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.

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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 ± 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 µmol/L; NRC: 139.6 ± 33.1 µmol/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 medullar 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.

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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 haematoxilin-eosin, periodic acid-schiff (PAS), Masson's trichrome, acid fuchsine 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, tubulointestitial 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 µmol/l, reference: 98-163 µmol/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.

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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. Steinbach[1], J. Weis[1], A. Schweighauser[2], T. Francey[2], R. Neiger[1]. [1]Small Animal Clinic (Internal Medicine), Justus - Liebig - University, GIESSEN, Germany, [2]Small 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 > 1.4mg/dl and/or urea > 59mg/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 difference 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. Jacinto[1], R.J. Mellanby[1], M.L. Chandler[1], N.X. Bommer[1], H. Carruthers[2], L.D. Fairbanks[3], A. Gow[1]. [1]Royal (Dick) School of Veterinary Studies, ROSLIN, MIDLOTHIAN, Scotland, [2]Tay Valley Veterinary and Equine Practice, PERTH, Scotland, [3]Purine 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.