CULTURE WITH ENTEROCOCCUS FAECIUM. S. Schmitz¹, N. Engelmann², M. Henrich³, R. Neiger², D. Werling⁴, K. Allenspach¹. ¹Royal Veterinary College, NORTH MYMMS, HATFIELD, United Kingdom, ²Small Animal Hospital (Internal Medicine) Justus-Liebig University, GIESSEN, Germany, ³Institute for Veterinary Pathology, Justus-Liebig-University, GIESSEN, Germany, ⁴Royal Veterinary College, Department for Pathology and Infectious diseases, NORTH MYMMS, HATFIELD, United Kingdom

Canine Inflammatory bowel disease (IBD) is thought to be partially caused by an aberrant immune response towards the intestinal microbiome. In humans and mice, administration of probiotics can alleviate IBD severity and/or prevent relapse by induction of a more "tolerant" microenvironment. The aim of this study was to investigate the effect of probiotic *Enterococcus faecium* NCIMB 10415 E1707 (EF) on gene expression and protein production in canine duodenal biopsies. Samples from 11 healthy Beagles and 8 IBD dogs were cultured *ex-vivo* with EF (1x10⁸ cfu/ml) or sterile nutrient broth/ PBS (negative control) for 5 hours. RNA extraction from biopsies and reverse-transcriptase quantitative PCR was performed in a SYBRGreen-based assay using specific primers for the following canine genes: TLR2, TLR4, TLR5, TLR9, IL-17A, IL-22, IL-10, TGF β , IL-4, IFN γ and TNF α ; using a 10-fold dilution of plasmid controls for each gene to assess assay efficiency. Relative quantification of gene expression was performed using three reference genes (GAPDH, SDHA, TBP). Protein content of IFN γ , IL-17A and TNF α was measured in culture supernatants using commercially available canine-specific ELISAs. A linear mixed model for each gene - with disease group and treatment set as fixed parameters - was chosen for statistical analysis using SPSS software. Significance was set at p < 0.05. No significant interaction between disease group and treatment was observed for any gene. Only expression of IL-4 was significantly increased in IBD dogs compared to healthy dogs (p = 0.022) in unstimulated samples. All other significant differences were independent of disease group, but depen-

dent on treatment with EF. Expression of the following genes was reduced by EF treatment: TLR 4 ($p = 0.003$), TLR5 ($p = 0.015$), TLR9 ($p = 0.005$), TGF β ($p = 0.006$), IFN γ ($p = 0.032$) and TNF α ($p < 0.001$). No significant amounts of IFN γ , IL-17A or TNF α protein were detected in culture supernatants. This is the first study demonstrating a profound effect of EF treatment on gene expression in *ex vivo* cultured canine duodenal biopsies. Down-regulation of several genes of innate immune receptors and pro-inflammatory cytokines was observed, with the most significant effect on suppression of TNF α expression. Effects were seen both in healthy and in IBD dogs. Whether this translates to a beneficial effect in a clinical situation needs further investigation.

GA-O-4

CHARACTERIZATION OF FECAL BACTERIAL DYSBIOSIS IN CATS WITH CHRONIC ENTEROPATHIES. J. Suchodolski¹, B.J. Marvel¹, W. Geiger¹, J.M. Steiner¹, C.B. Webb¹. ¹GI Lab, Texas A&M University, COLLEGE STATION, United States of America, ²Small Animal Clinical Sciences, CVM, FORT COLLINS, CO, United States of America

Recent molecular studies have revealed a highly complex bacterial microbiota in the intestine of cats. There is mounting evidence that microbes play an important role in the pathogenesis of chronic enteropathies, as compositional changes of the intestinal bacterial ecosystem have been associated with chronic intestinal inflammation in humans and dogs. The aim of this study was to characterize the bacterial microbiota in cats with chronic enteropathies. Faecal samples were obtained from healthy cats ($n=16$) and cats with histologically confirmed chronic enteropathies ($n=8$). The bacterial composition was analyzed by massive parallel 16S rRNA gene 454-pyrosequencing (yielding 194,000 sequencing tags), and selected quantitative PCR assays. Differences in microbial community structure between healthy and diseased cats were assessed by the phylogenetic Unifrac distance method, followed by Analysis of similarity (ANOSIM) of the distance matrix. Differences in bacterial groups between the disease groups were analyzed using Mann-Whitney U tests. The resulting P -values were corrected for multiple comparisons using the Benjamini & Hochberg's False Discovery Rate. An adjusted $P < 0.05$ was considered for statistical significance. The Unifrac distance metric indicated no significant clustering according to disease status. However, the relative proportions of sequences belonging to *Bacteroides* spp. were significantly decreased in the cats with chronic enteropathies compared to the healthy cats ($p=0.02$). The employed qPCR assays confirmed the sequencing results and also showed a significant decrease in proportions of *Bacteroides* spp. in the diseased cats. In addition, qPCR revealed also a significant decrease in *Turicibacter* spp. in cats with chronic enteropathies compared to the healthy cats ($p=0.04$). No significant differences in diversity indices were observed between healthy and diseased cats. In conclusion, the here used molecular approach revealed significant reductions in *Bacteroides* and *Turicibacter* spp. in cats with chronic enteropathies. Future studies are necessary to evaluate if these microbial changes correlate with functional changes in the intestinal microbiota.

GA-O-5

PROSPECT® CAMPYLOBACTER MICROPLATE ASSAY DETECTION OF C. UPSALIENSIS AND C. HELVETICUS IN SPIKED FAECAL SAMPLES. K. Bojanic¹, A. Midwinter², L.E. Rogers², P.J. Biggs², E. Acke¹. ¹Institute of Veterinary, Animal and Biomedical Sciences, PALMERSTON NORTH, New Zealand, ²Hopkirk Research Institute, Institute of Veterinary Animal & Biomedical Sciences, PALMERSTON NORTH, New Zealand

Campylobacter spp. represent a common cause of gastroenteritis in humans with *C. jejuni* and *C. coli* considered responsible

for the majority of clinical cases. Many human diagnostic laboratories use the ProSpecT[®] Campylobacter Microplate Assay (EIA) as a sole or screening test for detection of *C. jejuni* and *C. coli* as this technique is easier, faster and cheaper than *Campylobacter* spp. culture. *C. upsaliensis* can cause a diarrhoeal illness similar to that caused by *C. jejuni* in humans but methods routinely used for *C. jejuni* and *C. coli* detection, including the EIA, are not optimised or have not been evaluated for the detection of other *Campylobacter* species. *C. upsaliensis* and *C. helveticus* have been more commonly isolated from dogs and cats than *C. jejuni* and *C. coli* in most studies. *Campylobacter* spp. from pets are potentially zoonotic while the pathogenicity in pets remains uncertain. The significance of *C. upsaliensis* and *C. helveticus* infections may be underestimated in human medicine due to detection methods applied. The aim of this pilot study was to assess if the EIA detects *C. upsaliensis* and *C. helveticus* isolated from different pets in spiked human clinical samples. In addition, the ability of EIA to detect *Campylobacter* spp. in dog and cat faeces was assessed. Ten clinical human faecal samples and two healthy dog and cat faeces confirmed negative by EIA were tested by a range of culture methods to exclude presence of *Campylobacter* spp. Dilutions of eight *C. upsaliensis*, five *C. helveticus* cultures, and one *C. jejuni* and *C. coli* culture, all PCR confirmed, were added to aliquots of faecal samples to obtain a range of viable bacteria from 10^3 to 10^8 CFU/ml. EIA was performed following the manufacturer's instructions and in duplicates. Fifty out of 82 samples tested positive by EIA at various dilutions: 33/52 *C. upsaliensis*, 15/26 *C. helveticus*, 1/2 of each *C. jejuni* and *C. coli*. Detection limit varied between the isolates and was lower in watery than semi-solid faeces. In conclusion, EIA detected *C. upsaliensis* and *C. helveticus* in spiked faeces from human clinical cases and all *Campylobacter* spp. tested in healthy pets. EIA should not be used as a sole detection method and culture methods selected following a positive EIA result should enable detection of a wide range of *Campylobacter* spp. In addition, EIA may be a useful test in pets to rule out *Campylobacter* spp. infection and in epidemiological investigations.

GA-O-6

FEASIBILITY OF ESOPHAGEAL HIGH-RESOLUTION MANOMETRY IN AWAKE AND SEDATED HEALTHY DOGS. J. Kempf¹, H. Heinrich², C.E. Reusch¹, P.H. Kook¹. ¹Clinic for Small Animal Internal Medicine, ZÜRICH, Switzerland, ²Gastrointestinal Function Laboratory, University Hospital Zurich, ZÜRICH, Switzerland

High-Resolution Manometry (HRM) is the gold standard for the evaluation of functional esophageal motility disorders in humans. No information on this non-invasive technique is available in dogs. The aims of this study were to evaluate the feasibility of HRM in dogs, generate first normal values, and to examine the influence of a standard sedation on the esophageal pressure profile. The study population consisted of 20 healthy adult Beagle dogs (mean BW 12.85 kg), the study protocol was approved by the local ethics committee. HRM was performed in sitting position after a 6-h fast, lidocaine jelly at 2% was used as a lubricant. A solid-state catheter (Sierra Scientific, 2.75 mm diameter) with 36 circumferential pressure sensors spaced 1 cm apart was inserted intranasally, measurements were started after 5 minutes adaptation time. Real-time pressure imaging during catheter intubation enabled accurate placement. Each manometric protocol included 5 water and 5 canned food bolus swallows. The procedure was repeated 30 minutes after standard IM sedation with acepromazine and buprenorphine. Data were analysed using ManoView software and results (awake vs. sedated) were compared using the Wilcoxon test. Statistical significance was set at $p < 0.05$. HRM could successfully be performed in 12/20 dogs. Reasons for unsuccessful examinations were: defence reactions (5), inability to pass through the ventral meatus (2), reverse sneezing (1). Upper esophageal sphincter (UES) characterisation comprised: baseline pressure, residual pressure (nadir of the UES relaxation during swallowing), and relaxation duration. Tubular esophageal function characterisation comprised: peristaltic con-

tractile integral (PCI; amplitude x duration x length of the contraction wave) and the bolus transit time (BTT). Lower esophageal sphincter (LES) characterisation comprised: baseline pressure and residual pressure (lowest continuous 3 second mean LES pressure relative to intragastric pressure during swallow induced relaxation). The median values for water/food bolus swallows in awake (sedated) dogs were calculated i) UES: baseline pressure 11.5 mmHg (16.1), residual pressure -2.74/2.73 mmHg (-2.03/2.53) and relaxation duration 192.5/245 ms (230.25/324) ii) tubular esophagus function: PCI 478.15/1012 mmHg-cm-s (525.08/1605.4) and BTT 3.7/4.08 ms (4.85/5.82) iii) LES: baseline pressure 36.85 mmHg (16.8), residual pressure 7.2/5.64 mmHg (10.83/7). Significant differences were found for the UES relaxation duration (water) ($p=0.023$) and BTT (food bolus) ($p=0.008$). In conclusion, HRM is a feasible technique for the evaluation of esophageal function in dogs. Patients that require sedation can still be examined, however at this point it is not clear if sedation would affect the assessment of motility disorders in dysphagic dogs.

GA-O-7

WIRELESS AMBULATORY ESOPHAGEAL PH-MONITORING IN HEALTHY DOGS AND DOGS WITH HISTORICAL AND CLINICAL SIGNS INTERPRETED AS GASTRO-ESOPHAGEAL REFLUX. P.H. Kook, J. Kempf, C.E. Reusch. Clinic for Small Animal Internal Medicine, ZURICH, Switzerland

In humans ambulatory intraesophageal pH-monitoring utilizing the Bravo[®] capsule is the standard test for establishing pathological gastroesophageal reflux (GER). This technique not only provides information on esophageal acid exposure, but is also able to assess symptoms associated with GER. In dogs GER is poorly understood and it is not clear if GER actually represents a clinically relevant problem. The goals of this study were to examine the canine esophageal pH milieu in health and to examine esophageal pH in dogs presenting with signs commonly attributed to GER in the veterinary literature. Thirteen client-owned dogs (COD) of various breeds (median BW 20.3kg, 6.1-45; median age 5y, 1-11) were included. Clinical signs ultimately leading to pH-monitoring comprised: lip-smacking (6), repeated swallowing motions (3), chronic vomiting (3), cough (3), retching (2), regurgitation (2), sudden discomfort (2), excessive surface-licking (2), ptyalism (2), presumed postprandial pain (2), refusal to eat despite interest (2), history of esophageal foreign bodies (1), halitosis (1). Each dog showed a median of 3 (1-4) signs, 3 dogs had additional diarrhea. Six healthy Beagles (median BW 13.9kg, median age 1.5y) with unremarkable gastroduodenal evaluation served as controls (C). No prior antacid or prokinetic treatment was allowed. The capsule was endoscopically placed 4 cm above the lower esophageal sphincter, pH data were transmitted every 4s to a receiver attached to the dog's collar. Owners were instructed to press the individually predefined symptom-buttons on the receiver whenever indicated, and not to change the daily routine. Data were analysed using the RapidpH[®] software, reflux was defined as a single pH-measurement < 4. Results between groups were compared using non-parametric tests. The median pH-monitoring period (COD/C) was 47.49/43.17h. The following parameters (median, range for COD/C) were evaluated: Number of refluxes: 12 (1-86)/13.5 (1-65), number of longest (> 5min) reflux: 1 (0-14)/1 (0-4), duration of longest reflux (min): 7 (1-18)/6.5 (1-27), and fraction time pH < 4 (%): 0.5 (0.01-5.6)/0.5 (0-3.2). There were no differences between groups. The median number of button pushes was 6 (0-35), 3 dogs had reflux-positive pushes (2.8, 11, and 17.6% of pushes). Mild distal esophagitis was noted in 1 dog. Final diagnoses were: food-responsive IBD (6), steroid-responsive IBD (2), allergic skin disease (2), chronic laryngotracheobronchitis (2), muscular dystrophy (1). Dogs presenting with historical and clinical signs interpreted as GER may not have relevant reflux episodes. Considering normal values established in humans, none of the dogs would have been classified as abnormal.

GA-O-8

LABORATORY AND ULTRASONOGRAPHIC MONITORING OF DOGS WITH ACUTE PANCREATITIS. S. Corradini, A. Diana, F. Bresciani, M. Cipone, F. Fracassi. University of Bologna, Italy, OZZANO DELL'EMILIA, Italy

The aim of the present study was to evaluate the changes of some biochemical and ultrasonographic (US) parameters in a group of dogs with naturally occurring acute pancreatitis (AP) during the therapeutic follow-up. Dogs with clinical signs and abdominal US findings suggestive of AP associated with increased serum canine pancreatic lipase (cPL) activity were included into the study. In these dogs, the serum concentration of C-reactive protein (CRP), amylase and lipase were also measured. Severity indexes were established to semi-quantitatively evaluate the severity of clinical and US findings. In particular, a clinical score (0-3) for each of the following clinical parameters was given: presence and frequency of vomiting, appetite and general condition; an US score (0=normal, 1=abnormal) was assigned per each of the following parameters: pancreas (echogenicity, volume, echotexture and echogenicity of the mesentery), gastrointestinal tract, biliary ducts, lymph nodes and abdominal effusion (total score 0-14). All dogs were treated with fluid therapy, ampicillin-sulbactam, 15mg/kg IV q8h, buprenorphine, 0.01mg/kg q8h, and, if needed, maropitant 1mg/kg SC q24h. The two severity scores, serum CRP, amylase and lipase concentrations were measured at diagnosis (T0) and after 1 (T1), 3 (T3), and 5 (T5) days, and at discharge (Td) and 1 week after discharge (Td1). Nine client-owned dogs were included with a median (range) age of 10 years (8-14 years). Median (range) clinical and US scores were 8 (6-9) and 8.5 (3-13), respectively, at T0, and 0 (0-1) and 1 (0-3), respectively, at Td1. A significant, positive correlation was found between the clinical and US score ($p<0.001$, $r=0.68$). The median (range) serum concentration of CRP (mg/dl), amylase (U/L) and lipase (U/L) was 9.46 (3.36-30.4), 2,995 (776-6,458) and 889 (206-5,270), respectively, at T0, and 0.64 (0.01-3.07), 704 (563-1,002) and 302 (94-566), respectively, at Td1. On admission, serum CRP, amylase and lipase levels were increased in 100%, 77%, and 55% of dogs, respectively while they were increased in 50%, 12.5% and 0% of dogs, respectively, at Td1. Serum CRP and amylase, but not lipase, concentrations decreased during the follow up and were significantly ($p<0.05$) lower at Td1 compared to T0. Results suggest that US findings, and CRP and amylase concentrations are correlated with the recovery from the AP. Further studies are warranted to evaluate the usefulness of these parameters in the follow-up of AP in a wider population of dogs.

GA-O-9A

BLINDED RANDOMIZED CONTROLLED FIELD TRIAL TO DETERMINE THE EFFECT OF ENTERIC COATING ON THE EFFICACY OF ENZYME REPLACEMENT FOR CANINE EXOCRINE PANCREATIC INSUFFICIENCY. A. Mas¹, P.J.M. Noble¹, P.J. Cripps¹, D.J. Batchelor¹, P.A. Graham², A.J. German¹. ¹University of Liverpool, NESTON, United Kingdom, ²Nationwide Laboratories, POULTON-LE-FLYDE, United Kingdom

Enzyme replacement therapy is the mainstay therapy for exocrine pancreatic insufficiency (EPI) in dogs. 'Enteric-coated' preparations have been developed to protect the enzyme from degradation in the stomach, but their efficacy has not been critically evaluated. The hypothesis of the current study was that enteric coating would have no effect on the efficacy of pancreatic enzyme supplements for dogs with EPI. Thirty-eight client-owned dogs with naturally occurring EPI were included in this multicentre, blinded, randomised controlled trial. Dogs received either an enteric-coated enzyme preparation (test group) or an identical preparation without the enteric coating (control group) over a period of 56 days. There were no significant differences in baseline characteristics between test and control treatment groups. Body weight and body condition score increased in both groups during the trial ($P<0.001$) but the magnitude of increase was greater for the test treatment compared with the control treatment ($P<0.001$). By day 56, mean body weight increase was 17% (95% confidence interval 11-23%) in the treatment group and 9% (95% confidence

interval 4-15%) in the control group. The dose of enzyme used increased over time ($P < 0.001$) but there was no significant treatment group difference at any time point ($P = 0.225$). Clinical disease severity score decreased significantly over time for both groups ($P = 0.011$) and no significant difference was noted between groups ($P = 0.869$). No significant adverse effects were reported, for either treatment, for the duration of the trial. Adding an enteric coating to a pancreatic enzyme supplement conveys a therapeutic advantage, when treating dogs with EPI.

HE-O-1
SELF-RENEWAL FACTOR BM11 IS INVOLVED IN CANINE ADULT HEPATIC PROGENITOR CELL ACTIVATION AND HEPATOCELLULAR CARCINOMAS. L.C. Penning, B. Spee, H.S. Kruitwagen, I. vanGils, J. Rothuizen, B.A. Schotanus. Faculty of Veterinary Medicine, UTRECHT, The Netherlands

When liver injury is caused by toxins that inhibit hepatocyte replication, or when the proliferative potential of hepatocytes is exhausted due to the chronic condition of the disease, hepatocyte-dependent liver regeneration is strongly impaired. In this situation another cell compartment is activated to regenerate the liver: the hepatic progenitor cell compartment. Bipotent hepatic progenitor cells (HPCs) can differentiate into hepatocytes or cholangiocytes. Not only are HPCs activated during severe liver disease, they may well be the cells of origin for subtypes of hepatocellular carcinoma (HCC). The Polycomb Group protein Bmi1 is involved in murine HPC activation and has prognostic relevance in HCC. Therefore we investigated the expression of Bmi1 in canine liver diseases including HCC. Functional consequences of deregulated Bmi1 expression are included to reveal its feasibility in liver regenerative medicine. Immunohistochemistry (IHC) and laser microdissection followed by gene expression analysis were used to investigate the expression of Bmi1 in activated HPCs and HCC. To elucidate the role of Bmi1 in HPCs, *in vitro* gene silencing experiments followed by gene expression analysis, western blot analysis, and a proliferation assay (EdU-incorporation) were performed in the human HPC-like cell-line HepaRG. IHC and gene expression showed a strong nuclear expression of Bmi1 in activated HPCs in canine liver diseases. Keratin 19 is a marker for HPCs and cholangiocytes, and high expression is associated with poor prognosis in HCCs. Bmi1 staining was more intense in highly malignant hepatocellular carcinomas positive for Keratin 19 compared to Keratin 19 negative HCCs. Bmi1-silencing *in vitro* studies revealed a significantly reduced HPC proliferation and suggested a role of Bmi1 in differentiation (gene expression) of HPCs. These results indicate that Bmi1 is expressed in activated HPCs in all liver diseases tested. Bmi1 is needed for proliferation of HPCs *in vitro* and is potentially involved in HPC differentiation. Expression of Bmi1 in HCCs suggests a role in tumour development, potentially due to a persistent activation of HPCs. Therefore, enhanced activation of Bmi1 will lead to more progenitor cells (beneficial) but most likely also to more aggressive HCC with a HPC-signature.

HE-O-2
MAGNETIC ASSISTED CELL SORTING OF HEPATIC NON-PARENCHYMAL CELLS FOR CD133 ENRICHES FOR HEPATIC PROGENITOR CELLS. A. Gow¹, L.Y. Pang¹, D. Hay², D.J. Argyle¹. ¹The R(D)SVS & Roslin Institute, EDINBURGH, Scotland, ²MRC Centre for Regenerative Medicine, EDINBURGH, Scotland

Hepatic progenitor cells (HPC) are bipotential, forming cholangiocytes or hepatocytes. As a result, they express markers of both cell types. Various markers have been used to select for HPC's yet there is no specific cell marker. CD133, a transmembrane glycoprotein, has been identified as a organ stem cell marker and cancer stem cell marker, and used to select HPC's in rodents and humans. Canine HPC have been shown to have gene expression of CD133. This study aimed to assess if CD133 selection could enrich for canine HPCs. A wedge of liver from a healthy dog euthanased for behavioural reasons was digested by

collagenase perfusion. Hepatocytes were removed by pelleting at 50g for 5 mins. The remaining non-parenchymal cells (NPC) were then pelleted at 200g for 5 mins. Magnetic assisted cell sorting (MACS) for cells positive and negative for CD133 was performed according to the manufacturer's instructions. CD133 positive and negative NPC were cultured on bovine type I collagen-coated plates with Hepatocyte culture media (Lonza). Cell morphology was monitored. RNA was extracted and cDNA produced from cell pellets immediately after separation and also after 3 weeks of culture. Relative gene expression of CD133, cholangiocyte marker Keratin 7 (K7) and hepatocytes markers K18, albumin and CYP1A1 was performed using B2MG and RPL8 as reference genes. The CD133 positive fraction was 38% of the NPCs. Morphologically, CD133 positive cells formed more colonies of cells with a small cytoplasm to nucleus ratio, which then transformed to hepatoblastic appearance while the negative cells produced more fibroblastic cells. Compared to CD133 negative cells, initially CD133 positive cells showed a 2-fold increase in CD133, and 2.5-fold increase in cholangiocyte marker K7 as well as modest increases in hepatocyte markers albumin and CYP1A1 and a modest decrease in K18. After 3 weeks culture, positive cells expressed more albumin, CYP1A1, K7 & K18 compared to CD133 negative cultures. CD133 expression had reduced to a 1-fold increase after culture. The CD133 positive fraction expressed cholangiocyte and hepatocytes markers compared to negative cells initially after sorting. After 3 weeks culture, CD133 positive cells formed hepatocyte-like colonies, as well as continuing to have greater hepatocyte and cholangiocyte gene expression. CD133 expression decreased, consistent with differentiation. A large percentage of the NPC were positive for CD133. CD133 sorting also labels haematopoietic and mesenchymal stem cells therefore subsequently using FACS for other markers may further enrich for specifically the HPC compartment.

HE-O-3
NEW PROGNOSTIC CLASSIFICATION OF PRIMARY HEPATIC TUMOURS IN THE DOG. R.G.H.M. van Sprundel¹, F. Guscetti², O. Kershaw³, T.S.G.A.M vanden Ingh⁴, T.A. Roskams⁵, J. Rothuizen⁶, B. Spee⁶. ¹University Utrecht, UTRECHT, The Netherlands, ²Institute of Veterinary Pathology, University of Zürich, ZÜRICH, Switzerland, ³Institute of Veterinary Pathology, Freie Universität Berlin, BERLIN, Germany, ⁴TCCI Consultancy BV, UTRECHT, The Netherlands, ⁵Department of Morphology and Molecular Pathology, University Hospitals Leuven, LEUVEN, Belgium, ⁶Department of Clinical Sciences of Companion Animals, Utrecht University, UTRECHT, The Netherlands

Until now the hepatic neoplasms in dogs are classified as hepatocellular adenomas and carcinomas, cholangiocellular adenomas and carcinomas, mixed hepato- and cholangiocellular carcinomas and hepatic carcinoids. Over the past decade, many advances have been made in the characterization of primary liver tumours in man. This knowledge has resulted in a proposal for a new morphological and immunohistochemical classification of primary liver tumours which facilitates the diagnosis and categorization of these tumours including their aggressiveness and prognosis. The purpose of this study was to investigate the presence and relative incidence of the various morphological types of primary hepatic neoplasms in the dog and to determine whether the new human classification also can be applied to canine hepatic neoplasms. For this study 93 canine primary liver tumours were examined histologically and classified using several immunohistochemical markers including Keratin(K)19 (hepatic progenitor (stem) cell/bile duct epithelium marker), HepPar-1 (hepatocyte marker), EMA (MUC1; mucine producing biliary epithelium marker), pCEA (canalicular, ductular, and bile duct epithelium marker), NSE and Chromogranin-A (neuro-endocrine markers). In addition, the tumours were graded according to cellular and nuclear pleiomorphism and mitotic index (grade:0-3) and staged with respect to absence or presence of invasive growth, intrahepatic and/or distant metastases (stage:0-2). Of the 93 primary liver tumours, 80 had a hepatocellular origin (86%). These hepatocellular tumours could be subdivided in hepatocellular tumours with <10% positivity for K19 (65%) and tumours

with >10% positivity for K19 (22%). The hepatocellular tumours with >10% positivity for K19 were histologically poorly differentiated and often revealed lymphatic and vascular invasion in portal tracts and all showed intrahepatic and/or distant metastasis. In contrast the hepatocellular tumours with <10% positivity for K19 were almost always well differentiated and well demarcated and did not have evidence for vascular invasion, intrahepatic and/or distant metastasis. Eight of the 93 tumours were from cholangiocellular origin (9%). All of the cholangiocellular tumours were poorly differentiated (grade 2 and 3) and showed intrahepatic and/or distant metastases. The third group of primary liver tumours had neuroendocrine characteristics, consisted of five tumours (5%) and were classified as carcinoids. They all were histologically poorly differentiated and had intrahepatic and/or distant metastases. In conclusion, the morphological types of the primary hepatic neoplasm in the dog, including their aggressiveness and prognosis, are highly comparable to the situation in man. These findings indicate that the new human classification of primary hepatic neoplasms is applicable in the dog.

HE-O-4

ANTI-HISTONE ANTIBODIES IN DOBERMAN HEPATITIS.
H.E. Dygge¹, S. Meri², T. Spillmann¹, H. Jarva², M. Speeti¹.
¹University of Helsinki Finland, HELSINKI, Finland, ²Haartman Institute, University of Helsinki and HUSLAB, HELSINKI, Finland

Doberman hepatitis (DH) is a rare inflammatory liver disease characterized by female preponderance, elevated serum transaminase activity and increased hepatic copper content. Immune system involvement is suggested by the presence of lymphocyte infiltration, female predisposition, abnormal expression of major histocompatibility complex (MHC) class II antigens by hepatocytes and association of homozygosity for the MHC II risk allele DRB1*00601 of the dog leukocyte antigen system genotype. We investigated the possibility that autoantibodies are involved in DH. Serum samples from 25 subclinical and 13 clinical DH patients and 17 clinically healthy control Dobermans were included in an ELISA assay for detection of IgG autoantibodies against histones (AHA). The cut-off value for positivity in the anti-histone ELISA was 0.87, determined using the mean absorbance +2 SD of samples from healthy controls. The values for subclinical DH cases (mean ± SD: 1.36 ± 0.6; 95% confidence interval (CI) 1.11 to 1.61) and clinical DH cases (mean ± SD: 1.46 ± 0.49; 95% CI 1.17 to 1.76) were both significantly higher than values for controls (mean ± SD: 0.51 ± 0.18; 95% CI 0.42 to 0.6; p<0.05). No seropositivity was noted in the control group. Autoantibodies are the serological hallmark of autoimmune disease. Normally, the immune system has an extraordinary capacity for preventing self-antigens to stimulate an inflammatory reaction. The presence of autoantibodies is therefore the consequence of a breakdown or failure of B-cell tolerance toward the corresponding autoantigens. Since the appearance of AHA indicates possible presence of autoimmunity, our results support the assumption that DH is an autoimmune disease.

HE-O-5

EXTRAHEPATIC PORTOSYSTEMIC SHUNTS: MAPPING A COMPLEX DISORDER USING DIFFERENT DOG BREEDS. F.G. vanSteenbeek¹, P.A.J. Leegwater¹, I.J. Nijman², E. Cuppen², J. Rothuizen¹. ¹Utrecht University, UTRECHT, The Netherlands, ²Hubrecht Institute, Dept. of Genome Biology and Bioinformatics, UTRECHT, The Netherlands

Man's best friend (*Canis lupus familiaris*) is an ideal model organism for a broad variety of naturally occurring diseases. Dog breeds have a population structure suited for genetic studies of complex disorders. Haploblocks within dog breeds extend up to 100 times longer distances than in human populations. Related dog breeds often share phenotypes and causative mutations, allowing for finemapping and validation. The inbreeding and bot-

tlenecks of dog populations has led to an increased incidence of genetic diseases which remained incidental in the panmictic human populations. Extrahepatic portosystemic shunts (EHPSS) are large abnormal venous blood vessels connecting the portal vein with a major systemic vein. It results in almost complete diversion of the portal blood past the liver, leading to lack of liver function and liver growth, and hepatic encephalopathy due to brain neurotransmitter dysfunctions. There are only 173 reported human cases, whereas the disease is widespread in dogs. Shunts are more frequently diagnosed in purebred dogs than in crossbred dogs. The inheritance is complex without sex effect. A genome wide association study with 50K SNPs was performed on 48 Cairn terrier cases and 48 controls of the same breed. After quality control 42 cases and 39 controls were analyzed in 47702 SNPs. Allelic association was calculated with PLINK and GRAMMAS of the GenABEL package was used to correct for genetic kinship. Several chromosome regions were detected with close to significant association. Overlap between the two analysis methods was found on three genomic regions covering about 8.4 Mb. Finemapping was conducted by analyzing more SNPs in a larger group of Cairn terriers and in cases and controls of 8 other breeds. The finemapping resulted in two genomic regions covering 300 and 997 kb that were associated with significant p-values. Comparison of haplotypes of cases from different breeds confirmed the association signals. The regions of interest are analyzed by NGS of 48 cases and 48 controls.

IM-O-1

EFFICACY OF RIFAMPIN IN THE TREATMENT OF EXPERIMENTAL ACUTE CANINE MONOCYCYTIC EHR-LICHIOSIS: A PILOT STUDY OF A 3-WEEK REGIMEN.
K. Theodorou¹, M. Mylonakis¹, V. Siarkou², L. Leontides³, A. Koutinas¹, C. Koutinas², M. Kritsepi-Konstantinou⁴, G. Batziias⁵, E. Flouraki¹, O. Eyal⁶, V. Kontos⁷, S. Harrus⁶. ¹Veterinary Faculty, Aristotle University of Thessaloniki, THESSALONIKI, Greece, ²Laboratory of Microbiology and Infectious Diseases, Faculty of Veterinary Medicine, THESSALONIKI, Greece, ³Laboratory of Epidemiology, Biostatistics and Animal Health Economics, School of, KARDITSA, Greece, ⁴Diagnostic Laboratory, Faculty of Veterinary Medicine, Aristotle University of T, THESSALONIKI, Greece, ⁵Laboratory of Veterinary Pharmacology, Faculty of Veterinary Medicine, Aristotle, THESSALONIKI, Greece, ⁶Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, JERUSALEM, Israel, ⁷Department of Veterinary Public Health, National School of Public Health, ATHENS, Greece

Historically, doxycycline has been the first line drug for the treatment of canine monocytic ehrlichiosis (CME). Some studies have shown that dogs may remain carriers despite doxycycline treatment, therefore investigation for other anti-ehrlichial agents may be warranted. Rifampin was suggested as a promising alternative for the treatment of CME, though its efficacy in clearing the infection has not been thoroughly evaluated. The purpose of this study was to assess the efficacy of rifampin in achieving clinicopathological recovery and clearing the ehrlichial infection from the blood and other tissues in dogs with experimentally-induced acute CME. Of the 16 purpose-bred Beagle dogs that were included in the study, 5 dogs with acute experimental CME were treated with rifampin (10 mg/Kg, SID, PO, for 3 weeks), 9 infected dogs received no rifampin (infected controls) and two dogs served as uninfected controls. Fourteen days after the completion of rifampin treatment, dexamethazone (0.5 mg/Kg, IV, once) was given to the 5 rifampin-treated dogs. Clinical score, platelet counts, anti-*E. canis* immunofluorescent antibody titers (IFA) and polymerase chain reaction (PCR) detection of *E. canis*-specific deoxyribonucleic acid in the blood, bone marrow and spleen aspirates were evaluated between the treated and untreated infected dogs on day 21 post-inoculation (PI) (start of rifampin), on day 42 PI (end of rifampin) and day 98 PI (end of post-treatment monitoring). By day 21 PI, all infected dogs became clinically ill and thrombocytopenic, seroconverted and became PCR-positive in at least one tissue. The median clinical score and IFA titers did not differ between the treated and untreated dogs at any of the three time points. Median platelet

counts were significantly higher in the treated compared to the untreated infected dogs on day 42 PI (251,000/μl versus 168,000, $P=0.0233$) and day 98 PI (254,000/μl versus 205,000/μl, $P=0.0195$) (two-sample Wilcoxon rank-sum [Mann-Whitney] test). On day 42 PI, 2 treated and 2 untreated infected dogs were PCR-positive, while on day 98 PI, 3 treated and 6 untreated infected dogs remained PCR positive in at least one of the tissues tested. As administered in this study, rifampin hastened hematological recovery of the infected dogs, but was inconsistent in clearing the experimentally-induced acute *E. canis* infection.

IM-O-2

ACUTE PHASE PROTEINS: POTENTIAL PREDICTORS OF AN IMMUNE-MODULATION IN NATURAL RETROVIRAL-INFECTED CATS RECEIVING RECOMBINANT INTERFERON-OMEGA THERAPY. R.A.O. Leal¹, S. Gil¹, N. Sepúlveda², D. Mcgahie³, A. Duarte¹, M.R.E. Niza¹, L. Tavares¹. ¹CHISA/FMV, LISBOA, Portugal, ²London School of Hygiene and Tropical Medicine, LONDON, United Kingdom, ³Virbac, CARROS, France

Acute phase proteins (APP) are considered one of the hallmarks of the inflammatory response. Among their major functions, APPs seem to modulate innate immune system efficiency. In cats, serum amyloid A (SAA) and α 1-glycoprotein (AGP) are two major positive APPs that are increased during inflammation. This rise is presumed to be secondary to various cytokines that are involved in the innate inflammatory response. Recombinant Feline Interferon- ω (rFeIFN- ω) is an immune-modulator drug that is commonly used in cats naturally infected with retroviruses, namely feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV). Several studies have been performed to clarify the clinical benefits of rFeIFN- ω therapy in naturally infected FIV and/or FeLV cats. Our group has previously described that C-reactive Protein (CRP) increased in naturally retroviral-infected cats under rFeIFN- ω therapy. However, the role of APPs such as SAA, AGP and CRP in the innate immune response, remains unknown. The aim of this study was to evaluate SAA, AGP and CRP serum levels in naturally retroviral-infected cats under rFeIFN- ω therapy. Sixteen naturally retroviral infected cats (7 FIV, 6 FeLV and 3 co-infected FIV/FeLV stray cats) housed in a Lisbon Animal Rescue Shelter were submitted to rFeIFN- ω therapy. The licensed protocol was used: 3 courses of 1MU/kg SC administered once daily for 5 days, beginning on days 0, 14 and 60. Blood samples were collected for SAA, AGP and CRP quantification before, during and after treatment (at D0, 10, 30, 65). SAA was quantified by ELISA (Phase SAA, Tridelta) and AGP was determined by single radial immunodiffusion (AGP, Tridelta). Feline CRP was quantified by ELISA (Kamiya Biomedical Company). APP serum levels were compared before and after rFeIFN- ω therapy. A statistically significant increase of SAA and AGP ($p=0.0005$ and $p=0.012$ respectively - Friedman test) was observed at D65 in comparison to D0. These findings corroborate the significant increase of CRP serum levels previously described ($p < 0.0001$ - Friedman test). All the APPs tested behaved similarly, showing an evident increase in their serum values after rFeIFN- ω therapy. These results suggest a possible immune modulation effect induced by rFeIFN- ω which seems to maximize the efficiency of innate immune response. Further studies correlating these findings with the cytokine profile will extend our knowledge about the efficiency of rFeIFN- ω therapy in naturally retroviral infected cats.

IM-O-3

CANINE THEILERIOSIS: CLINICAL MANIFESTATIONS. C. Rosa, P. Pazzi, S. Nagel, V. McClure, J. Christie, M. Troskie, E. Dvir. Faculty of Veterinary Science, University of Pretoria, PRETORIA, South Africa

Canine theileriosis is a tick-borne disease caused by protozoan parasites of the genera *Theileria* that has been associated

with anaemia and/or thrombocytopenia. The clinical manifestation of this disease in the dog is poorly described. This disease of emerging importance has been diagnosed in several dogs, emphasizing the need to elucidate the specific pathogenic species and characterize the clinical manifestations of the disease. This retrospective study describes the clinical characteristics, diagnostic tests, treatment and outcome of six client owned clinically ill dogs diagnosed with canine theileriosis at the Onderstepoort Veterinary Academic Hospital in South Africa during 2010-2011. Canine theileriosis was diagnosed by Polymerase Chain Reaction (PCR) on whole-blood followed by a Reverse Line Blot (RLB) hybridization assay. Other tick-borne diseases and neoplastic conditions were excluded. The most common clinical findings were pale mucous membranes (5/6 dogs), lethargy (3/6 dogs) and oral bleeding (3/6 dogs). All dogs had thrombocytopenia with a median of $59.5 \times 10^9/l$ (range: 13 - 199) and 5/6 dogs had anaemia with a median haematocrit of 18% (range: 5 - 32). The anaemia was regenerative in 3/5 dogs and non-regenerative in 2/5 dogs. One dog was positive on an in saline auto-agglutination test. Bone marrow cytology and core biopsies were performed in two dogs with severe non-regenerative anaemia and showed myelofibrosis. *Theileriasp.* were detected in four dogs and *Theileria equi* in two dogs. Imidocarb dipropionate was administered in all dogs as treatment of choice for the theileriosis. Five dogs that received the complete treatment achieved clinical cure. PCR post-treatment was performed in three dogs and was negative. Prednisolone and azathioprine was administered in all dogs for suspected immune-mediated haematological disorders secondary to the theileriosis. One dog was euthanased one week after diagnosis. Canine theileriosis should be considered a differential diagnosis for dogs with thrombocytopenia and/or anaemia in endemic tick-borne disease areas. PCR is a versatile tool for diagnosis and treatment monitoring in theileriosis. In our study, imidocarb dipropionate was effective in sterilizing the parasitic infection. The bleeding tendency seen in the theileriosis cases is most likely secondary to the thrombocytopenia and/or concurrent thrombocytopathy as described in canine ehrlichiosis. Further studies are required to determine the possible links between thrombocytopenia, anaemia and myeloproliferative disorder observed in canine theileriosis.

IM-O-4

THE EFFICACY OF THE PARAMUNITY INDUCER PIND-ORF IN THE TREATMENT OF CANINE PARVOVIRIOSIS. A.L. Proksch¹, S. Unterer¹, U. Truyen², R.S. Mueller¹, K. Hartmann¹. ¹Clinic of Small Animal Medicine, LMU University of Munich, MUNICH, Germany, ²Institute for Animal Hygiene and Veterinary Public Health, University of Leipzig, LEIPZIG, Germany

Canine parvovirus is a common and severe disease, especially in puppies, and there is a need for drugs that can decrease severity of symptoms and accelerate recovery. The paramunity inducer PIND-ORF stimulates the immune system. Therefore, the aim of the study was to investigate whether PIND-ORF, used as an additional drug, leads to faster recovery in dogs with parvovirus. In total, 40 dogs with parvovirus were randomly assigned to two groups (20 dogs each). In all dogs, infection with canine parvovirus was diagnosed by fecal ELISA or polymerase chain reaction (PCR). Also, all dogs had clinical signs. The study was performed as prospective placebo-controlled, double-blinded trial. All dogs received either PIND-ORF or placebo, and additional standardized treatment for canine parvovirus. Clinical scores, complete blood count, and serum protein and albumin were evaluated daily (day 0 - 7) and at day 14. Viral shedding was measured on day 0, 3, 7, and 14 by fecal PCR and virus isolation. No significant difference could be found in clinical scores, most blood parameters, and duration of virus shedding when comparing dogs receiving PIND-ORF and dogs receiving placebo. The only significant difference was an increase in lymphocyte counts observed in the PIND-ORF group. Three dogs receiving placebo did not survive, but no significant difference between groups was determined concerning survival rate. In this study, no significant influence of the paramunity inducer

PIND-ORF on the course of parvovirus was determined. Therefore, there is no indication to recommend PIND-ORF therapy in canine parvovirus.

IM-O-5

COMPARISON OF DIFFERENT DIAGNOSTIC TOOLS FOR THE DETECTION OF BORRELIA BURGDORFERI ANTIBODIES IN DOGS. C. Barth¹, I. Krupka², R.K. Straubinger², E. Müller³, C. Sauter-Louis⁴, K. Hartmann⁵. ¹Clinic of Small Animal Medicine, LMU University of Munich, Germany, MUNICH, Germany, ²Institute for Infectious Medicine and Zoonotic Diseases, LMU University Munich, MUNICH, Germany, ³LABOKLIN Veterinary Diagnostic Laboratory, BAD KISSINGEN, Germany, ⁴Clinic for Ruminants with Ambulatory Clinic and Herd Health Management, LMU, MUNICH, Germany, ⁵Clinic of Small Animal Medicine, LMU University of Munich, MUNICH, Germany

Antibody tests are frequently used in the diagnosis of canine Lyme borreliosis, including immunofluorescence assays (IFA) detecting immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies, kinetic enzyme linked immunosorbent assays (KELA), and Western blot (WB). Recently, the SNAP[®]4Dx[®] test, an in house test using C₆ technology, came on the market. There are no studies so far comparing the diagnostic value of these methods. Aim of the study was to compare different diagnostic tools like IFA, KELA, SNAP[®]4Dx[®] test, and WB, and to determine sensitivity and specificity when compared to the gold standard WB. Two hundred canine sera were tested for the presence of *Borrelia* antibodies with the above mentioned tests. Sensitivity and specificity of IFA IgG was 76.6% (95% CI 46.87-86.72) and 87.1% (95% CI 80.06-91.90). Sensitivity and specificity of IFA IgM was 26.3% (95% CI 11.81-48.79) and 81.0% (95% CI 73.64-86.71). Sensitivity and specificity of KELA was 100% (95% CI 83.18-100) and 75.4% (95% CI 67.02-82.09). Sensitivity and specificity of SNAP[®]4Dx[®] was 84.2% (95% CI 62.43-94.48) and 98.5% (95% CI 94.83-99.60). SNAP[®]4Dx[®] showed almost perfect agreement with WB results (kappa 0.847). IFA IgG and IgM had very low sensitivity and specificity and cannot be recommended to diagnose *Borrelia* infection. KELA showed excellent sensitivity and can be recommended as screening test, but positive results require confirmation. SNAP[®]4Dx[®] had very good sensitivity and specificity and can replace the more labor-intensive WB, at least in untreated patients.

IM-O-6

MOLECULAR CHARACTERIZATION OF LEPTOSPIRA SEROVARS FROM CLINICALLY ILL DOGS AND COMPARISON WITH THE INFECTING SEROGROUP DETERMINED BY MICROSCOPIC AGGLUTINATION TEST. G. Hazart, Z. Djelouadji, C. Pouzot-Nevoret, A. Barthélémy, A. Kodjo, I. Goy-Thollot, M. Hugonnard. Vet Agro Sup, University of Lyon, MARCY L'ETOILE, France

The Microscopic Agglutination Test (MAT) is currently considered as the gold standard for the diagnosis of leptospirosis in dogs. However, it is not a perfect tool to predict the infecting serogroup as cross-reactions and paradoxical reactions do exist. The objective of this study was to determine the infecting serovar in 29 dogs with a positive Polymerase Chain Reaction (PCR) on one or more biological sample(s) by molecular typing and to compare the results with those provided by the highest MAT titer for each dog. Forty-one positive PCR biological samples (20 urine samples, 19 blood samples, one kidney sample and one cerebrospinal fluid -CSF- sample) from 29 dogs with a clinical suspicion of leptospirosis between 2008 and 2011 and at least one positive PCR on blood, urine, kidney or CSF (Kit Taqvet Pathogenic Leptospira, LSI, France) were submitted to molecular typing. The genomospecies were first determined by partial *rpoB* or partial 16S rRNA gene sequencing. The serovar was further identified by Multiple Loci Variable Number Tandem Repeat Analysis (MLVA). Three

Variable Number Tandem Repeat (VNTR) loci were used as markers for serovar identification. The genomospecies were *Leptospira interrogans* sensu stricto in 36 samples belonging to 25 dogs, *Leptospira borgpetersenii* in three samples (three dogs) and *Leptospira kirschneri* in two samples (two dogs). Interestingly, for one dog, we found a different species in the blood and in the urine. MLVA could unequivocally determine infecting serovar in 14 samples belonging to 13 dogs: Australis in one dog, Muenchen in three dogs, Fugis in one dog, Canicola in two dogs, Autumnalis in six dogs. For only two dogs among those 13, the infecting serovar identified by MLVA belonged to the infecting serogroup identified by MAT. For 16 samples belonging to 15 dogs, MLVA failed to identify the infecting serovar because one or more marker(s) could not be amplified. For 11 samples belonging to 9 dogs, amplification profile suggested coinfection or infection with a serovar that had not been previously characterized by MLVA. It must be noted that for some dogs, we were able to characterize the serovar in a single kind of sample. Despite lack of sensitivity of MLVA applied to clinical strains in our study, this rapid method could contribute to a better knowledge of the epidemiology of canine leptospirosis with some adaptations in the choice of markers.

IM-O-7

IMPACT OF TRICHOMONADS ON FECES QUALITY IN PUPPIES IN FRENCH BREEDING KENNELS. L. Diallo¹, A. Grellet², E. Viscogliosi³, B. Polack¹. ¹Université Paris-Est, Ecole Nationale Vétérinaire d'Alfort, MAISONS-ALFORT CEDEX, France, ²Royal Canin Research Center, AIMARGUES, France, ³Institut Pasteur de Lille, Centre d'Infection et d'Immunité de Lille, Université, LILLE CEDEX, France

Recently, two Trichomonads have been identified in diarrheal stool of puppies: *Pentatrichomonas hominis* (PH) and *Trichomonas foetus* (TF) [1]. TF infection in cats results in a chronic colitis. However in dogs, pathogenicity of TF and PH has never been studied. So the objective of this study was to evaluate the association between Trichomonads' infection in puppies and the presence of diarrhea. Faecal samples were collected prospectively from 273 puppies (4 to 13 weeks of age) in 3 French breeding kennels. For each puppy, a rectal swab was performed and the fecal consistency was evaluated using a 15-point numerical scale (1 = liquid feces, 15 = hard feces) [2]. Detection of Trichomonads was performed by using a commercially available system "In PouchTM TF test" (BioMed Diagnostics, Oregon USA). Evaluation of this media was done as already described [3]. Observation of motile Trichomonads organisms in the system culture was considered as a positive result. Nine positive culture systems, from one kennel, were frozen and single-tube nested PCR assays were performed on them in order to sequence and identify the Trichomonads. 29.7% (81/273) of the cultures were positive. 32.6% of the puppies (89/273) had gastrointestinal troubles. Puppies infected by Trichomonads had significantly more digestive problems than puppies not infected (49.4% vs 25.5%; $p < 0.05$). PH was systematically isolated in the 9 positives cultures. PH was the only Trichomonads isolated in the nine culture system tested by single-tube nested PCR assay. These results show the poor specificity of the medium to distinguish TF from PH. This observation underlines the necessity to use PCR for precise identification of type of Trichomonads. Trichomonads are significantly associated to the presence of digestive disorders in puppies. Some etiological studies on the subject (by considering the co-infection with parasites and viruses and by fulfilling Koch's postulates) are needed to determine whether the canine Trichomonads are etiological agents of diarrhea. Gookin JL *et al.* - Molecular characterization of trichomonads from feces of dogs with diarrhea. J. Parasitol., 2005, 91: 939-43 Grellet A *et al.* - Validation of a fecal scoring scale in puppies during the weaning period. Prev. med. vet (accepted for publication), 2012 Gookin JL *et al.* - Use of commercially available culture system for diagnosis of *Trichomonas foetus* infection in cats. J. Am. Vet. Med. Assoc., 2003, 222(10), 1376-79

IM-O-8

PROSPECTIVE MEDICAL EVALUATION OF 7 DOGS PRESENTED WITH FLY BITING. D. Frank, MC Bélanger, V. Bécuwe-Bonnet, J. Parent. Université de Montréal, SAINT-HYACINTHE, Canada

Fly snapping, fly-biting or jaw snapping are names given to a syndrome in which dogs appear to be watching something then suddenly leaping and snapping at it. Fly-biting dogs are generally referred to neurologists or behaviourists because the abnormalities are often interpreted as focal seizures or as obsessive compulsive disorder (OCD). There is one published case report of fly biting presumably caused by dietary intolerance in a Cavalier King Charles Spaniel. The aims of this case series were 1) to characterize fly biting, 2) perform a complete medical evaluation of dogs presented with fly biting, and 3) evaluate the outcome of this behaviour following appropriate treatment of the underlying medical condition. Seven dogs presented for fly-biting behaviour (FB) were assessed. All dogs underwent a complete medical and behavioural history as well as physical and neurological examinations. Further investigation was performed if an abnormality was found on examination or if the history was suggestive of an underlying problem. Based on clinical presentation, physical examination, neurologic examination, and laboratory test results, a diagnosis was made and a specific treatment recommended. Response to treatment was monitored and evaluated following phone conversations with owners at day 30, 60 and 90 from onset of treatment. Many gastrointestinal disorders were found in FB dogs which included eosinophilic and lymphoplasmacytic infiltration of the stomach and small bowel, delayed gastric emptying and gastroesophageal reflux. Complete resolution of the FB was observed in 5/6 dogs diagnosed and specifically treated for the underlying gastrointestinal (GI) disease. One dog was diagnosed with Chiari malformation and responded temporarily to pain management. In conclusion, this prospective case series indicates that fly biting behaviour may be caused by an underlying medical disorder, GI disease being the most common. Resolution of this behaviour is possible following specific treatment of the underlying medical condition.

IM-O-9

USEFULNESS OF SERUM ACUTE PHASE PROTEINS (APPS) IN CATS WITH BODY CAVITY EFFUSIONS TO HELP WITH A DIAGNOSIS OF FELINE INFECTIOUS PERITONITIS (FIP). K. Hazuchova, S. Held, R. Neiger. Small Animal Clinic Justus-Liebig-University, GIESSEN, Germany

Although several diagnostic tests have been developed to diagnose FIP, there are still difficulties to differentiate between FIP and diseases with similar clinical appearance in vivo. FIP is an inflammatory disease, therefore, as in other inflammatory conditions, the concentrations of APPs are expected to be increased. The aim of this study was to evaluate the ability of the APPs to distinguish FIP from other diseases. Serum samples from 88 cats presented with effusion were obtained for measurement of three APPs. The diagnostic work-up was performed with respect to FIP (JVIM 2011; 25: 1505) and further diagnostic procedures were performed depending on the medical condition. 20 cats were diagnosed as having FIP and 68 cats had another disease (cardiac 22, tumor 24, other 22). Serum amyloid A (SAA) and haptoglobin (Hp) were measured by automated analyser using feline validated assays (Eiken and Tridelta, respectively), alpha-1-acid glycoprotein (AGP) was measured using a manual method based on single radial immunodiffusion (Tridelta). The median concentrations of SAA, Hp and AGP were significantly ($p < 0.001$) higher in cats with FIP compared to cats without FIP (SAA: 98.5; range 1.3-163.4 $\mu\text{g/ml}$; 7.6; range 0.1-163.8 $\mu\text{g/ml}$), (Hp: 2.0; range 2.0-9.0 mg/ml ; 1.8; range 0.0-2.0 mg/ml), (AGP: 2900; range 960-5040 $\mu\text{g/ml}$; 690; range 120-4500 $\mu\text{g/ml}$). All major feline APPs seem to be useful diagnostic tools to help in differentiating FIP from other diseases. However, the concentration of APPs in some diseases (septic processes, disseminated neoplasias) was as high as in FIP.

IM-O-10

CANINE PROTOTHECOSIS IN THE NORTH OF ITALY: 4 CASES (2009-2011). E. Mercuriali¹, E. Bottero², F. Abramo³, B. Dedola⁴, E. Zini¹. ¹Istituto Veterinario di Novara, NOVARA, Italy, ²Clinica Albese, CUNEO, Italy, ³Università di Pisa, PISA, Italy, ⁴Clinica Veterinaria, MANTOVA, Italy

Protothecosis is an uncommon disease of people and animals caused by *Prototheca* spp., an unicellular aerobic algae. To date, about 30 cases have been described in dogs in North America and Australia. In Europe, only 4 cases have been documented in the last 2 decades (Poland, Italy, Greece and Spain). Affected dogs show signs referable to the gastro-intestinal tract, particularly the colon, but ocular and neurologic signs are also reported. The disease has an insidious onset, a slow progression and fatal course. The aim of the present study is to describe clinical and laboratory findings in 4 cases of canine protothecosis from the north of Italy, diagnosed between 2009-2011. Medical records were retrieved and information pertaining history, clinical and instrumental data, as well as follow-up, were collected. The median age of the 4 dogs was 8 years (range: 5-11), 3 of them were female and 2 were Boxers. Major complaints were chronic large bowel diarrhea with hematochezia and weight loss observed since a median time of 3 months (range: 1 to 7). Previous treatment with gastrointestinal diets, antiparasitic drugs and antibiotics yielded no improvement. Additionally, 2 dogs developed uveitis during the disease course. In all dogs a complete blood count, a serum biochemical profile, including protein electrophoresis, and abdominal ultrasound were performed; serum cTLI, folate and cobalamin were available in 3 dogs and urinalysis in one. The results of the above laboratory tests were normal. Ultrasonography was unremarkable in 2 dogs and showed increased colon wall thickness in the other 2. Definitive diagnosis was obtained from endoscopic biopsies of the colon and/or rectal scrapings in 3 dogs and from biopsies of the colon at necropsy in one. In each case spheroid, ovoid or irregularly-shaped organisms suggestive of *Prototheca* spp. were observed. Different treatments were attempted without benefit in 3 dogs. In one dog transient improvement was obtained with itraconazole. The median survival time was 5 months (range: 2-12). The present work indicates that protothecosis should be included in the list of differential diagnosis in dogs with large bowel diarrhea, especially in those with chronic refractory colitis or developing ocular signs. Dogs infected with *Prototheca* spp. have a guarded prognosis. Diagnosing protothecosis in 4 dogs over a 2-year period may suggest that the disease is emerging in some southern European countries.

IM-O-11

CCL2 AS A SERUM BIOMARKER OF IDIOPATHIC PULMONARY FIBROSIS IN DOGS. E. Krafft¹, E. Roels¹, H. P. Heikkilä², M.J. Day³, M.M. Rajamäki², C. Clercx¹. ¹Faculty of veterinary medicine, University of Liège, LIEGE, Belgium, ²Department of Equine and Small Animal Medicine Faculty of Veterinary Medicine, HELSINKI, Finland, ³School of Veterinary Sciences University of Bristol, BRISTOL, United Kingdom

Idiopathic pulmonary fibrosis (IPF) is an interstitial fibrotic pulmonary disease, mainly described in the West Highland White Terrier (WHWT). The diagnosis is challenging and ultimately relies on lung histopathology. Identification of biomarkers specific for the disease would be very helpful. CCL2 (MCP-1) is a chemotactic cytokine for monocytes. It is a known biomarker in human IPF. In dogs with IPF, increased CCL2 gene expression has been described in lung tissue. The aim of the present study was to compare serum CCL2 concentration in dogs with IPF versus healthy dogs and dogs with other chronic pulmonary diseases. Thirteen dogs with IPF (ten WHWTs, two Scottish Terriers, one Yorkshire) mean age 12 years, range 8-15), nine dogs with eosinophilic bronchopneumopathy (EBP) (various breeds, 5 years, 1-12), ten dogs with chronic bronchitis (CB) (various breeds, 9 years, 1-13) and ten healthy WHWTs (9 years, 3-14) entered the study. Diagnosis

was established after clinical, radiographical, bronchoscopic (and BALF analysis) examinations, as well as, in dogs with IPF, either lung high resolution computed tomography (six dogs) or histopathology (three dogs) or both (four dogs). CCL2 concentration in serum was determined by ELISA (Canine CLL2/MCP-1Quantikine[®], R&D Sytems). Results in the different groups were then compared using non-parametric test (Mann-Whitney rank sum test). Serum CCL2 concentration was elevated in dogs with IPF (median; interquartile range = 528.8 pg/mL; 444.7-692.0) compared to healthy WHWTs (344.0; 254.5-415.5), ($p < 0.001$). Serum CCL2 value in IPF dogs was higher than in EBP dogs (281.6; 163.9-416.5) ($p = 0.009$) and than in CB dogs (277.7; 137.3-364.7) ($p = 0.003$). The present study shows that (1) serum CCL2 values are significantly elevated in IPF dogs compared to healthy WHWTs; (2) serum CCL2 values are significantly elevated in IPF dogs compared to EBP and CB, suggesting that serum CCL2 could be a useful diagnostic biomarker of canine IPF.

IM-O-12

TRANSFORMING GROWTH FACTOR- BETA 1 AND ITS ACTIVATING PATHWAYS IN CANINE IDIOPATHIC PULMONARY FIBROSIS. E. Krafft¹, H.P. Heikkilä², M.J. Day³, I.R. Peters³, K. McEntee⁴, D. Peeters¹, M.M. Rajamäki², C. Clercx¹. ¹Faculty of veterinary medicine, University of Liège, LIEGE, Belgium, ²Department of Equine and Small Animal Medicine Faculty of Veterinary Medicine, HELSINKI, Finland, ³School of Veterinary Sciences University of Bristol, BRISTOL, United Kingdom, ⁴Faculté de Médecine, Université Libre de Bruxelles, BRUXELLES, Belgium

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial fibrotic disease, described in humans and in dogs. Etiology and pathogenesis of IPF are poorly known in both species, even if a genetic basis is suspected in dogs because of the predisposition of the West Highland white terrier (WHWT). Serum transforming growth factor beta 1 (TGFB1) concentration is elevated in both healthy WHWTs and WHWTs with IPF, as compared to healthy dogs of various breeds. In human IPF, pathways involving TGFB1, a cytokine with profibrotic properties, seem to be central in the pathogenesis and are considered as potential therapeutic targets. TGFB1 is produced as a pro-protein and usually stored as a latent complex. Activation of the latent complex is an important step that regulates TGFB1 function. Multiple activation mechanisms have been identified including binding to integrins and thrombospondin 1 (THBS1). The aim of the present study was to quantify TGFB1 expression, as well as expression of proteins involved in TGFB1 activation, by quantitative RT-PCR, in lung tissue from dogs with IPF versus control dogs. Total RNA was extracted from lung tissues from 14 dogs with IPF (12 WHWTs, 1 Scottish terrier, 1 Lhasa Apso) and 11 control dogs (various breeds). IPF was confirmed by histopathology on all samples. Expression of TGFB1, 2 integrins (ITGB6 and ITGB8) and THBS1 was measured by qRT-PCR. For each gene, a relative copy number was calculated for each sample and results were normalised using two stably expressed housekeeper genes (RPS18 and TBP). Statistically significant differences between the groups were assessed using a Student t-test or a Mann-Whitney Rank sum test with significance defined as a $p < 0.05$. Expression of TGFB1 and ITGB6 was not statistically different between the two groups. Expression of ITGB8 was significantly lower ($p < 0.001$) while THBS1 expression was significantly higher ($p = 0.016$) in the IPF group relative to controls. Results of the present study could not confirm that increased gene expression of TGFB1 by lung tissue is the source of the high circulating TGFB1 level in IPF. This study highlights different activating pathways of TGFB1 in IPF lungs compared to control lungs with a shift toward an increased activation via THBS1 in canine IPF.

IM-O-13

EFFECT OF BODY WEIGHT LOSS ON PULMONARY FUNCTION ASSESSED BY 6-MINUTE WALK TEST AND ARTERIAL BLOOD GASES IN OBESE DOGS. J. Manens¹, R. Ricci², C. Damoiseaux³, S. Gault³, M. Diez³, C. Clercx¹. ¹University of Liege, LIEGE, Belgium, ²University of Padoua, PADOVA, Italy, ³University of Liège, LIEGE, Belgium

Obesity is the most common nutritional problem in dogs, and its detrimental effect on basal lung function parameters has been recently shown using whole-body barometric plethysmography. The 6-Minute Walk Test (6MWT) has been recently demonstrated to be a non-invasive easy-to-perform test in clinical settings, able to discriminate between healthy dogs and dogs with pulmonary disease. The aim of this study was to investigate the effect of body weight loss (BWL) on pulmonary function assessed by 6MWT and arterial blood gas values. Six experimental Beagles and 6 privately-owned dogs, all obese but otherwise healthy, were enrolled in a diet-induced BWL program. Physical examination, BW and Body Condition Score (BCS) assessment, arterial blood gas analysis and 6MWT were performed when dogs were obese (BCS 8-9/9), and repeated with animals in the middle of their BWL program (overweight, BCS 6-7/9) and at the end of it (lean, BCS 5/9). For the 6MWT, dogs were walked for 6 minutes, along an inside 53m-long hallway. Heart rate (HR) and oxygen saturation (SpO₂) were measured by pulse oximetry before the test (pre-test value), after three minutes of walk (mid-test value) and at 0, 1, 2, 3 and 5 minutes post-test. All dogs concluded the BWL program (initial BW: 27.3±2.9 kg; final BW: 20.85±2.9, means±SE, $P \leq 0.001$). BWL caused a significant increase in the walked distance (lean: 581.8±40.9m; overweight: 582.7±44.4m; obese: 500.4±40.0m; means±SE, $P \leq 0.05$) and a decrease in pre-test respiratory rate (RR) (lean: 33±3.3/min; overweight: 40±3.6/min; obese: 49±4.1/min; means±SE, $P \leq 0.05$). Resting arterial blood gas results were not influenced by BWL and neither did the pre-test HR and SpO₂ values measured by pulse oximetry. Obese dogs showed significant higher HR mid-test values compared to overweight and lean dogs (lean: 122.0±7.5/min; overweight: 119.8±7.2/min; obese: 167.2±8.2/min; means±SE, $P \leq 0.001$). Moreover, SpO₂ values recorded at 0 and 1 minute post-test were significantly higher in overweight and lean dogs, compared to obese dogs. Also, HR values registered at 1, 2, 3 and 5 minutes post-test were all lower in overweight and lean dogs. In conclusion, obesity negatively affects the blood oxygenation level during and shortly after physical exercise in dogs, with subsequent HR increase. BWL induces a significant decrease in resting RR and it improves pulmonary function during exercise, even before achieving the targeted ideal BW. The 6MWT, but not pre-test arterial blood gas values, is an efficient tool to demonstrate the efficacy of BWL.

IM-O-14

MULTIPLATE CAN BE USED TO DETECT INCREASED PLATELET REACTIVITY IN DOGS WITH DISEASES KNOWN TO PREDISPOSE FOR HYPERCOAGULABILITY AND THROMBOSIS. C.B. Marschner¹, A.T. Kristensen¹, E.H. Spodsberg¹, L.R. Jessen¹, B. Wiinberg². ¹Copenhagen University, FREDERIKSBERG, Denmark, ²Novo Nordisk A/S, MAALOEV, Denmark

There are few diagnostic laboratory methods available for evaluation of platelet function and contribution to thrombotic events in the clinical setting. The impedance whole blood platelet aggregometer Multiplate[®] has recently become available. Although it is being marketed for monitoring effect of antiplatelet therapy, it can also be used for assessment of platelet aggregation in response to various agonists, reflecting platelet function, activity and reactivity in response to disease. The purpose of this study was therefore to investigate Multiplate[®] as a diagnostic tool for detection of variations in platelet aggregation in dogs with diseases known to predispose to hypercoagulability and thrombosis and to evaluate whether there is a correlation

between Multiplate aggregation response and the maximal amplitude (MA) measured by thromboelastography (TEG). Twenty clinically healthy dogs and eighteen diseased dogs with neoplasia, generalized inflammation or protein losing enteropathy or -nephropathy admitted to the University Hospital for Companion Animals, University of Copenhagen, were included in the study. Citrated and heparinised blood samples were collected. Multiplate® aggregations were performed on diluted heparinised whole blood for 12 minutes using ADP, Collagen (COL) and Arachidonic Acid (AA) as agonists and NaCl as buffer control. Results were recorded as area under the curve (AUC). Dilute (1:50000) Tissue Factor TEG analyses were performed on citrated whole blood. Diseased dogs had significantly increased AUC compared to healthy dogs for NaCl buffer control ($p=0.0005$), ADP ($p<0.0001$) and COL ($p=0.0048$) whereas no significant difference was obtained for AA as agonist ($p=0.3116$). TEG-MA was significantly higher ($p=0.0114$) in diseased dogs compared to healthy dogs. A significant correlation was not found between TEG-MA and Multiplate AUC using ADP ($p=0.1720$, $r=-0.3366$), COL ($p=0.2274$, $r=-0.2994$) or AA ($p=0.4304$, $r=-0.1982$). These results demonstrate that Multiplate® aggregation responses are significantly increased in a population of diseased dogs with diseases known to predispose to hypercoagulability and thrombosis, but results are not significantly correlated to TEG-MA. This suggests that the Multiplate method can be used to detect increased platelet reactivity in dogs with diseases known to predispose to hypercoagulability and thrombosis and that Multiplate provides additional information on platelet function than TEG alone in this patient group. Further studies are needed to determine how Multiplate and TEG-MA results correlate to thrombosis and whether there may be an added benefit of using them in combination.

IM-O-15

THE USE OF 20% HUMAN SERUM ALBUMIN IN 60 DOGS TREATED FOR HYPOALBUMINAEMIA: A REVIEW OF THE SIDE EFFECTS ENCOUNTERED AND INFLUENCE ON OUTCOME. M. Dunning¹, M. Augusto², J. Hurley², C.P. Sturgess³. ¹University of Nottingham, LEICESTERSHIRE, United Kingdom, ²Anderson Moores Veterinary Specialists, WINCHESTER, United Kingdom, ³Vet Freedom, BROCKENHURST, United Kingdom

Hypoalbuminaemia is a commonly identified biochemical dyscrasia. The clinical impact of this can be far reaching, particularly in severely affected animals. Problems recognised to ensue include altered colloid osmotic pressure and cavity effusions, clotting abnormalities, altered carriage of drugs, hormones and electrolytes, along with acid-base disturbances. The aim of the study was to determine the incidence of side effects encountered when administering 20% intravenous human albumin to dogs suffering with hypoalbuminaemia. Animals were presented to a specialist referral centre in Hampshire, UK for various conditions resulting in hypoalbuminaemia. Hypoalbuminaemia was considered to be present when the serum albumin concentration was $<20\text{g/l}$. A total of 69 albumin infusions were given to 60 dogs presenting with a serum albumin concentration of 17g/l or lower. Albumin was given as an intravenous infusion of 800mg (4ml)/ kg following premedication with chlorphenamine. The duration of administration was between 30 minutes and 4 hours. The dogs were monitored for potential adverse reactions during the administration of albumin and in the post-infusion period. Potential adverse reactions included hypotension, hyperthermia, tachycardia, tachypnea, peripheral oedema, agitation/restlessness and collapse. None of the animals showed adverse reactions during the administration of albumin or in the post-infusion period. One animal demonstrated mild hyperaesthesia that resolved prior to completion of the infusion. Of the animals presented, 39 survived to discharge, 15 animals were euthanased and 6 died. Each dog received an average of 1.23 (SD 0.46) albumin infusions during the period of hospitalisation. There was no significant difference in the starting albumin concentrations between the survivors and non-survivors. There was no significant difference in the increase in albumin concentration post-infusion between survivors and

non-survivors. There was no significant difference in the number of albumin infusions between the survivors and non-survivors. The concentration of albumin pre-infusion did not negatively impact on survival and discharge from the hospital. The results of this study demonstrate no significant complications during or following administration of 20% Human albumin solution in dogs. There was no association between the administration of albumin, number of albumin infusions or amount of albumin administered in any patient and outcome. Albumin infusion may improve the chances of severely hypoalbuminaemic dogs surviving to be discharged from the hospital. The use of human albumin for this purpose enables the limited supplies of canine plasma to be reserved for dogs needing plasma transfusion for other reasons.

NU-O-1

DO OBESE DOGS SUFFER FROM METABOLIC SYNDROME? A. Tvarijonavičiute¹, J.J. Ceron¹, S.L. Holden², V. Biourge³, P.J. Morris⁴, A.J. German². ¹University of Murcia, MURCIA, Spain, ²University of Liverpool, NESTON, United Kingdom, ³Royal Canin Research Center, AIMARGUES, France, ⁴The WALTHAM Centre for Pet Nutrition, MELTON MOWBRAY, United Kingdom

Recently, metabolic syndrome has gained attention in human medicine given its associations with development of diabetes mellitus and cardiovascular diseases. Canine obesity is associated with the development of insulin resistance, altered lipid profiles, and mild hypertension, but the authors are not aware of any existing studies examining the existence of MS in obese dogs. Thirty-five obese dogs were assessed before and after weight loss. The guidelines of the International Diabetes Federation were modified in order to produce a definition for canine metabolic syndrome (CMS), which included a measure of adiposity (using a 9-point body condition score [BCS]), systolic blood pressure, plasma cholesterol, plasma triglyceride, plasma glucose, and urine protein:creatinine ratio (UPCR). By way of comparison, total and regional body fat mass were assessed by dual-energy X-ray absorptiometry, whilst adiponectin, insulin, and high-sensitivity C-reactive protein (hsCRP) were also assessed with validated assays. Systolic blood pressure ($P=0.008$), cholesterol ($P=0.003$), triglyceride ($P=0.018$), insulin ($P<0.001$), and UPCR ($P=0.034$) all decreased after weight loss, whilst plasma adiponectin increased ($P=0.001$). However, hsCRP did not change with weight loss. Prior to weight loss, 10 dogs were defined as having CMS. There was no difference in total or regional body fat mass between these dogs and those who did not fit the definition of CMS. However, plasma adiponectin concentration was less ($P=0.004$), and plasma insulin concentration was greater ($P=0.01$) in CMS dogs. In this study, up to a third of obese dogs suffer from CMS, and this is characterized by hypoalbuminaemia and hyperinsulinaemia. These studies can form the basis of further investigations to determine pathogenetic mechanisms and the health significance for dogs, in terms of disease associations and outcomes of weight loss.

RE-O-1

PERCUTANEOUS FLUOROSCOPIC-ASSISTED PERINEAL APPROACH FOR RIGID CYTOSCOPY IN 9 MALE DOGS. C. Weisse, A. Berent. The Animal Medical Center, NEW YORK, United States of America

Cystourethroscopy has greatly enhanced the diagnosis and treatment of numerous conditions in veterinary medicine. Rigid telescopes used in female cytoscopy provide well-illuminated highly detailed images using rod lens system technology. The flexible ureteroscope has been used for male urethrocytoscopy but is limited in image quality and procedural abilities due to the fiberoptic system, diminished illumination, and smaller working channel. The purpose of this study was to describe the technique, efficacy, and complications using a novel percutaneous

perineal approach to the male urethra in order to gain access for rigid cystoscopy. The perineal approach was performed ten times in nine dogs for ectopic ureter laser ablation of idiopathic renal hematuria sclerotherapy. The dogs were placed in dorsal recumbency. Using fluoroscopic guidance, an 18 gauge renal access needle was advanced trans-perineally into the pelvic urethra. Guidewire access was obtained and the access site dilated to accept a 16Fr peel-away sheath. A rigid cystoscope was then placed through the sheath to perform the procedures. Urinary catheters were placed following three of ten procedures for three to eighteen hours. The only identified peri-operative minor complication included urination from the perineal site approximately six hours post-operatively once in a single dog. No signs of stranguria or pollakiuria or incisional complications were identified in any of the 9 dogs post-operatively at follow-up examination or contact (range 4 to 1248 days). The percutaneous perineal approach in male dogs for rigid cystoscopy appears to be a safe and effective means of facilitating endoscopic procedures.

RE-O-2

RENAL SPARING TREATMENT OF IDIOPATHIC RENAL HEMATURIA (IRH): ENDOSCOPIC SCLEROTHERAPY. A. Berent¹, C. Weisse¹, E. Branter¹, D. Bagley², R. Berg³, L. Adams⁴. ¹The Animal Medical Center, NEW YORK, United States of America, ²Thomas Jefferson University, PHILADELPHIA, United States of America, ³Stromsholm Small Animal Referral Hospital, STROMSHOLM, Sweden, ⁴Purdue University, WEST LAFAYETTE, United States of America

IRH results in chronic upper urinary tract bleeding. In humans, ruptured renal pelvic hemangiomas/angiomas are typically the cause. Although benign, anemia, ureteral and urethral obstruction(s) can ensue. With the advent of endourology renal-sparing therapies like ureteropyeloscopic-guided electrocautery or sclerotherapy has replaced ureteronephrectomy. The objective is to describe the use of endoscopic-fluoroscopic-guided sclerotherapy for the treatment of IRH in dogs and report the first clinical outcomes. Each UVJ was identified cystoscopically. Once the bleeding was confirmed a retrograde ureteropyelogram was performed. A ureteropelvic junction balloon was used for ureteral occlusion and pelvis filling volumes were recorded. Four dwells were performed (2 5% povidone iodine mixture; and 2 sterile liquid 0.5-1% silver nitrate). A double-pigtail ureteral stent was placed. Seven dogs had sclerotherapy. Five unilateral, 1 bilateral, and 1 developed contralateral bleeding (n=9 units). Five were right and 4 left-sided. There were 6 males and 1 female. The median age and weight was 6 years and 27.5kg, respectively. Median procedure time was 150 minutes. There was 1 complication of severe renal discomfort and pyelectasia in an unstented dog. Cessation of hematuria occurred in 6/9 renal units (median 12 hours). Two had recurrence within 3 weeks; both resorted to intermittent mild hematuria. Two failed treatment. Median follow-up time was 5 months (range, 1.5-19). Overall, topical sclerotherapy for IRH can be safe and effective. This is the first report of local sclerotherapy for IRH in dogs and could be considered a valuable endoscopic-guided therapy prior to ureteronephrectomy. Further investigation is required.

RE-O-3

INTRARENAL ENDOSCOPIC NEPHROLITHOTOMY FOR REMOVAL OF COMPLICATED NEPHROLITHIASIS IN 9 DOGS AND 1 CAT. A. Berent¹, C. Weisse¹, A. Aarhus¹, D. Bagley². ¹The Animal Medical Center, NEW YORK, United States of America, ²Thomas Jefferson University, PHILADELPHIA, United States of America

Percutaneous nephrolithotomy (PCNL) is considered the standard of care for removal of nephroliths >1.5 cm in people, minimizing morbidity and preserving renal function. Success rates are reported to be 90-100%. Most veterinary nephroliths remain clinically silent and removal is only recommended for complicated

stones. Morbidity of nephrotomy can be severe. The objective is to describe endoscopic-guided nephrolithotomy (ENL) in canine and feline patients and report clinical outcomes, hypothesizing it is safe and effective. Patients that had either PCNL or surgically-assisted endoscopic nephrolithotomy (SENL) were retrospectively evaluated. A renal puncture needle and balloon-dilation-sheath combination was used for tract formation. A nephroscope provided visualization for intracorporeal lithotripsy. Stone fragments were removed and a ureteral stent was placed. Nine dogs and 1 cat (12 renal units) were included. Four had PCNL and 6 SENL. Indications included recurrent UTIs (4), worsening azotemia (4), and ureteral-outflow obstructions (2). Median weight was 8.2 kg (3.1-26.9). Stone composition was calcium oxalate (6), mixed struvite (2), urate (1), and cystine (1). Median stone size was 2 cm (0.7-5). Median pre- and 3 month post-operative creatinine was 1.3 (0.8-9.1) and 1.1 mg/dL (0.6-6.1), respectively. The median procedure time was 165 minutes. Successful removal of all stones were documented in 11/12 (91.6%). Procedure-related complications occurred in 3 units, all were easily managed. Median follow-up time was 150 days (4-2007). Four patients are still alive. No patient died from the procedure. Overall, ENL can be safely performed in dogs and cats, yielding similar success rates to people. Advanced endourologic experience is recommended.

RE-O-4

SURVIVAL OF CATS WITH NEWLY DIAGNOSED CHRONIC KIDNEY DISEASE (CKD) IS ASSOCIATED WITH PLASMA FIBROBLAST GROWTH FACTOR 23 (FGF-23) CONCENTRATION. R.F. Geddes, J. Elliott, H.M. Syme. Royal Veterinary College, LONDON, United Kingdom

FGF-23 is a key regulator of plasma phosphate concentration. It is elevated in cats with naturally occurring CKD and increases as renal function declines. Elevated FGF-23 concentrations are an independent predictor of survival time in human haemodialysis patients, but this association has not previously been examined in cats with CKD. This study investigated if FGF-23 was independently associated with survival time (all cause mortality) in cats with newly diagnosed CKD. Cats diagnosed with CKD at two London-based first opinion practices between 2000 and 2011 were identified. CKD was defined as plasma creatinine concentration >177µmol/l with concurrent urine specific gravity (USG) <1.035 or plasma creatinine concentration >177µmol/l on two consecutive visits. Cats were excluded if no residual EDTA plasma was available to measure plasma FGF-23 concentration within 42 days of the date of diagnosis of CKD. FGF-23 concentrations were measured using a previously validated human intact FGF-23 ELISA. Plasma FGF-23, creatinine, phosphate and total calcium concentrations, packed cell volume (PCV), systolic blood pressure (SBP), USG and age were entered into univariable Cox regression models of survival time. FGF-23 concentrations were logarithmically transformed due to a highly skewed distribution. Statistical significance was defined as P<0.05. Variables with P<0.05 were carried forwards into a backwards, stepwise multivariable Cox regression analysis of survival time. Ninety-one cats were included in the study. At the end of the follow-up period (February 2012), 64 cats had been euthanased or died (median (range) survival time 236 (0 - 1766) days) and 27 cats were alive or lost to follow-up (median (range) survival time 696 (42 - 1311) days). Median (range) age at diagnosis (n=85) was 14.0 (6.6 - 18.3) years. Univariable Cox regression analysis indicated that plasma creatinine (P<0.001), phosphate (P<0.001) and log-FGF23 (P<0.001) concentrations were negatively associated with survival time, and that PCV (P<0.001) and USG (P<0.001) were positively associated with survival time. In the multivariable model (n=82), plasma logFGF23 (hazard ratio (HR)=1.327, 95% confidence interval (CI) for HR=1.072-1.644; P=0.009) and creatinine concentration (HR=1.003, 95% CI for HR=1.002-1.004; P<0.001) were negatively associated with survival time, and PCV (HR=0.936, 95% CI for HR=0.885-0.990; P=0.020) was positively associated with survival time. Plasma FGF-23 concentration is a novel prognostic indicator in feline CKD, independent of other factors including plasma creatinine concentration and PCV. Future studies should investigate whether

FGF-23 can be used as a biomarker to improve the management of phosphate homeostasis in feline CKD, thus potentially increasing survival time.

RE-O-5

PROSPECTIVE EVALUATION OF RAGDOLL AND CONTROL CATS FOR KIDNEY DISEASE BY ROUTINE LABORATORY PARAMETERS AND ULTRASONOGRAPHY. D. Paepe, V. Bavegams, A. Combes, J. Saunders, S. Daminet. Faculty of Veterinary Medicine, University of Ghent, MERELBEKE, Belgium

Ragdoll breeder organizations often forewarn Ragdoll cat owners that renal problems may develop due to polycystic kidney disease (PKD), chronic interstitial nephritis, familial renal dysplasia or nephrocalcinosis. In several European countries, screening of Ragdoll cats for kidney disease is already performed for years, without scientific evidence. Therefore, we aimed to investigate if Ragdoll cats are predisposed for kidney disease. This prospective study evaluated serum creatinine and urea concentrations, routine urinalysis and renal ultrasonography in apparently healthy Ragdoll cats (RC), and compared their findings with apparently healthy age-matched non-Ragdoll cats (NRC). All Ragdoll cats also underwent genetic PKD testing. In total, 133 Ragdoll (mean \pm SD 2.7 ± 1.8 years, 4.2 ± 0.9 kg) and 62 non-Ragdoll (2.7 ± 1.6 years, 4.1 ± 0.8 kg) cats were included. Serum creatinine (RC: 145.5 ± 29.1 μ mol/L; NRC: 139.6 ± 33.1 μ mol/L) and urea (RC: 7.6 ± 1.5 mmol/L; NRC: 8.0 ± 1.3 mmol/L) concentrations did not differ significantly between groups. Serum creatinine exceeded the reference interval in three Ragdoll and one non-Ragdoll cats. Serum urea concentration exceeded the reference interval in two Ragdoll and one non-Ragdoll cats. Urine specific gravity was significantly lower in non-Ragdoll cats (RC: 1.056 ± 0.009 ; NRC: 1.049 ± 0.013 ; $P < 0.001$). Based on the laboratory parameters, one Ragdoll cat was diagnosed with IRIS stage 2 chronic kidney disease (CKD). Renal infarcts were detected significantly more often in Ragdoll cats (RC: 9/133; NRC: 0/62; $P = 0.029$). For the other renal ultrasonographic parameters (kidney size, renal capsule, renal shape, cortical and medullary echogenicity, corticomedullary distinction, medullary rim sign, dystrophic mineralization, cavitary lesions, solid mass or nodule, and renal pelvis), significant differences were not found between Ragdoll and non-Ragdoll cats. Although not significant, the ultrasonographer diagnosed CKD in six cats, all Ragdoll cats ($0.5 < P < 1$). One of these six cats was the Ragdoll cat with IRIS stage 2 CKD. In one Ragdoll cat, PKD could not be excluded on ultrasonography because one cyst was detected in one kidney. However, none of the Ragdoll cats was genetically positive for PKD. Based on this study, PKD and CKD appear to be uncommon in Ragdoll cats residing in Belgium and the Netherlands. However, renal infarcts were seen more commonly in Ragdoll cats compared to an age-matched control group. The clinical significance of this finding is currently uncertain and requires further investigation.

RE-O-6

RENAL MORPHOLOGY AND FUNCTION IN CATS WITH DIABETES MELLITUS. E. Zini¹, S. Benali², L. Coppola³, F. Guscetti⁴, M. Ackermann⁵, T.A. Lutz⁶, C.E. Reusch¹, L. Aresu². ¹Clinic for Small Animal Internal Medicine, University of Zurich, ZURICH, Switzerland, ²Department of Comparative Biomedicine and Food Sciences, University of Padova, PADOVA, Italy, ³Department of Animal Medicine, Production and Health, University of Padova, PADOVA, Italy, ⁴Institute of Veterinary Pathology, University of Zurich, ZURICH, Switzerland, ⁵Institute of Virology, University of Zurich, ZURICH, Switzerland, ⁶Institute of Veterinary Physiology, University of Zurich, ZURICH, Switzerland

In humans, diabetes mellitus (DM) is an important cause of renal damage. Main lesions include thickening of the glomerular basement membrane and mesangial expansion, whereas tubular atrophy and vascular hypertrophy are less frequent. In cats, although diabetes is a common endocrinopathy, it is yet

unknown whether DM causes renal damage. The aim of the present study was to compare renal histopathological features and clinical parameters of kidney function in diabetic cats against a well-matched control population. Formalin-fixed, paraffin-embedded kidney samples were retrieved from diabetic and control cats that died between 1997 and 2009 due to any disease at the Clinic for Small Animal Internal Medicine, University of Zurich (Switzerland), and in which a post-mortem examination was performed. Control cats were selected to be matched for age, sex, breed and body weight. Serum creatinine and urea levels were analyzed if they had been measured within 10 days before death. Kidney sections were stained with haematoxylin-eosin, periodic acid-schiff (PAS), Masson's trichrome, acid fuchsin orange-g (AFOG), and periodic acid methenamine silver (PAMS). With optical microscopy glomerular, tubulointerstitial and vascular parameters were identified and scored using a grading scale. Data were analyzed with contingency tables and t-tests. Thirty-two diabetic cats and 20 matched controls were included. With optical microscopy, scores of glomerular lesions (i.e., sclerotic glomeruli, mesangial or endocapillary hypercellularity, increased mesangial matrix, immunodeposits, glomerular basement membrane thickening, mesangial interposition), tubulointerstitial lesions (i.e., inflammation, fibrosis, tubular atrophy, necrosis and lipidosis, intratubular mineralizations) and vascular lesions (i.e., small or large artery hypertrophy) did not differ between the 2 groups. Overall, glomerular, tubulointerstitial and vascular lesions were observed in 43.8%, 57.9% and 6.3% of diabetic cats and in 57.9%, 78.9% and 15.7% of the controls. Similarly, serum creatinine and urea levels were not different between groups (creatinine: 197 ± 42 vs. 199 ± 46 μ mol/l, reference: 98-163 μ mol/l; urea: 18.2 ± 2.5 vs. 18.4 ± 4.6 mmol/l, reference: 7.4-12.6 mmol/l). The results suggest that DM in cats does not lead to microscopically detectable renal lesions or clinically relevant renal dysfunction when compared to a well-matched control group. We hypothesize that the short life expectancy of diabetic cats and the low prevalence of hypertension are main reasons for the difference to human diabetics.

RE-O-7

NON-INVASIVE DIAGNOSTIC EVALUATION INCLUDING QUALITATIVE PROTEINURIA TO DETECT AN EARLY RENAL DAMAGE IN CANINE LEISHMANIASIS. A. Buono¹, J. Duque², E. Ferlizza¹, C. Zaragoza², R. Barrera², G. Isami¹, F. Dondi¹. ¹Alma Mater Studiorum - University of Bologna, OZZANO DELL'EMILIA, Italy, ²Dept. of Vet. Internal Medicine - HCV - University of Extremadura, CACÉRES, Spain

Urine markers are advocated to early detect kidney damage in the clinical practice, nevertheless histology remains the *gold standard*. The aim of this study was to evaluate quali-quantitative proteinuria and possible renal damage using different non-invasive tests in dogs affected by leishmaniasis. Based on clinical signs and serology/cytology, 26 affected dogs (Leish) were included. Fifteen healthy, non-proteinuric dogs were selected as Control. Upon admission, all dogs underwent to physical examination, Systolic Blood Pressure (SBP) measurement, clinicopathological evaluation (CBC, Urea, Creatinine, ALT, ALP, Glucose, Calcium, Phosphorous, Sodium, Potassium, Cholesterol, Triglyceride, Albumin, Total Protein), serology, urinalysis, ultrasound examination and Renal Resistive Index (RRI) determination. Urine Total Protein and Urine Albumin to Creatinine ratios (UPC; UAC), urine High Resolution agarose and Silver Staining Sodium-Dodecyl-Sulphate-PolyAcrylamide gel electrophoresis (HRE; SDS-PAGE) were performed. A cut-off of 66 kDa was selected to classify bands in High or Low Molecular Weight (HMW; LMW). Data were analyzed with non-parametric statistics and ROC curve analysis (ROC). A difference was considered significant for $p < 0.05$. In 9/26 dogs Creatinine concentration was above the reference interval (Median 0.85, Mean 1.84, range 0.2-12.8, R.I. 0.65-1.4 mg/dl) and in 15/26 the Urine Specific Gravity (USG) was < 1030 (Median 1025, Mean 1031, range 1012-1050). Proteinuria (UPC > 0.5) was detected in 16/26 dogs (P), 5/26 were borderline proteinuric (BLP; UPC 0.2-0.5) and 5/26 were non-proteinuric (NP, UPC < 0.2). Leish dogs presented significantly higher UPC (Mean 3, Median 1.29) and UAC (Mean 1.62, Med-

ian 0.29). RRI values were significantly higher in Leish (Mean 0.72) than Control (Mean 0.64). RRI was significantly correlated to WBC ($r=0.51$), Hemoglobin ($r=0.52$) and Albumin concentrations ($r=0.61$), USG ($r=0.60$) and UPC ($r=0.48$). HRE and SDS-PAGE protein patterns allow to distinguish P from NP and Control dogs. SDS-PAGE revealed a significantly higher number of bands in Leish dogs (35-40) than in Control (25-30). NP and BLP dogs presented a significantly lower number of LMW bands than P. Number of bands was significantly correlated to UPC ($r=0.66$) and UAC ($r=0.64$). Using a cut-off value of 32 SDS-PAGE bands to discriminate between Leish and Control, ROC showed for UPC >0.17 , 89% Sensitivity and 88% Specificity and for UAC >0.013 , 94% Sensitivity and 82% Specificity. The Areas under the Curve for UPC and UAC were 0.89 and 0.92, respectively. Non-invasive methods, particularly urinary SDS-PAGE, could be useful to detect an early renal damage in canine leishmaniasis. Further studies are required to correlate these findings to renal histology.

RE-O-8

PLASMA AND URINE NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) IN DOGS WITH ACUTE KIDNEY INJURY (AKI) OR CHRONIC KIDNEY DISEASE (CKD). S. Steinbach¹, J. Weis¹, A. Schweighauser², T. Francey², R. Neiger¹. ¹Small Animal Clinic (Internal Medicine), Justus - Liebig - University, GIESSEN, Germany, ²Small Animal Internal Medicine, Vetsuisse Faculty, University of Bern, BERN, Switzerland

Early diagnosis of AKI and differentiation from non-renal disease or CKD remains challenging in veterinary medicine. In human medicine NGAL is used as a real time indicator of AKI but few data exist in veterinary medicine. In this study plasma and urine NGAL was measured in 18 healthy dogs with normal GFR (plasma inulin clearance) and 83 dogs with renal azotemia (creatinine $> 1.4\text{mg/dl}$ and/or urea $> 59\text{mg/dl}$ persisting at least 24 hours after correction of prerenal factors). Based on history, clinical course, laboratory and ultrasonographic findings, azotemic dogs were diagnosed with AKI ($n=53$) or CKD ($n=30$). Urine and plasma NGAL was measured with a dog NGAL ELISA Kit (Bioporto[®] Diagnostics A/S, Gentofte, Denmark). Intra-assay variability for plasma and urine NGAL was 3.1% and 4.8%, respectively. Azotemic dogs had significantly higher plasma NGAL concentrations and urine NGAL-creatinine ratios compared to healthy dogs ($P < 0.001$, Mann-Whitney U-Test). Median (min-max) plasma NGAL concentration in healthy dogs, dogs with AKI and CKD was 10.7 (2.5 - 21.2) ng/ml, 49.1 (5.7 - 469.0) ng/ml and 35.3 (7.7 - 97.9) ng/ml, respectively. Using a multiple linear regression model in the azotemic dogs with NGAL as dependent and age, weight, sex, AKI vs. CKD, dialysis and survival as independent variables revealed a significant differ-

ence only for AKI vs. CKD ($P = 0.005$). In conclusion, NGAL can be measured successfully in plasma and urine of healthy dogs and dogs with kidney disease. Dogs with AKI had significantly higher plasma NGAL concentration compared to dogs with CKD.

RE-O-9

URINE CONCENTRATIONS OF PURINE METABOLITES IN UK CAVALIER KING CHARLES SPANIELS. A.M.L. Jacinto¹, R.J. Mellanby¹, M.L. Chandler¹, N.X. Bommer², H. Caruthers², L.D. Fairbanks³, A. Gow¹. ¹Royal (Dick) School of Veterinary Studies, ROSLIN, MIDLOTHIAN, Scotland, ²Tay Valley Veterinary and Equine Practice, PERTH, Scotland, ³Purine Research Laboratory, St Thomas Hospital, LONDON, United Kingdom

Xanthine urolithiasis is a rare condition accounting for 0.1% of all canine urolithiasis in one study. This pathology has been reported as a primary disorder in dogs, most notably in Cavalier King Charles Spaniels (CKCS). Xanthine is an intermediate product of purine metabolism, which is converted from hypoxanthine by xanthine oxidase. Xanthine is only slightly soluble in urine and therefore hyperxanthinuria may lead to urolith formation. It has been speculated that some CKCS have an inherited mutation in the xanthine oxidase gene. In humans, isolated deficiency of xanthine oxidase occurs rarely and approximately 50% of individuals are asymptomatic, despite having significant xanthinuria. Therefore we hypothesised that asymptomatic xanthinuria may be commonplace in the UK population of CKCS. In support of this, a previous case report of a symptomatic CKCS reported significant xanthinuria occurring in an asymptomatic sibling. In order to examine the prevalence of xanthinuria in CKCS, urine concentrations of hypoxanthine and xanthine metabolites as well as creatinine were measured in 35 client-owned Cavalier King Charles Spaniel dogs and 24 dogs of other breeds from three first-opinion veterinary practices in the UK. Urine samples were collected by free catch and purine metabolites were measured by high-performance liquid chromatography. Ratios of xanthine/creatinine and hypoxanthine/creatinine from the two populations were compared by Mann Whitney U test and were found not to be significantly different ($p=0.41$ and $p=0.59$ respectively). In the control population, the xanthine/creatinine ratio ranged from 0.00018 to 0.01611 (median 0.00069), while in the CKCS population it ranged from 0.000154 to 0.005794 (median 0.000435). These results are markedly lower than the previously reported case of xanthine urolithiasis in a UK CKCS dog, which utilised the same reference laboratory (xanthine/creatinine ratio 0.406). These data suggest that asymptomatic xanthinuria is not prevalent in the UK CKCS population.