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LEFT VENTRICULAR HYPERTROPHY IN A CLOSED COLONY OF 1 PERSIAN CATS. L. Martin, E. VandeWoude, J. Soren, D. Brown, College of Veterinary Medicine, Colorado State University, Fort Collins, CO.

Hypertrophic cardiomyopathy (HCM) associated with left ventricular hypertrophy (LVH) may be a hereditary disease in cats. A family of Maine coon cats which carries this defect has been described. Familial forms of HCM have been documented in man and appear to be autosomal dominant. A defect in the beta-heavy chain myosin gene has been identified as a cause of this disease in humans. The purpose of this study was to determine if the etiology of LVH in a closed colony of cats was genetic. A partially inbred colony of Persian-anxiety cats was noted to have a high incidence of heart murmurs. These cats were either hetero- or homozygous for Gheekish Higashi Syndrome, an autosomal recessive lysosomal fusion defect which has not been associated with cardiac pathology in cats or other species. Echocardiography of colony members revealed that 15 of 28 cats (54%) had LVH, some identified as young as 4 months of age. Seventeen of 28 cats (61%) also had altered blood flow kinetics detected by color flow and continuous wave doppler. Fourteen animals were followed with echocardiography over a 4-12 month period. Seven of these cats showed progression of cardiac disease, either by increase or development of LVH. Serum chemistry profiles, complete blood counts and serum thyroid hormone levels were within normal limits. Plasma atrial natriuretic factor levels in 4 LVH-affected cats were significantly elevated (p < 0.05) with respect to 5 control cats. Direct blood pressure measurements were normal to slightly elevated relative to published normal values, but were not significantly different when colony members were compared to control cats. Autopsy, histologic, and histopathology of retinal renal and pulmonary vasculature have not revealed any changes suggestive of hypertensive disease.

The high incidence of LVH in this colony suggests that the disease is inherited in an autosomal dominant pattern and may serve as a model of the disease in humans. The relationship of this syndrome with hypertension warrants further investigation.

COLOR FLOW DOPPLER ESTIMATION OF MITRAL 3 REGURGITATION USING THE PROXIMAL FLOW CONVERGENCE METHOD IN DOGS WITH CHRONIC DEGENERATIVE MITRAL VALVE DISEASE (CDMDV). W. A. Brown and M. D. Kittleson. School of Veterinary Medicine, University of California, Davis, CA.

Previous basic and human clinical studies have demonstrated that mitral regurgitant stroke volume (RSV) and fraction (RF) can be accurately estimated using the proximal flow convergence region (PFCR) method. To document the magnitude of MR in dogs with CDMDV, a study utilized the PFCR method to estimate RF in dogs with different clinical stages of CDMDV. A blinded observer judged the clinical severity of MR to be mild, moderate, or severe using radiographic and echocardiographic assessment of left heart size, presence of an episode of heart failure, and size of the MR color Doppler jet. The RSV index (I), forward SVI, and RF were calculated using the PFCR method and aortic Doppler and area measurements. These were compared with the clinical assessment and were regressed to other indices of MR severity (left atrial diameter/aortic diameter [LA/AO], LA surface area [SA/AO]).

Five dogs had clinically mild MR. Four of these dogs had an RF<45% (21-42%) while 1 dog had an RF of 72%. Three dogs had moderate MR. All had an RF between 45% and 75% (45- 72%). All 9 dogs with clinically severe MR had an RF > 75% (77- 88%). Regression analysis revealed a good correlation between LA/AO and RF (r=0.86) and between LSA/AO and RF (r=0.78).

In conclusion, dogs with clinically severe MR have hemodynamically massive regurgitation (RF's >75%) consistently while dogs with clinically mild to moderate disease have lesser RF's. There is a reasonable correlation between LA size and PFCR calculated RF in dogs with CDMDV.

ECG AND PATHOLOGIC CHARACTERIZATION OF RABBIT CORONAVIRUS INFECTION. 'L K Alexander, 'DW Keene, 'O Gertz, 'Y Youn, 'DS Small, and 'RS Baric University of North Carolina School of Public Health, 'School of Medicine, and the 'North Carolina State University College of Veterinary Medicine, Raleigh, NC.

This study describes ECG changes and cardiac pathology observed following infection of 31 NZ white rabbits with coronavirus (RbCV). Six lead ECGs were recorded for at least 5 minutes 2x daily with rabbits gently restrained in stalls. Recordings started 2 days before RbCV infection and continued on survivors through day 50, when all survivors were euthanized. Specimens for cardiac pathologic and morphometric exams were obtained within 12 hours of death. The ECG and pathologic changes following RbCV infection were divided into three phases. Ten of the 31 rabbits died in the acute phase of infection (days 1-5), characterized by mild cardiomyopathy with scattered degeneration and necrosis of cardiac myocytes. In the acute phase ECGs, sinus tachycardia (74%), ventricular (V) (10%) and supraventricular (SV) (6.5%) ectopy as well as 1° and 2° AV block and right bundle branch block were observed. The subacute phase (days 6-12) was fatal to 7 rabbits. Pathologic examination revealed severe biventricular dilation, myocarditis, pulmonary venous congestion, and pleural effusion. Persistent sinus tachycardia (90%) with significantly reduced QRS and T wave voltages, occasional V and SV tachyarrhythmias, and 1° and 2° AV block were observed. No animals died spontaneously during the chronic phase (days 13-50), characterized by biventricular dilation, interstitial and replacement myocardial fibrosis with myocyte hypertrophy and ongoing myocarditis. The sinus rate and QRS and T wave voltages returned toward normal, although V and SV arrhythmias and conduction disturbances persisted in approximately 20% of animals.

We conclude that pathologic and ECG changes observed during RbCV infection mimic those of canine or human myocarditis, heart failure, and dilated cardiomyopathy.

INOTROPIC EFFECTS OF MEDETOMIDINE IN AUTONOMICALLY-BLOCKED DOGS. H.S.A. de Morais, W.W. Mair Jr, Ohio State University, Columbus, OH.

Medetomidine is a new sedative drug that acts primarily by stimulating alpha-adrenoreceptors. The effects of medetomidine upon load-dependent and load-independent indexes of left ventricular contractility and hemodynamics were studied in 8 chloralose-anesthetized, autonomicomically-blocked dogs. Left ventricular volume was obtained by the impedance catheter technique and left ventricular and aortic pressure were obtained by micromanometer catheter. Left ventricular contractility was assessed by the maximum rate of increase in ventricular pressure (dP/dtmax), the slope of the end-systolic pressure volume relationship (Ees), preload recruitable stroke work (PRSW) and dP/dtmax-end-diastolic pressure relation (SDP). Dogs received 5 or 10 μg/kg of medetomidine IV. The dP/dtmax increased significantly 30 minutes after either dose of medetomidine. The Es did not change. Both SDP and PRSW increased 5 minutes after either dose of medetomidine. Mean arterial pressure, left-ventricular end-diastolic and end-systolic pressure, peripheral vascular resistance and effective arterial elastance (Es) increased 5 minutes after either dose of medetomidine. Stroke volume, cardiac output and stroke work decreased 5 minutes after medetomidine administration. End-diastolic volume did not change. End-systolic volume increased but the difference was not significant. Our study suggests that medetomidine increases inotropy and vascular resistance in autonomicomically-blocked dogs and that both ventricular and vascular responses to pharmacologic manipulation must be considered for a complete understanding of a drug's cardiovascular effects.
DILTZIAZEM PHARMACOKINETICS AND 5 PHARMACODYNAMICS IN CATS. Atkins, C, Johnson, L, Keene, B, Bai, S. College of Veterinary Medicine, North Carolina State University, Raleigh, NC.

Diltiazem (D) is currently used to treat hypertrophic cardiomyopathy in cats and may also have use in the management of hypertension and supraventricular arrhythmias. Because there are neither pharmacokinetic (PK) nor dynamic (PD) data regarding this drug in cats, and because it is assumed that tit dosing is required, we sought to evaluate the PK and PD effects of D and a long acting form (CD), each at steady state (SS), in normal cats.

Four healthy female cats were studied, each receiving D IV (0.2 mg/kg), D PO (1 mg/kg tid), or CD PO (10 mg/kg q24h) in random order with at least 10 T1/2 elapsing before the subsequent drug was administered. Drug concentrations ([D]) were determined by HPLC. PD effect over 24 hours was evaluated by hem rate from cats receiving no drug (C) and at D and CD.

Mean PK data for D (and CD) were: bioavailability- 94% (38%); volume of distribution- 1.88 Ukg; clearance- 14.4 ml/min/kg; T1/2-125 (395) min. Peak [D] and [CD] were reached at 30 min and 6 hrs, respectively. [D] and [CD] remained in the prolonged therapeutic range (50-300 ug/ml) for 5 and 24 hrs, respectively. Mean 24 hr and 1st hr HR and PR interval (PR), using automatic hourly ECG, obtained from cats receiving no drug (C) and at SS for D and CD.

We conclude that probable therapeutic blood concentrations can be obtained with D and CD at the doses utilized. D should be administered tid and CD q24h. The lack of a demonstrable PD effect may be due to the small numbers of cats or the insensitivity of the tests for PD, but might also have been due to the lack of a pharmacologic effect.

FELINE ENDOCARDITIS: A CLINICAL/PATHOLOGICAL STUDY

Endocarditis (EMC) was first described histopathologically in 1974. The purpose of our study was to identify risk factors and reliable clinical diagnostic criteria consistent with the gross and histologic features of EMC. The diagnosis was confirmed in 26 cats based on post mortem evidence and suspected in 18 others with clinical features similar to those of the necropsied cats. Signalements were compared to those of the total hospital population. History, signalment, seasonal incidence, clinical signs, thoracic radiographs, ECG, M-mode and 2D echo variables were evaluated and correlated with histologic findings. Cats with confirmed EMC were young (mean 3.4 years). A male predisposition was observed (62%). Respiratory distress was part of the clinical presentation in 96% of confirmed cases. A recent stressful event (declaw, vaccination, neutering) 5-10 days prior to presentation occurred in 62% of this group. 73% of all 44 cats presented during the months of Aug.-Nov. Cardiomegaly (62%) and an increased interstitial/alveolar lung pattern (74%) were evident radiographically. Echocardiographically, there was mild thickening of the left ventricular free wall and septum (0.6-0.7 cm) (82%) and mild LA enlargement (1.5-1.7 cm) (82%). The (sub)endocardium appeared strikingly hyperechoic in 91% of confirmed and 95% of suspected cats. There was fibroplasia and/or inflammation of the endocardium in all necropsied cats and interstitial pneumonia in 65%. In conclusion, our findings describe a subset of myopathic cats that are typically young males in respiratory distress, recently preceded by a stressful event. A hyperechoic (sub)endocardium appears to be a key clinical marker of this important feline cardiac disease.

CHARACTERIZATION OF TRANSIENT DYSRHYTHMIEGENIC AND CHRONOTROPIC EFFECTS OF ATROPINE IN BRADYCARDIC DOGS.

Atropine administration in the treatment of vagally mediated bradycardia has been reported to be dysrhythmogenic and to transiently potentiate the bradycardia. To characterize these phenomena, we examined the effects of atropine administration in 6 dogs with bradycardia (HR<70 bpm) induced with a combination of morphine and fentanyl. Atropine was administered at 0.02 mg/kg by SQ, IM or IV routes, and ECGs were recorded continuously. All routes of administration resulted in an increase in the atrial rate prior to any increase in ventricular rate, thus inducing transient AV block. IV route induced 2nd AV block most consistently (6/6 dogs), with mean duration of 4.6±3.2 (SEM) min., compared with IM route (4/6 dogs, 8.4±4 min.), or SQ route (4/6 dogs, 17.1±4 min.). AV block persisted with the SQ route in 2 dogs for the duration of the study (40 min.). In 33% of the studies, all routes of atropine administration produced transient potentiation of the ventricular bradycardia during the AV block. Duration of the bradycardia was longer with SQ route (10.5±1.8 min.) than with IV (2.0±1.5 min.) or IM routes (4.5±1.6 min.). Mean decrease in ventricular rate during this period was 9% of baseline and briefly decreased below 40 bpm in only one study. These results show that atropine causes transient AV block with all routes of administration. This is most consistently seen, but is of shortest duration, with the IV route. Mild potentiation of the bradycardia occurs inconsistently with all routes. While these transient effects appear to be clinically unimportant, they should be anticipated when atropine is administered to treat vagally mediated bradycardia.
AMLODIPINE BESYLATE THERAPY IN CATS WITH SYSTEMIC ARTERIAL HYPERTENSION SECONDARY TO CHRONIC RENAL DISEASE. 

L.A. Holtz, P.S. Snyder, L.M. Volk. 
University of Wisconsin School of Veterinary Medicine, Madison, WI.

Twelve cats (five females; seven males) with systemic hypertension secondary to chronic renal disease were treated with amlodipine besylate (AML) (0.625 mg PO qAM), a dihydropyridine calcium antagonist drug, as a single agent. Nine of the 12 cats were receiving combinations of enalapril, propranolol, and phenoxycobenzamine, and became refractory or developed adverse effects to antihypertensive therapy. These drugs were discontinued when AML therapy was initiated. Systolic arterial blood pressure (SBP) was measured indirectly using a Doppler technique. The average systolic BP measurement for the 12 cats prior to the institution of AML was 201 mmHg (range 159-246). The average systolic BP of the 12 cats decreased significantly to 158 mmHg (range 104-188) during AML treatment of at least 1 week's duration (p = 0.00003 using a paired t-test).

Body weight and serum potassium and creatinine concentrations were compared using paired t-tests before and during AML therapy. Significant differences were not detected (p > 0.05). Results suggest that AML is an effective and safe treatment for the control of systemic arterial hypertension secondary to chronic renal disease in cats when used once daily as a single drug.

EVALUATION OF CARDIAC RYANODINE BINDING SITES IN TAURINE DEFICIENT CATS WITHOUT MYOCARDIAL FAILURE. P.D. Pion, K. Costas A. Edinger, M.D. Kittleson, Q.R. Rogers, J.G. Morris, I.N. Pessah. School of Veterinary Medicine, University of California, Davis, CA.

Taurine deficiency in cats causes a reversible reduction in myocardial function similar to dilated cardiomyopathy in approximately 30% of cats. The mechanism by which taurine acts remains unknown. In this study, high affinity ryanodine binding site density and affinity, and the Ca+ dependence of ryanodine binding was measured in crude cardiac membranes prepared from 7 age matched pairs of female cats. Each pair consisted of one cat fed a taurine-free diet and one cat fed an identical diet with 0.15% taurine for at least 2 years. The taurine deficient cats were selected from a larger initial group on the basis of having normal left ventricular pump function as assessed by echocardiogram. Although all echocardiographically determined dimensions were within the limits of normality, left ventricular end-systolic diameter was significantly larger in TAU- cats (mean±SD difference = 2±2.17 mm). There was no significant difference in body weight, LV weight, LV/BW ratio, or protein yield of the crude membrane preparations. There was no significant difference in the calcium dependence (EC50) for calcium activation of binding) or binding affinity (Kd) for [3H]-ryanodine between groups. When expressed as receptor per g ventricle, TAU- cats had significantly decreased receptor density (-4.8±2.84 pmol/g). We conclude that under these assay conditions there is no significant change in the structure of the cardiac ryanodine binding sites in taurine depleted cats without myocardial failure.

The decrease in receptor density in TAU- cats with mild, albeit detectable echocardiographic changes, is consistent with findings in cardiac sarcoplasmic reticulum preparations from spontaneous and induced cardiac diseases that result in myocardial hypertrophy/remodelling.
ELEVATED CONCENTRATION OF TUMOR NECROSIS FACTOR IN DOGS WITH CONGESTIVE HEART FAILURE. Lisa M. Freeman, John E. Rush, Don J. Brown, and Ronenn Roubenoff. Tufts University School of Veterinary Medicine, North Grafton, MA and USDA Human Nutrition Research Center, Boston, MA

Cardiac cachexia, the accelerated loss of lean body mass, is commonly associated with congestive heart failure (CHF), and is a predictor of survival in human patients with this syndrome. Cytokines appear to play a major role in the pathogenesis of cachexia, and elevated circulating concentrations of tumor necrosis factor (TNF) have been found in human CHF patients. The purpose of this study was to determine whether elevated TNF concentrations are present in dogs with CHF. Fifteen adult dogs with CHF secondary to dilated cardiomyopathy or mitral insufficiency, and without concurrent disease, were studied. Blood was collected from each dog upon admission and the activity of TNF was measured in plasma using the WEHI-164 clone cytotoxicity assay. Blood from 15 age-matched, healthy dogs was used as a control. Eleven of 15 CHF patients were subjectively judged to be below their optimum body weight. Eight of fifteen CHF patients had detectable circulating concentrations of TNF (X = 35.27 ± 62.1 pg/ml), compared to none of the controls (p = 0.045). This study demonstrates that plasma TNF is increased in some dogs with CHF, and future studies on the mechanisms of cytokine-mediated changes in body composition and modes of intervention are warranted.

DIURNAL VARIATION IN BLOOD PRESSURE AND HEART RATE IN BEAGLE DOGS MEASURED BY TELEMETRY. A.M. Gelzer & H.A. Ball, Univ. of Birm, Veterinary Dept. & Cardiovasc. Res. Dept., Ciba-Geigy, Basel, Switzerland

Blood pressure measurements from the dog have generally been obtained at one point in time by direct arterial puncture or cuff, an approach which in itself may affect blood pressure & heart rate. In order to continuously measure haemodynamic parameters in the undisturbed male Beagle dog we used a subcutaneously-placed telemetric system to record femoral artery blood pressure & ECG (lead II). Systolic, mean & diastolic blood pressure (SBP, MBP & DBP), heart rate (HR), and LQ-interval (an index of cardiac contractility) & locomotor activity (LA) were recorded (8 min intervals) over five days, & 1 hour averages calculated (mean ± SEM, n = 6). There were distinct diurnal variations in MBP (peak/ trough of 115 ± 3/ 97 ± 4 mmHg, at 7.00 h/ 18.00 h), HR (peak/ trough of 112 ± 4/ 74 ± 3 bpm, at 10.00 h/ 4.00 h) and LA (peak/ trough of 92 ± 19/ 9 ± 4 units, at 11.00 h/3.00 h). QA-interval did not change. The 1 hour variability of all these parameters (coefficient of variation) was constant over 24 h indicating the effectiveness of the baroreflex mechanism during both daytime activity and sleep. In conclusion, continuous & undisturbed recording by telemetry revealed diurnal variations in BP, HR & LA, demonstrating the utility of this model, which may allow further pharmacological investigation of the mechanisms of BP regulation.
The effects of a recombinant interleukin-2 (IL-2) gene therapy in tumor-bearing dogs was evaluated using cationic liposome-mediated gene therapy. Significant luciferase activity was found in all injected tumor sites except those injected with DNA alone. In tumors treated with liposome-DNA complexes, the efficiency of gene transfer and expression was determined by assaying luciferase activity. The tumors were treated for 24-48 hours following injection and the efficiency of gene transfer and expression was determined by assaying luciferase activity. Significant luciferase activity was found in all injected tumor sites except those injected with DNA alone. In tumors treated with liposome-DNA complexes, the efficiency of gene transfer and expression was determined by assaying luciferase activity.
INHIBITION OF MYELOMA GROWTH IN
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VITRO BY INTERLEUKIN-6 (IL-6) AND IL-6 RECEPTOR ANTISENSE. E.T. Keller and M. A. Ershler. Institute on Aging, University of Wisconsin, Madison, WI.

IL-6 stimulates proliferation of various tumors including myeloma, renal cell carcinoma and melanoma. Development of methods to inhibit IL-6 action on these cancers should inhibit their proliferation. IL-6 and IL-6 receptor (IL-6R) antisense oligodeoxynucleotides (ODN) were examined for their effects on proliferation of an IL-6 dependent (U266) and independent (RPMI 8226) myeloma cell line. Cell lines were grown in both the presence or absence of IL-6. The cells were exposed to either sense, antisense, or no IL-6 ODN or IL-6R ODN. The sense nucleotides control for non-specific effects of ODN. Cells were evaluated for proliferation (3H-thymidine uptake) and steady state levels of both IL-6 and IL-6R mRNA (competitive polymerase chain reaction (C-PCR)).

Proliferation of U266 cells was markedly decreased by IL-6 antisense ODN in the absence of IL-6, but not in its presence. In case ODN inhibited proliferation of U266 cells both in the presence and absence of IL-6. IL-6 and IL-6R ODN had no effect on proliferation of RPMI 8226. C-PCR demonstrated a marked decrease of IL-6 mRNA and IL-6R mRNA upon exposure of cells to IL-6 ODN and IL-6R ODN, respectively. These results demonstrate the efficacy and specificity of IL-6 and IL-6R antisense ODN for inhibiting the proliferation of an IL-6 stimulated cancer cell line.

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HYPERTHERMIA AND RADIOLABELED TUMOR-SPECIFIC MONOCLONAL ANTIBODIES. M.I. Hauck, M.R. Zalutsky. Duke University Medical Center, Durham, NC.

The utility of radiolabeled monoclonal antibodies for diagnostic and therapeutic applications has been limited by low levels of uptake in tumor. A 2-3 fold increase in antibody (Ab) uptake has been demonstrated when radiolabeled Abs are injected with a concurrent 4-hr 42°C hyperthermia treatment in a mouse xenograft model. The purpose of this study was to determine whether heat induced changes in Ab binding kinetics could be at least partially responsible for the increase Ab uptake seen in the in vivo study.

Antigen-positive and antigen-negative live cells were incubated with varying concentrations of Ab under normothermic (37°C) and hyperthermic (42°C) conditions for three hours. Scatchard analyses were employed to determine the association constant (Kd) at both temperatures, as well as the number of Ab molecules bound/cell. Timed incubations with a fixed concentration of Ab were performed to determine the effect of 42°C on the rate of the reaction.

Results of these assays with an intact, anti-tenascin IgG2 mAb shows an increase in the Kd, from (4.2 ± 0.2)x10^6 to (6.9 ± 0.3)x10^6 at 42°C. The significant difference in the affinity constant at 42°C suggests that besides the postulated hemodynamic effects of hyperthermia on Ab delivery and penetration, hyperthermia may affect the binding kinetics of the radiolabeled mAb as well.

IMMUNOSTAINING OF LYMPHOID TISSUE FROM DOGS WITH LYMPHOMA. COMPARISON OF FINE NEEDLE ASPIRATION AND NEEDLE BIOPSY SAMPLES. J.L. Flaherty, D. Maydan, L.L. Warner, P.P. Moore. Veterinary Medical Teaching Hospital, University of California, Davis.

The purpose of this study was to make a systematic comparison between histologic and cytologic samples utilizing immunostaining techniques in dogs with lymphoma. By comparing same site samples, the specific reactivity of selected antibodies to cell surface markers and intermediate filaments was evaluated with regard to their utility as an aid in cytologic diagnosis. A total of 12 biopsy aspirate specimens were collected from the same lymph node of 11 dogs with peripheral lymphadenopathy for which the presumptive diagnosis was untreated lymphoma. Cytologic specimens were suspended in physiologic buffered saline and multiple cytocentrifuged slides were prepared, fixed in acetone and stored up to one month at -70°C for the same time period. Sections were cut (4-6 μm) just prior to staining. A panel of 15 antibodies was applied to the specimens and positive and negative controls were run simultaneously. Staining of neoplastic cells was classified as either positive or negative. Results were considered discrepant when staining differed between corresponding cytologic and histologic preparations. Cytologic slides were interpreted first without knowledge of the primary antibody used. Out of 132 comparisons, four discrepant findings occurred, however, these did not alter the immunophenotype diagnosis for any individual case. These diagnoses included eight 8-cell tumors, one 7-cell tumor, one reactive lymph node and one metastatic carcinoma. Immunocytochemical staining correlated well with immunohistologic staining and is a simple, non-invasive technique that is useful for determining the immunophenotype of lymphoma in dogs.

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HYPOGLYCEMIA ASSOCIATED WITH INTRA-ABDOMINAL SMOOTH MUSCLE TUMORS IN 6 DOGS. R.S. Bagley, L.K. Levy, D.E. Malley.* Washington State University, *North Carolina State University.

Severe paraneoplastic hypoglycemia in dogs is usually associated with the pancreatic islet cell tumor, insulinoma. Infrequently, other tumors which do not produce insulin also cause hypoglycemia by unknown mechanisms. We report 6 dogs bearing large intra-abdominal smooth muscle tumors that presented for clinical signs associated with severe hypoglycemia. There were 4 males and 2 females, and age ranged from 5.5-10 years (median 9). Clinical signs included weakness or collapse (2), seizures (3), weakness or collapse (3), salivation (2), tremor (2), and ataxia or staggering (2). Large abdominal masses were palpable in 6 cases. Profound hypoglycemia (≤32 mg/dl) was identified in all dogs. Insulin concentrations were sub-normal or low-normal in the 4 dogs evaluated. Cytologic examination of mass aspirates from 4 dogs revealed only blood (3) or suppurative inflammation (1). Thoracic radiographs showed no evidence of metastatic disease, and abdominal radiographs confirmed a large abdominal mass in all cases. Ultrasonographic examination revealed a hypo- or hyperechoic mass with cystic areas in the 4 dogs examined. Exploratory laparotomy was performed in 5 cases, and 1 dog was euthanatized and necropsied. Masses ranging from 12-24 cm in greatest dimension were identified in all dogs and were resected in the operated dogs. Biopsy revealed leiomyoma originating from the jejenum, duodenum, pylorus, and liver and leiomyosarcoma of the stomach and jejunum. One dog died post-op with mesenteric varices. Blood glucose and clinical status returned to normal by the day following surgery in the 4 surviving dogs. At 12 months post-op, 1 dog died of unknown causes, and 1 was euthanatized for unrelated reasons. Recurrence of PU/PD and lethargy signaled pulmonary metastases 28 months post-op in 1 dog; signs resolved when the tumors were resected. A fourth dog was normal 18 months post-op.
Inflammatory bowel disease (IBD) is among the most common clinical diagnoses in dogs with chronic gastrointestinalitis, and the expected histologic lesion is lymphocytic-plasmacytic enteritis. Endoscopic biopsies of small intestine from 28 dogs were evaluated for lamina propria cellularity using immunoperoxidase techniques. Dogs were classified into 3 groups: I, IBD group having signs of chronic gastrointestinalitis and histologic evidence of epithelial/glandular alterations (n=11); II, chronic nonspecific gastrointestinalitis (n=8); III, normal dogs (n=9). Paired duodenal villi were divided vertically into 3 regions for morphometric analysis of IgA, IgG, and T-cells by immunoperoxidase staining. The predominant proprial cell in all groups. Significant differences in the villus distributions of IgA, IgG, and T-cells within dog groups were not present. Group I dogs had significantly (p<0.05) higher IgA cells as compared to Group III dogs. Significant (p<0.05) group differences for IgG cells were present with the Group I dogs having the lowest cell counts. Group III dogs had significantly (p=0.05) higher T-cell counts as compared to groups I and II dogs. These results indicate that techniques of morphometric analysis may be used to evaluate endoscopic biopsies of the canine intestine in a quantitative fashion. Increased lamina propria cellularity of IgA, IgG, and T-cells is not a stable characteristic in the histologic assessment of canine IBD.
**31 BLIND PERCUTANEOUS GASTROSTOMY: A NEW TECHNIQUE.** S.L. Marks, M. Richwot, C.J. Henry, S.T. Kanaly. Washington State University, College of Veterinary Medicine, Pullman, WA.

A modification of non-endoscopic ("blind") gastric tube placement is described. Although several techniques for this procedure have been described previously, this technique utilizes a new instrument specifically designed for this procedure. The Eld Gastrostomy Tube Applicator was developed for use in dogs and cats. The major difference between this technique and all other modifications is the use of an internal trocar. Gastrostomy tubes (20 F) were placed using this device in 15 anesthetized healthy adult cats. All gastrostomy tubes were placed within 10 minutes. Tube placement was evaluated by necropy. The gastrostomy tubes were located along the greater curvature of the stomach in all cats. This anatomic position is comparable with endoscopically placed gastric tubes in cats. Complications associated with this procedure consisted of minor hemorrhage at the time of tube placement and omental perforation in 3/15 cats. The animals were euthanized within 1 hour after tube placement, so long-term complications were not evaluated. Postmortem examination after tube placement revealed no visceral entrapment or trauma in any cats. Blind percutaneous gastrostomy with the Eld Gastrostomy Tube Applicator is safe, fast, and effective and should be considered when surgical or endoscopic gastrostomy is not indicated or feasible.

**30 ENDOSCOPIC COMPARISON OF PROTECTIVE EFFECTS OF OMEPRAZOLE VERSUS CIMETIDINE VERSUS MISOPROSTOL VERSUS SUCRALFATE ON GASTRIC MUCOSAL INJURY INDUCED BY FLUNIXIN PLUS PREDNISONE IN DOGS.** JP Paula, RG Sherding, SE Johnson, KW Simpson*, Ohio State University, Columbus, OH,*Royal Veterinary College, UK

The purpose of this study was to compare the efficacy of omeprazole, cimetidine, misoprostol, and sucralfate in preventing gastric mucosal injury induced by flunixin plus prednisone in dogs. Five groups of six adult male mixed breed dogs were evaluated: all dogs received flunixin meglumine 1.1 mg/kg q 12 hours by IM injection and prednisone, 0.55 mg/kg q 12 hours PO. Group 1 dogs received no additional medications. Group 2 dogs received omeprazole, 1.0 mg/kg PO q 24 hours. Group 3 dogs received cimetidine, 10 mg/kg PO q 6 hours. Group 4 dogs received misoprostol 5 μg/kg PO q 6 hours. Group 5 dogs received sucralfate, 1 g/mldog PO q 6 hours. All medications were given for 10 days. Endoscopy was performed prior to treatment, and on treatment days 4, 7, and 11. Regions of the stomach (cardia, body, pyloric antrum) were evaluated endoscopically and video-recorded. Videotapes were reviewed retrospectively by two of the authors who were unaware of the treatment groups. Stomach regions were scored qualitatively from 0 to 5 for the presence of hemorrhage, erosion, or ulceration. Scores from each evaluator were averaged for statistical analysis. Comparisons between treatment groups at the same time intervals were made.

Results showed variation in the response to treatment within and between treatment groups. The lowest mean scores were found in Group 4 dogs which received misoprostol. We conclude that there is variability in the degree of gastric mucosal injury induced by flunixin and prednisone. Misoprostol was associated with less severe mucosal lesions as detected by endoscopy.
Acute pancreatitis (AP) in dogs may be difficult to diagnose and is of unpredictable severity. The pathophysiology of AP is thought to involve the intra-pancreatic activation of trypsinogen with the release of the highly-specific trypsinogen activation peptide (TAP), Asp-Asp-Asp-Asp-Lys. The aim of this study was to develop a rapid and accurate ELISA for TAP and to evaluate its use in the specific diagnosis of AP in dogs.

Carboxy-terminal specific anti-TAP antibodies were produced in rabbits immunised with synthetic TAP coupled to thyroglobulin by its amino-terminal. The assay uses solid phase TAP, linked to rabbit serum albumin, which competes with TAP in the sample for binding to free anti-TAP antibodies. The proportion of antibody bound to the solid phase is quantitated spectrophotometrically by use of anti-rabbit IgG-biotin conjugate, extravidin-alkaline phosphatase and a colorimetric substrate. Urine from normal dogs and dogs with AP was collected in 10mM EDTA and 0.1% sodium azide. 

To determine the effect of diet on colonic ultrastructure, cell height, cell area, microvillus membrane width were measured. Measurements were taken on ten cells per animal; means were evaluated using ANOVA and Duncan’s multiple comparison test. The value of cell height for the highly digestible group was significantly greater than the other groups. No other significant differences were found. The biological relevance of a significantly greater cell height is difficult to evaluate, as other parameters that would indicate an alteration in maturation or proliferation of the colonic epithelial cells were not significantly different. Therefore, we conclude that commercial diets do not have an effect on the colonic ultrastructure of normal dogs. Although no effect of diet was found, this study does provide morphometric measurements that can be used as a basis for future ultrastructural studies of colonic mucosa.

Spherical, polyethylene radiopaque markers (RMs) with a diameter of 1.5 mm and 5.0 mm have been developed to aid in the diagnosis of gastrointestinal (GI) motility disorders and partial obstructions in the private practice setting. The gastric emptying rates of RMs in healthy dogs has been reported previously. Preliminary data suggest RMs are a useful clinical tool for the diagnosis of functional or physical obstructions. The GI transit of RMs in dogs and cats with a variety of GI and non-GI diseases was studied. RMs were administered with a test meal (% daily calorie requirements of canned Prescription Diet™ d/d®) but if the animal was vomiting RMs were administered in a gelatin capsule on an empty stomach. Delayed GI transit of RMs was observed in patients with uraemia, megacolon, paracetamol, pyloric disorders and in dogs with surgically corrected gastric dilation-volvulus. In animals with adynamic ileus, RMs are either retained in the stomach or are evenly distributed throughout the entire upper GI tract. Conversely, in animals with either naturally occurring or surgically created partial obstructions the RMs tend to bunch in the loop of bowel immediately oral to the site of obstruction. This "stagnant loop sign" strongly suggests a physical obstruction. In comparison to barium suspensions we found RMs to be non-invasive and of unpredictable severity. The pathophysiology of AP is thought to involve the intra-pancreatic activation of trypsinogen with the release of the highly-specific trypsinogen activation peptide (TAP), Asp-Asp-Asp-Asp-Lys. The aim of this study was to develop a rapid and accurate ELISA for TAP and to evaluate its use in the specific diagnosis of AP in dogs.

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Quantitative duodenal culture is the benchmark for diagnosis of bacterial overgrowth in the canine small intestine. This study compared duodenal counts in healthy adult dogs sampled by either endoscopy or intraoperative permucosal aspiration.

Duodenal fluid was collected from six Beagles and five pet dogs, all previously adapted to the same commercial dry maintenance diet. Fluid was aspirated endoscopically via sterile polyethylene tubing inserted into the endoscope's biopsy channel, which was disinfected and rinsed between dogs. A second sample from the same dog was then collected intraoperatively by permucosal aspiration with sterile needles and syringes. Samples were plated on non-selective media and duplicates incubated aerobically and anaerobically.

Both aerobic and anaerobic bacterial concentrations (CFU/ml) exceeded those previously reported in the literature. Comparison of endoscopic aerobic counts (median = 4.1 x 10^6; mean = 4.42 x 10^7) with permucosal aerobic (median = 1.98 x 10^7; mean = 3.18 x 10^7) and anaerobic counts (median = 1.41 x 10^7; mean = 1.28 x 10^11) demonstrated no quantitative difference between the methods.

Results suggest that bacterial levels currently deemed diagnostic of canine duodenal overgrowth should be re-examined, and that endoscopy and permucosal aspiration give equivalent quantitative results. The objectives of this study were to determine the sensitivity of young adult dogs to aspirin-induced gastrointestinal (GI) injury and the time course for occurrence of such damage. Five male (7.8-14.9 Kg) and five female (6.3-14.3 Kg) Beagles, less than 2 years of age, were given 250mg of aspirin 3 times daily over a 4-week period. Endoscopic examination was performed pretreatment and on days 2, 9, 16 and 30 of dosing. Ulceration of the gastric mucosa in 4 dogs and hemorrhagic lesions in another dog were observed after the fourth 250mg dose of aspirin; the latter dog showed gastric mucosal ulceration by day 9, and 2 additional dogs had ulcers by Day 30. These dogs had normal gastric mucosa within 1-2 weeks of removal from dosing. The 3 remaining dogs, which were also the heaviest dog, had moderate to extensive hemorrhagic lesions in the stomach and the occurrence of gastric ulceration in the dog.
Hypophosphatemia (HP) is uncommon in cats, but has been reported in association with diabetes mellitus and hepatic lipidosis. HP can cause hemolysis, rhabdomyolysis, depression, seizures, and coma. The purpose of this study was to identify cats with low serum phosphate (<2.5 mg/dl) subsequent to enteral alimentation, to determine the prevalence of this phenomenon, and to identify characteristics which may predispose these cats to HP. Over 6000 feline serum chemistries from July 1990 through December 1991 were reviewed. The medical records of all cats with HP were examined for history of enteral alimentation. Diabetic cats were excluded from the study. Nine cats were identified, ranging in age from 3 to 17 years. All cats had normal serum phosphorus values before tube feeding began. Onset of HP occurred 12-72 hours after initiation of alimentation. Phosphate concentrations in affected cats ranged from 0.4-2.4 mg/dl. Five cats had primary liver disorders, one cat had intestinal adenocarcinoma, and one cat had transitional cell carcinoma. The primary problem was undiagnosed in two cats. Hemolysis occurred in six of the affected cats. HP secondary to enteral alimentation is a relatively unusual phenomenon. Cats with high hepatic transaminases, bilirubinemia, and weight loss should be closely monitored for HP during the first 72 hours of alimentation.

EVALUATION OF INTRAOSSEOUS ADMINISTRATION OF TOTAL PARENTERAL NUTRITION IN CATS. R.D. Davies-Dean, RC DeNovo, GB Daniel, ACVIM ABSTRACTS 42.

Intravenous catheterization is a useful method of providing nutritional or emergency support to patients. However, complications can be common and may include infection at the catheter site and catheter dysfunction. An alternative method of parenteral delivery is by intraosseous administration. This technique involves the placement of an intraosseous catheter into the medullary cavity of the proximal femur under aseptic conditions. Needle placement was confirmed radiographically and by aspiration of marrow. Cats assigned to the experimental group (N=6) received an infusion of TPN through the needle for 6 days. Cats in the control group (N=4) received an infusion of an isotonic solution (Normosol-R) for 6 days. All cats were necropsied at the end of the study. Major complications occurred in only one cat. This cat (in the experimental group) developed an infection at the needle site and became septic which made removal of the study prior to completion necessary. Minor complications occurred in both groups and included: leakage of fluid around the needle (9), mild discomfort of the leg (6), transient fever (2), and mutilation of the fluid line or catheter by the cat (4). Histopathologic examination showed variable degrees of inflammation within the medullary cavity of the femur in all cats. It was concluded that intraosseous TPN is tolerated by normal cats. The complication rate suggests traditional routes of administration should be exhausted before using this route.

44. SERUM CREATINE KINASE CONCENTRATIONS IN ANORECTIC CATS. A. Faceejj, G. Mauldin, and N. Mauldin. The Animal Medical Center, New York, NY. There are no available biochemical analyses which will reliably identify malnourished cats, or enable monitoring during supportive alimentation. Human studies suggest that creatine kinase (CK) may be elevated in malnourished patients, and may decrease in response to nutritional intervention. The purpose of this study was to determine the significance of serum CK concentrations in anorectic cats, and to assess the usefulness of this test in monitoring nutritional support in these patients. Serum CK was determined for nonanorectic cats (Group 1, N=25). In hospitalized anorectic cats with a variety of disorders, that received nutritional support (enteral feeding formula) through a nasogastric tube (Group 2, N=25), serum CK was determined at the time of tube placement (time 0) and every 24 hours thereafter until discharge from the hospital. Serum CK was determined at the time of recheck visits whenever possible. Statistical analyses were performed by Mann Whitney or Kruskal Wallis tests, with P<0.05 considered significant. Correlations between serum CK at time 0 and hematologic and serum biochemical parameters were also examined in Group 2 cats using a Spearman correlation test. Anorectic cats had a significantly higher serum CK (median=2292.0 U/L) than the control group (median=175.0 U/L, p<0.001). There was a significant, positive correlation between serum CK at time 0 in Group 2 cats, and the number of days of anorexia prior to the onset of nutritional support (r=0.67; p<0.001). There were significant, positive correlations between serum CK and both SGOT (p<0.01; R=0.89) and LDH (p<0.05; R=0.41). Serum CK was significantly lower in anorectic cats after 48 hours of nutritional support than at time 0 (p<0.05), and eventually returned to normal with continued support. Serum CK may serve as a useful marker in assessing and monitoring nutritional status in the cat.

43. INTAKE IN THE DOG. B. E. Justus, A. E. Hohenhaus, Animal Medical Center, NY, NY. Hypophosphatemia (HP) is uncommon in dogs, but has been reported in association with diabetes mellitus and hepatic lipidosis. HP can cause hemolysis, rhabdomyolysis, depression, seizures, and coma. The purpose of this study was to identify dogs with low serum phosphate (<2.5 mg/dl) subsequent to enteral alimentation, to determine the prevalence of this phenomenon, and to identify characteristics which may predispose these dogs to HP. Over 6000 canine serum chemistries from July 1990 through December 1991 were reviewed. The medical records of all dogs with HP were examined for history of enteral alimentation. Diabetic dogs were excluded from the study. Eleven dogs were identified, ranging in age from 2 to 10 years. Dogs had normal serum phosphorus values before tube feeding began. Onset of HP occurred 12-72 hours after initiation of alimentation. Phosphate concentrations in affected dogs ranged from 0.4-2.4 mg/dl. Seven dogs had primary liver disorders, one dog had intestinal adenocarcinoma, and one dog had transitional cell carcinoma. The primary problem was undiagnosed in two dogs. Hemolysis occurred in six of the affected dogs. HP secondary to enteral alimentation is a relatively unusual phenomenon. Dogs with high hepatic transaminases, bilirubinemia, and weight loss should be closely monitored for HP during the first 72 hours of alimentation.

EFFECT OF LEVEL OF DIETARY FIBRE ON FOOD INTAKE IN THE DOG. B. E. Justus, Waltham Centre for Pet Nutrition, Melton Howbury, Leics. UK.

The study was designed to evaluate the effect of different levels of insoluble (IF) and soluble (SF) dietary fibre on food intake in the dog. Test diets included two standard low calorie canine diets (CLC1 and CLC2), two with increased levels of IF (IF7 and IF10) and two with increased levels of SF (SF2 and SF4) (Table 1). Dietary fibre content of test diets g/1000kcal CLC1 CLC2 IF7 IF10 SF2 SF4

| IF   | 3.7 | 3.9 | 55.7 | 90.3 | 5.5 | 10.4 |
|------|-----|-----|------|------|-----|------|
| SF   | 9.2 | 11.7| 9.8  | 8.2  | 14.7| 31.2 |

Each test diet was fed for a period of 12 days to a group of six dogs in a Latin square design, and in amounts that correspond to the food allowance recommended for weight reduction. On two occasions during each test period, exactly three hours following feeding of the test diet, dogs were presented with a challenge meal consisting of a standard canned food (CF) ad libitum. At the end of each 12 day feeding period all dogs entered a six day washout period in which they were offered CF and Librum. Food intake and bodyweight were monitored over the duration of the study. There was no significant (p>0.05) effect of diet on percentage intake of food offered or energy intake of test diets, on percentage weight loss, intake of challenge or intake during the washout period. Results of this study indicate that high levels of IF or SF have no effect on food intake in dogs not receiving an energy intake appropriate to weight reduction.

* WALTHAM VETERINARIUM* Canine Calorie Control Diet (Effem, Belmont) 1
  1. Nardelli, P.J. et al Clinical studies in the management of obesity in dogs and cats. Int. J. Ob. (in press)
Clinical signs of hypokalemic polyneuropathy have been observed in dogs with chronic renal disease and in cats fed vegetarian diets. The purpose of this study was to examine the effects of an experimentally prepared diet containing adequate animal requirements for all nutrients with the exception of potassium on five, female, young, adult cats. Taurine concentration of the diet was 0.5 g/kg. Cats were fed the diet for 90 days. Blood was collected biweekly for clinical pathology assays and taurine analysis. The cats were examined daily for evidence of muscle weakness. Body weights were recorded weekly. Electromyographic, electrocardiographic, and cardiac ultrasound studies were performed immediately prior to euthanasia. Muscle samples of the neck, fore and hind limb were obtained for histological studies.

All cats had decreased serum potassium concentrations 30 days after diet was initiated (5.4 mg/dl). Serum creatinine kinase levels were markedly increased. Plasma taurine levels decreased by 50% or greater during the study. These cats demonstrated clinical signs of muscular weakness after 60 days of ingesting the diet. Electromyographic studies revealed abnormal electrical activity. Abnormalities, including positive sharp waves and fibrillation potentials, were more apparent in the neck and front limbs than hind limbs. Pathological changes observed in skeletal muscle were mild; primarily in muscle from the front and front limbs; and observed in cats demonstrating muscular weakness at the time of examination. Clinical signs were cyclic even though dietary changes were not performed.

Hypokalemic polyneuropathy was produced in five cats fed an experimental diet with potassium restriction. Taurine levels decreased and clinical signs were similar to those seen clinically. This study represents the first complete study of the reproduction of this disease in the cat.

ERETHROCYTE STABILITY AND MEMBRANE

46 COMPOSITION IN TOCOPHEROL DEFICIENT CATS

David A. Williams, Purdue University, West Lafayette, IN; Claire Mannella, Kansas State University, Manhattan KS; J. R. Mehta, & W. Kelly, Auburn University, Auburn, AL.

Eight kittens were fed a casein-, sucrose- and lard-based tocopherol-deficient diet for 2 years. Four of the kittens served as controls and were given supplemental tocopherol. Serum tocopherol concentrations were assayed by HPLC and erythrocyte resistance to oxidative hemolysis was assessed in vitro by exposure to dialic acid, 500 mg/L. Erythrocyte membrane fluidity was evaluated by steady state fluorescence anisotropy using diphenyl-1,3,5-hexatriene (DPH) and trimethylammonium DPH (TMA) probes, and membrane lipid composition was determined by gas chromatographic analysis.

After 45 weeks serum tocopherol concentrations in all unsupplemented cats were <2 mg/L whereas concentrations in control cats were >5 mg/L. Erythrocytes from deficient cats exhibited hemolysis when exposed to dialic acid, whereas control erythrocytes did not. After 2 years state state fluorescence anisotropy R values (mean ± SEM, deficient, control) were lower in tocopherol deficient cats (DPH 0.18 ± 0.01, 0.19 ± 0.02 p = 0.01; TMA 0.20 ± 0.004, 0.24 ± 0.005 p = 0.01), indicating increased fluidity. In deficient cats the membrane cholesterol to phospholipid ratio was lower (0.72 ± 0.02, 0.89 ± 0.02 p = 0.01), percent content of C17 (0.37 ± 0.07, 0.27 ± 0.08 p = 0.05) and C18 (31 ± 6.01, 41, 28 ± 0.05, 20.8 ± 0.05 p = 0.05) saturated fatty acids was greater, and percent content of polyunsaturated fatty acids content was lower (7.75 ± 0.08, 12.78 ± 0.36 p = 0.05) than in control cats.

These findings are consistent with the hypothesis that tocopherol plays a role in maintaining normal erythrocyte membrane cholesterol and fatty acid content, with an associated beneficial effect on membrane rigidity. Loss of rigidity may contribute to increased susceptibility to hemolysis in the presence of mild oxidizing agents. Oxidizing agents may cause hemolytic anemia in cats deficient in tocopherol secondary to either dietetic deficiency or malabsorption.
EVALUATION OF DIETARY N-6 TO N-3 FATTY ACID RATIOS ON LEUKOTRIENE B SYNTHESIS IN DOG SKIN AND NEUTROPHILS, D.M. Vaughan, M.A. Reinhardt, S.F. Swain, S.D. Lauten, M.K. Boudreaux, J.S. Spano, and C. Hoffman. College of Veterinary Medicine, Auburn, Alabama, and Research and Development, The Lens Company, Lewisburg, Ohio.

The effects of five diets supplemented with increasing ratios of n-6 to n-3 polyunsaturated fatty acids on leukotriene B synthesis in dog skin and neutrophils were evaluated. The dogs were normalized for 2 months on a diet with an n-6 to n-3 fatty acid ratio of 28:1. The experimental diets containing n-6 to n-3 ratios of 5:1, 10:1, 25:1, 50:1 and 100:1 were fed to 30 beagles (6 dogs/group), for 12 weeks. Leukotriene B$_4$ (LTB$_4$) and leukotriene B$_3$ (LTB$_3$) concentrations were quantitated in skin stimulated with lipopolysaccharide, and neutrophils at the end of the 2 month control diet and again at 6 and 12 weeks of treatment feeding. After feeding the 5 diets, skin and neutrophils synthesized 30-33% less LTB$_4$ (P<0.05) and 370-500% greater LTB$_3$ (P<0.05) at 6 and 12 weeks, but had no change in the release of superoxide anions during respiratory burst. LPS-stimulated dog skin synthesized 48-62% less LTB$_4$ (P<0.05) and 46-79% more LTB$_3$ (P<0.05) at 12 weeks. These results demonstrate diets containing a 5:1 and 10:1 ratio of n-6 to n-3 fatty acids resulted in decreased concentrations of proinflammatory LTB$_4$ and increased concentrations of the less inflammatory LTB$_3$ in dog skin and neutrophils.

COMPARISON OF CONTINUOUS VS. INTERMITTENT ENTERAL FEEDING IN DOGS. M.L. Chandler and W.O. Guilford, Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Auburn, Alabama. The purpose of this study was to compare the GI side effects, better weight gain and nitrogen (N) balance, and less glucose intolerance than bolus feeding. The dogs were fed either continuously or in 3 bolus meals/day for 30 days. The dogs were weighed daily. Pre and post trial serum chemistry panels, glucose tolerance tests (GTT) and serum insulin concentrations (sI) were performed. During each trial, fecal dry matter (DM), serum osmolality (sOsm), and serum electrolytes (sElec) were determined another 3 times. Urine specific gravity (USG) was checked intermittently. Hydrogen (H) breath tests were done on days 0, 3 and 10. During the last 6 days of each trial period, feed digestibility and N balance were determined.

In conclusion, this study provides no support for the preferential use of continuous enteral intragastric feeding over bolus feeding in healthy dogs. It is likely that feeding jevity in the amounts used in this study leads to slight over-hydration of dogs.

EFFECT OF DIET ON FATTY ACID SUPPLEMENTATION 52 ON LIPIDS AND LIPOPROTEINS IN CANINE RENAL DISEASE. J.Bauer, D.Zoren, K.Bigley, D.Senior, J.Harte. Texas A&M and Louisiana State Universities, USA, & Waltham Centre for Pet Nutrition, UK.

Elevations in serum total cholesterol (CHOL) have been reported in dogs and humans with renal failure. Dietary polyunsaturated fatty acids can modify serum lipoproteins (LP) and these effects are species specific. This study was conducted to characterize lipid metabolic changes in canine renal failure and to evaluate effects of dietary n-6 and n-3 fatty acids. Dogs with chronic renal failure were recruited into the study. After a 3 week "wash-out" period, the dogs were randomly assigned to be fed either continuously or in 3 bolus meals/day for 10 weeks. Leukotriene B$_4$ (LTB$_4$), and leukotriene B$_3$ (LTB$_3$) concentrations exceeded 400 mg/dl. Similarly, triglyceride concentrations exceeded 400 mg/dl. Lipoprotein cholesterol distributions showed a significant (p<0.05) decrease in the LDL and HDL fractions of the test group compared to the control group. In conclusion, continuous feeding of dietary n-6 and n-3 fatty acids is effective in modifying serum lipids in canine renal failure.
CHARACTERIZATION OF DIET-INDUCED OBESITY AND SUBSEQUENT WEIGHT LOSS IN CATS. M.K. Jackson, ID Kurzman, DL Panciera, EG MacEwen, Univ. of Wisconsin, School of Veterinary Medicine, Madison, WI.

The purpose of this study was to characterize the metabolic and hepatic effects of diet-induced obesity (DIO) and subsequent weight loss in the cat. Seventeen neutered male cats were fed a high fat diet (4.7 kcal ME/g, 44% of calories from fat) ad libitum to induce obesity, defined as a minimum increase in body weight of 20%. Following DIO, cats were caloricly restricted (25% of calculated maintenance energy needs for initial body weight). Pretreatment, post-obesity, and post-weight loss hepatic biopsies were obtained for histomorphometric evaluation and quantitative evaluation of hepatic triglyceride content. Fasting serum cortisol, insulin, thyroxine (T4), and triiodothyronine (T3) levels were determined at monthly intervals. All cats became obese within 16 weeks, and then returned to initial body weight within 18 weeks. There was marked individual variation in weight gain (20-55%). There was a trend toward increased hepatic lipid content with DIO, and a significant increase in hepatic lipid content following weight loss, compared to initial values (initial hepatic triglyceride content 7.09 +/- 4.5 mg/dl, 24.46 +/- 4.89 mg/dl, post-weight loss, p < 0.05). Morphometric analysis also revealed a trend toward increased hepatic lipid content during DIO, and a significant increase in hepatic lipid content following weight loss, compared to initial values (initial volume fraction of lipid 12.6 +/- 2.6%, 24.5 +/- 2.2% post-weight loss, p < 0.05). Serum cortisol increased over time during DIO, then returned to baseline values during weight loss (initial serum cortisol 9.00 +/- 1.5 ug/dl, 7.76 +/- 1.6 ug/dl post-obesity, p < 0.05). Serum T4 increased significantly during DIO, and remained above baseline following weight loss (initial T4 14.44 +/- 0.92 ng/ml, 18.41 +/- 0.54 ng/ml, post-obesity, 21.1 +/- 1.07 ng/ml post-weight loss, p < 0.05). Serum T3 also increased significantly during DIO. Serum insulin did not change significantly.

These results suggest that obesity and rapid weight loss are risk factors for the development of hepatic lipidosis in cats, and that cortisol and thyroid hormones may play a role in the pathogenesis of this disease.

MEASUREMENT OF SERUM IRON, TOTAL IRON-BINDING CAPACITY AND TRANSFERRIN IN 21 DOGS WITH CONGENITAL PORTOSYSTEMIC SHUNTS. S.E. Bunch, M.C. McGahan, North Carolina State University, Raleigh, NC.

The reason for microcytosis in dogs with congenital portosystemic shunts (PSS) is unclear. Previous studies of iron (Fe) status in these patients have shown that absolute Fe deficiency is not causative, and that the most consistent change is low total iron-binding capacity (TIBC) and transferrin concentration. The purpose of this investigation was to determine if low TIBC is associated with absolute and percentage body weight loss, and absolute and percentage body fat. LBTL decreased by an average of 154 g (mean +/- SEM). 86% of the total weight loss was from fat, compared with only 12.3% from LBTL. Average body composition of the cats changed from 35.8% fat and 61.9% LBTL at the start, to 24.1% and 73.6% respectively at the end of the study. It was concluded that the feeding regimen effectively brought about weight reduction in overweight cats, with the majority of the loss occurring from fat, and not lean, tissue.

WALTHAM VETERINARY CANINE CALORIE CONTROL DIET (Secretary, Bolton) A study of obese cats on a weight reduction programme. Vet. Rec. (in press)
Criteria for inclusion were previously healthy dogs that developed clinical total sol exposure. Heat induced illness is a common, seasonal occurrence in dogs. History, physical examination findings, initial packed cell volume (PCV), and urinalysis were evaluated. Comparisons between survivors (discharge from the hospital) and nonsurvivors (death or euthanasia) were made for each of the parameters measured.

Clinical parameters of 42 dogs with heat-induced illness were studied. Criteria for inclusion were previously healthy dogs that developed clinical abnormalities during exposure to a hot environment. Data evaluated from the medical records included time of year of presentation, signalment, history, physical examination findings, initial packed cell volume (PCV), total solids (TS), whole blood glucose concentration, whole blood sodium and potassium concentrations, serum chemistry values, initial platelet counts, partial thromboplastin times, prothrombin times, fibrin split products concentrations, and urinalysis. Comparisons between survivors (discharge from the hospital) and nonsurvivors (death or euthanasia) were made for each of the parameters measured.

There were no significant differences between survivors and nonsurvivors in initial platelet counts, coagulation parameters, red blood cell numbers or parameters, white blood cell count, and alanine aminotransferase as well as initial body temperature, and duration of exposure. Heat induced illness is a common, seasonal occurrence in dogs in hot environments. The clinical findings in a large number of such dogs have not been studied previously. Dogs with the most severe biochemical abnormalities or organ dysfunction had a poorer prognosis for survival.

| Group | Alb (g/dl) | Platelets | ALT | Tcreat | BUN |
|-------|------------|------------|-----|--------|-----|
| A (8) | 1.9 (2)    | 115,000 (8)| 248 (3) | 0 (0) | 0 (0) |
| B (9) | 1.6 (7)    | 42,000 (9) | 352 (9) | 10.3 (9) | 94 (9) |

In grp B, thrombocytopenia always occurred prior to or concomitantly with azotemia. All but 1 dog with a platelet count <40,000/ul became azotemic. In grp A, 28 dogs had no proteinuria (SSA); urine protein-to-creatinine ratios (U/Pc) were determined in 5 dogs: 25 were >1. In grp B, 59 dogs had U/Pc performed; 45 were >1 (mean 3.9). Eight of 9 dogs in B were euthanatized (7/8 due to uremia). One of 8 dogs in A was euthanatized due to hepatic complications. From this small study, we concluded that CRGV is diagnosed clinically, dogs with platelet counts less than 40,000 usually become azotemic. Most, but not all dogs with renal azotemia and CRGV, do not recover with conservative therapy.

The purpose of this study is to describe the clinical and pathologic manifestations and progression of disease in dogs with CRGV. Greyhounds with deep cutaneous ulcers and thrombocytopenia (group A) and greyhounds with deep cutaneous ulcers and renal insufficiency (group B), were included. The presence and degree of anemia (PCV <49%), hyperbilirubinemia (<2.0mg/dl), thrombocytopenia (<100,000/ul), increased serum ALT (>1.5X normal) concentration, and presence of proteinuria were evaluated. The severity of the cutaneous and the survival of the dogs was described.

The relationship between patients with and without renal azotemia and CRGV, do not recover with conservative therapy.

The purpose of this study is to describe the clinical and pathologic manifestations and progression of disease in dogs with CRGV. Greyhounds with deep cutaneous ulcers and thrombocytopenia (group A) and greyhounds with deep cutaneous ulcers and renal insufficiency (group B), were included. The presence and degree of anemia (PCV <49%), hyperbilirubinemia (<2.0mg/dl), thrombocytopenia (<100,000/ul), increased serum ALT (>1.5X normal) concentration, and presence of proteinuria were evaluated. The severity of the cutaneous and the survival of the dogs was described.

In this study, we compared the clinical and pathologic manifestations and progression of disease in dogs with CRGV. Greyhounds with deep cutaneous ulcers and thrombocytopenia (group A) and greyhounds with deep cutaneous ulcers and renal insufficiency (group B), were included. The presence and degree of anemia (PCV <49%), hyperbilirubinemia (<2.0mg/dl), thrombocytopenia (<100,000/ul), increased serum ALT (>1.5X normal) concentration, and presence of proteinuria were evaluated. The severity of the cutaneous and the survival of the dogs was described.

Creating a model for outcome prediction

Heat induced illness in dogs: A retrospective study of 59 cases. K. Drobatz, D. MacIntire. School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA. Dogs with heat-induced illness were studied. Criteria for inclusion were previously healthy dogs that developed clinical abnormalities during exposure to a hot environment. Data evaluated from the medical records included time of year of presentation, signalment, history, physical examination findings, initial packed cell volume (PCV), total solids (TS), whole blood glucose concentration, whole blood sodium and potassium concentrations, serum chemistry values, initial platelet counts, partial thromboplastin times, prothrombin times, fibrin split products concentrations, and urinalysis. Comparisons between survivors (discharge from the hospital) and nonsurvivors (death or euthanasia) were made for each of the parameters measured.

There were no significant differences between survivors and nonsurvivors in initial platelet counts, coagulation parameters, red blood cell numbers or parameters, white blood cell count, and alanine aminotransferase as well as initial body temperature, and duration of exposure. Heat induced illness is a common, seasonal occurrence in dogs in hot environments. The clinical findings in a large number of such dogs have not been studied previously. Dogs with the most severe biochemical abnormalities or organ dysfunction had a poorer prognosis for survival.

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Comparison of the canine syndrome

Objective prediction of survival, that could be applied to all critically ill patients regardless of disease, at an early stage of hospitalization. Such a system would allow risk assessment of groups according to probability of survival for experimental studies, and might allow us to avoid expenditure of scarce clinical resources on animals with little chance of survival. The prospective study included 200 critically ill dogs: 93 females and 107 males, representing 62 breeds. With survival defined as alive 30 days after admission to ICU, the overall mortality rate was 40.3% (81 of 200 dogs). Data collected included signalment, parameters that reflected vital organ function, the severity of physiologic derangement, and the extent of physiologic reserve. We recorded the worst value for each of 23 parameters within the first 24 hours of admission to ICU. Logistic regression analysis was used to analyze four different weighting systems. The best model had a concordance of 86.3% with outcome, and was then re-evaluated to determine whether individual variables could be eliminated without losing predictive accuracy. Five variables could be eliminated, resulting in a final model that had 86.3% concordance with outcome. At a 0.5 cut-off for predicted risk, the model had sensitivity of 69%, specificity of 86%, a positive predictive value of 77%. A receiver operating curve was constructed using serial cut-offs for predicted outcome from 0.2 to 0.9. Thus, a linear equation was generated that allowed outcome prediction in critically ill dogs. The statistical result gives an estimation of the probability of survival. Since they are most appropriately applied to groups, such outcome predictors must be used with great caution to determine clinical decisions for individual animals.

Characterization of the canine syndrome

Of acute respiratory distress: 19 cases (1985-1993). C. Parent, L.O. King, T. Van Winkle, L. Walker. School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

We retrospectively identified 19 dogs with histologic lesions consistent with ARDS and who had died after exhibiting acute dyspnea. We characterized the management and progression of the respiratory failure. Ages of the subjects ranged from 2 months to 10 years with a mean of 4.5 ± 3.6 years prior to presentation. Oxygenation rate ranged from 36 to 140 bpm (mean 58 ± 31 bpm) and bilateral crackles were auscultated frequently (n=7). Oxygen supplementation or ventilation was required in all dogs as respiratory status worsened. Thoracic radiographs showed diffuse bilateral alveolar infiltrates in 13 dogs. Hypeoxia was present in 4 dogs breathing room air (PaO2 range 54.8 to 80.7 mmHg) and the alveolar-arterial oxygen tension gradient was elevated in all dogs (P(a)-P(Aa)O2 measured 39.6 ± 9.7 mmHg). In 6 dogs ventilated with FiO2 of 1.0, the mean P(A-a)O2 was 570.5 ± 107.4 mmHg. The arterial to inspired oxygen tension ratio (P(a)/FiO2) calculated in 2 dogs was <300 (mean 280 ± 18) and in 6 dogs <200 (mean 59 ± 19). The most common associated conditions identified were infectious pneumonia (n=7), sepsis (n=5), aspiration of gastric contents (n=4), and prolonged hypotension (n=4). More than one factor was present in 12 dogs. The index of suspicion for ARDS should be high in dogs with these conditions that develop respiratory distress. The syndrome is characterized clinically by an acute and progressive dyspnea, bilateral alveolar infiltrates, and severe oxygenation defect.
CYCLOSPORINE INHIBITS THE DEVELOPMENT OF AIRWAY HYPERRESPONSIVENESS AND AIRWAY INFLAMMATION AFTER CHRONIC ANTIGEN CHALLENGE IN CATS. P. A. Padrid, R. A. Mitchell, P. Cozier, J. M. Ndukwu, P. Shiue, J. Solway and A. R. Leff. Section of Pulmonary and Critical Care Medicine, Department of Medicine, The University of Chicago, Chicago IL.

We determined the effect of high dose cyclosporine (CsA) treatment in antigen (Acaris suum, AA) sensitized and chronically challenged (EXP cats) on the development of airway hyperreactivity (AHR) and airway inflammation. Airway reactivity to nebulized acetylcholine (ACh) was determined before AA sensitization, 24 hr following acute AA challenge by nebulization, and 72 hrs following the last AA challenge in EXP (n = 7) or sham (n = 4) challenged cats. Four additional sensitized cats were given CsA twice daily beginning prior to the first AA challenge to maintain trough blood levels > 500 ng/ml. EXP cats developed AHR in vivo, demonstrated by a 1.5 log shift to the left in response to nebulized ACh 24 hrs after acute, and 72 hrs after final AA challenge, compared to baseline. In contrast, reactivity to ACh after both acute and chronic AA challenge was equivalent between CsA treated and control cats. Airway smooth muscle from EXP, but not control or CsA treated cats was also hyperresponsive in vitro. Maximal response to electrical field stimulation expressed as % maximal contraction of each tissue to 63mM KCl (% KCl) was 65 ± 10 % KCl for tracheal smooth muscle (TSM) from control cats, 68 ± 10 for TSM from CsA treated cats, and 100 ± 3 % KCl for TSM from EXP cats (P < 0.05 vs control and CsA). Similarly, maximal response to electrical field stimulation was 88 ± 5 % KCl for bronchial smooth muscle (BSM) from control cats, 86 ± 10 % KCl for BSM from CsA treated cats, and 125 ± 5 % KCl for BSM from EXP cats (P < 0.05 vs control and CsA). EXP cats developed goblet cell hypertrophy and hyperplasia, submucosal gland hyperplasia, airway smooth muscle thickening, and epithelial erosion with eosinophil infiltrates. Airways from CsA treated cats were equivalent to control tissues. These data suggest that T cell activation is necessary for the development of AHR and airway inflammation in this model of feline asthma.

U.S. FIELD EFFICACY OF A CYCLOSPORINE (CsA) OPHTHALMIC OINTMENT IN THE TREATMENT OF CANINE CHRONIC IDIOPATHIC KERATOCONJUNCTIVITIS SIICCA (KCS). C.K. Johnson, P.W. Lockwood, and A.J. Weingarten. Schering-Plough Animal Health Research, Union, NJ.

One hundred and thirty two dogs with chronic idiopathic KCS were enrolled in a controlled, double-blind clinical trial to evaluate the efficacy and safety of CsA ophthalmic ointment under field conditions. Eleven board-certified veterinary ophthalmologists in 9 states served as investigators. Dogs were randomly allocated to treatment with either an ophthalmic ointment containing 0.2% CsA or placebo (vehicle). Ophthalmic examinations were carried out on Days 0, 7, 21, 42, and 84 post-treatment. On Day 84 drug therapy was withdrawn. Treatment with CsA resulted in a larger (p ≤ 0.05) increase in tear production relative to placebo vehicle. This increase in Schirmer Tear Test was associated with improvement in conjunctival (reduction in hypertrrophy, hyperemia and discharge) and corneal (improved surface contour, reduction in edema and neovascularization) health. Treatment withdrawal resulted in worsening of the KCS in all dogs, while resumption of therapy resulted in clinical improvement in all but 2 dogs.

CsA ophthalmic ointment was effective for the treatment of chronic idiopathic KCS in dogs. There were no adverse reactions. Continual therapy was required for maintenance of clinical improvement.

MODULATION OF THE GROWTH OF HUMAN HEPATOCELLULAR XENOGRAFTS BY THE ANTI-P-GLYCOPROTEIN ANTI BODY, MRK16. C.B. Leveille-Webster, T. Tourov and Arias, I.M. Tufts Medical School, Boston, MA and University of Tokyo, Tokyo, Japan.

We have used a novel model to study multiple drug resistance in human hepatocellular carcinoma (HCC). Two HCC cell lines, Alex 0 which has a small amount of the multidrug transporter, p-glycoprotein, and a clone induced to overexpress this protein, Alex 0.5 were injected intrasplenicly into CB17 SCID mice. Within 6 weeks, hepatic tumors develop in 70% of the mice. The Alex cells contain an integrated human hepatitis B viral gene for the production of HBsAg. Both cell lines secrete HBsAg in direct proportion to cell growth. Serial determination of serum HBsAg levels permitted monitoring of tumor growth in the mice. In 20 mice with untreated HCC serum HBsAg titers increased progressively until the mice were euthanized due to overwhelming tumor burden. Nine mice with Alex 0 and 4 mice with Alex 0.5 tumors were treated with MRK 16, 500 ug IV weekly for 3 weeks. In the Alex 0 group, 4/9 mice showed no response, 4/9 showed a partial response (duration: 14-68 days) and one animal was cured as evidenced by negative autopsy 9 months after treatment. In the Alex 0.5 group, 1/4 mice showed a partial response (duration: 38 days) and 3/4 showed complete responses (duration: 20 days, 22 days and 66 days). Mice in both groups treated with a nonspecific isotype matched murine monoclonal antibody had no response to therapy. MRK 16 modulates the growth of HCC xenografts in SCID mice. The greater the surface expression of p-glycoprotein, the better the response to immunotherapy.

THYROID PROFILES IN HEALTHY PUPPIES FROM BIRTH TO 12 WEEKS OF AGE. M. L. Casal, C. A. Zerbe, P. F. Jezyk, K. R. Refsal, R. F. Nachreiner*. School of Veterinary Medicine, University of Pennsylvania and *Michigan State University.

Hypothyroidism in dogs less than 1 year of age is reported to occur only in 3.6% of all cases, while in humans the incidence of congenital hypothyroidism is 1/2800 live births. Since dogs and cats with congenital hypothyroidism may die within the first weeks of life, it is possible that this disease is more common, but goes undiagnosed and untreated. The dogs were followed up to age 12 weeks and their thyroid profiles were measured at 2 week intervals.

Plasma concentrations of thyroid (T3), triiodothyronine (T3), and reverse T3 (rT3) were measured by RIA. Free T4 (fT4) and fT3 (fT3) were estimated by direct, analog-based RIA.

Average T4 concentrations were 35, 73, 97, 99, 88, 68, 53, 47, 40, 37, 33, 31, and 38 nmol/l at birth, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 weeks, respectively (adult normal range: 20-40 nmol/l). Plasma T3 concentrations had a nearly identical pattern with a peak at the third week of life (1.6 nmol/l), followed by a gradual decrease into the adult normal range (0.41-0.95 nmol/l) by week 10. Changes in fT3 were similar but less dramatic than for T4 and rT3 with values within the adult normal range at all times. Both T3 and fT3 concentrations were much lower than adult normal values in all dogs at birth from which point on both increased. The lower limit of adult normal values of T3 and rT3 had been reached in >50% of the puppies by the 5th and 6th week, respectively.

Plasma thyroid hormones differ between puppies and adult dogs and also differ significantly with time during the first 12 weeks of life. Therefore, the use of a standard reference range for adult dogs is inappropriate. Additionally, these studies show high T3 values (up to 3-fold increase when compared to adult averages) with low T3 and fT3 concentrations during the first 3-5 weeks of life suggesting that, although the thyroid is able to produce these hormones, the process of peripheral conversion of T4 to T3 may not be completely developed at this age.
MENT OF SERUM FREE THYROXINE BY MODIFIED EQUILIBRIUM DIALYSIS IN DOGS. TREATMENT WAS A 120-DAY ADMINISTRATION OF MED, E. C. Scott-Norrie, R. M. W. DeNicola, S. Neal, Purdue University, W. Lafayette, IN; University of California, Davis, CA; University of Georgia, Athens, GA.

Serum free thyroxine (FT4) was measured by modified equilibrium dialysis (MED), equilibrium dialysis (ED), and analog RIA kit utilizing magnetic separation, and serum total T4 (TT4) by analog RIA kit in 74 dogs. Dogs were healthy (31), hypothyroid (11), or euthyroid with concurrent problems (hyperadrenocorticism (10), obesity (9), hypoponulinemia (8), megaesophagus (5)). Diagnoses were based on history, physical exam, appropriate diagnostics, TSH stimulation testing, and need for thyroid hormone treatment.

Mean (±SD) FT4 measured by MED was significantly higher in healthy vs hypothyroid dogs (2.0±0.8 vs 0.2±0.2 ng/dl, P<0.001) and dogs with hyperadrenocorticism (1.4±0.6 ng/dl, P<0.02). There was no significant difference between healthy dogs and euthyroid dogs with other concurrent problems. In healthy dogs, mean FT4 was similar between MED and ED (2.2±0.9 ng/dl) but was significantly higher for MED vs RIA FT4 (0.9±0.2 ng/dl, P<0.001). Using means derived from healthy dogs as the normal range for MED, ED, RIA FT4, and TT4, the accuracy (defined as hypothyroid dogs with positive test results and euthyroid dogs with negative test results/total dogs tested) for MED, ED, RIA FT4, and TT4 was 0.97, 0.85, 0.94, and 0.79, respectively. Based on these results, MED can be used to assess thyroid gland function in dogs.

TREATMENT OF FELINE THYROID CARCINOMAS WITH SURGERY AND 131-IODINE. L. C. Gillill, C. Scott-Norrie, L. Janovits, W. Blevins, S. Yohn, D. D'Amico. School of Veterinary Medicine, Purdue University, W. Lafayette, IN.

The efficacy of surgical debulking followed by high dose (30 mCi) 131I in achieving remission of localized thyroid follicular cell carcinomas in cats was investigated. Seven cats with thyroid carcinomas were treated with surgery and 30 mCi radioactive iodine (131I). Each cat was treated with 131I 1 to 10 months (mean 2.6 months, median 1 month) after its last surgical thyroidectomy. Six cats were hypothyroid; one had a nonfunctional tumor. Pre-and post-treatment evaluation included but was not limited to serum T4 assays, technetium scans, and physical examinations; technetium scans were not made of 2 cats prior to surgery.

No complications were associated with the high-dose 131I treatment. All cats responded to treatment with complete resolution of clinical signs. Technetium scans made 6 weeks after 131I treatment showed no radioiodine uptake in the thyroid region or mediastinum of 3 cats. Small areas of uptake equal to or less than the intensity of uptake in salivary glands were seen in the thyroid or mediastinal region of the other 4 cats. These areas of uptake did not increase in size or intensity over a 6 to 18 month period. All 7 cats became hypothyroid after treatment and 4 of 7 cats required L-thyroxine supplementation. One cat was euthanatized due to unrelated disease 10 months after treatment for thyroid carcinoma. The other 6 cats are alive 8–32 months after treatment. The combination of surgical debulking followed by treatment with 30 mCi 131I appears safe and effective in achieving remission of thyroid follicular cell carcinomas.
CHANGES IN RENAL FUNCTION ASSOCIATED WITH TREATMENT OF HYPERTHYROIDISM IN CATS. T.K. Gray, R.B. Olivier, R.F. Nachreiner and J.M. Kruger. College of Veterinary Medicine, Michigan State University, East Lansing, MI.

Based on the clinical impression that cats sometimes develop renal failure following correction of thyrotoxicosis, we hypothesized that treatment of feline hyperthyroidism could lead to a drop in glomerular filtration rate (GFR) which might unmask underlying renal failure. To test this hypothesis we measured GFR estimated by plasma disappearance of 125I-diethylenetriaminepentaacetic acid, serum concentrations of T₄, creatinine, and urea nitrogen, and urine specific gravity in 13 cats (7M, 6F, mean ± SD age = 12.7 ± 2.1 years) before and 30 days following treatment of naturally-occurring hyperthyroidism by bilateral thyroidectomy, as well as in a group of 11 control cats (6M, 5F, mean ± SD age = 11.0 ± 1.7 years).

Mean ± SD serum T₄ concentration decreased from a pre-treatment value of 120.16 ± 39.21 nmol/L to a post-treatment value of 12.15 ± 6.26 nmol/L (normal range = 10 - 48 nmol/L). Treatment of hyperthyroidism resulted in decreased GFR, in all cats, with a mean metabolic clearance rate of 2.51 ± 0.69 ml/kg/min to a post-treatment value of 1.40 ± 0.41 ml/kg/min. Mean serum creatinine concentration increased from 1.26 ± 0.34 mg/dl before thyroidectomy to 2.05 ± 0.60 mg/dl after thyroidectomy. Mean serum urea nitrogen concentration increased from 26.62 ± 16.83 mg/dl to a mean post-thyroidectomy concentration of 34.92 ± 8.95 mg/dl. All of these changes were significant.

Two cats developed overt renal azotemia following bilateral thyroidectomy, as well as in a group of 11 control cats (6M, 5F, mean ± SD age = 11.0 ± 1.7 years). The length of the AG, but not the height or width, was found to be correlated with BW, aortic diameter and kidney length in normal dogs. This was significantly greater in dogs with PDH except for the length of the left AG. The length difference was identified with the width and height of the AG, with p-values < 0.001. The width of the left AG was the most consistent in differentiating normal versus PDH dogs. By using 7.5 mm as the upper limit of normal size for the width of the left AG (maximum in normal dogs) sensitivity was 81% with a specificity of 100% (k8.95). There was significant difference between the length of the AG in dogs with PDH and in normal dogs when the aortic diameter and the age of the dog were included in the multiple regression analysis. Results of this study indicate that ultrasonography is a valuable procedure in the evaluation of dogs suspected of having hyperadrenocorticism.
EFFECTS OF NONADRENAL DISEASE ON THE RESULTS OF DIAGNOSTIC TESTS FOR HYPERADRENOCORTICISM IN DOGS. A.J. Kaplan, M.E. Peterson, and W.J. Kumpainen. Department of Medicine, The Animal Medical Center, New York, NY, and College of Veterinary Medicine, Auburn University, AL.

Although a variety of pituitary-adrenal function tests have been recommended for hyperadrenocorticism (HAC) in dogs, there have been few studies concerning the effect of nonadrenal disease on the results of these tests. The purpose of this study was to assess 3 commonly employed screening tests for HAC, including the low-dose dexamethasone suppression test (LDDST), ACTH stimulation test, and urinary cortisol/creatinine ratio (UCCR) in dogs with a variety of nonadrenal diseases. We evaluated 100 dogs in this study: 59 with nonadrenal disease, 20 with pituitary-dependent HAC, and 21 normals.

Of the 59 dogs with nonadrenal disease, 20 (34%) had high basal serum cortisol concentration (above reference range), and 22 (38%) and 33 (56%) failed to show normal cortisol suppression at 4 and 8 hours, respectively, during the LDDST. Compared with the normal dogs, dogs with nonadrenal disease had significantly (P < 0.05) higher mean serum cortisol concentration at both 4 and 8 hours during the LDDST. There was no significant difference between the mean 8-hour cortisol concentration of the sick dogs and of dogs with HAC. After ACTH stimulation, only 9 (15%) of the dogs with nonadrenal disease had high serum cortisol concentration. No significant difference existed between mean ACTH-stimulated cortisol concentration of the normal and sick dogs. Of the 59 dogs with nonadrenal disease, 45 (76%) had a high UCCR. When compared with normal dogs, nonadrenal disease had a significantly higher mean UCCR, but no significant difference existed between the mean UCCR of sick dogs and that of the dogs with HAC. Conclusions: Many dogs with nonadrenal disease have false-positive test results for HAC if tested with the commonly employed pituitary-adrenal function tests. Because false-positive test results were observed for all of the commonly used screening tests, the definitive diagnosis of HAC should never be based solely on the results of one or more of these screening tests alone, especially in dogs without classical clinical signs of the disease or in those with known nonadrenal disease.

CENTRAL DIABETES INSIPIDUS (CDI) IN 20 DOGS. M. Harb, R. Nelson, E. Feldman, C. Scott-Manneff. University of California, Davis, CA; Purdue University, W. Lafayette, IN.

CDI was diagnosed in 20 dogs based on history, physical findings, clinical pathology, modified water deprivation test (MWDT), and response to DDAVP. Signalment included 13 pure and 4 mixed breeds, 11 males and 9 females, and a mean age of 6.6 yrs. Six dogs were < 3 yrs and 14 were > 6 yrs old. Clinical signs included severe PU/PD (20) and urinary incontinence (7). Duration of signs prior to diagnosis of CDI ranged from < 1 wk to 3 yrs (median, 5 mos). The range (mean) for clinical pathologic parameters included: BUN, 3-23 (14) mg/dl; creatinine, 0.5-1.8 (1.2) mg/dl; SAP, 30-349 (99) IU/L; ALT, 18-202 (67) IU/L; serum sodium, 141-155 (148) mmol/L. Urine specific gravity (USG) ranged from 1.001 to 1.010 (mean, 1.005). Tests of the pituitary-adrenocortical axis were normal in all dogs. The range (mean) for USG during MWDT was: pre-tinting, 1.001-1.016 (1.006); post-dehydration, 1.001-1.023 (1.017-1.036 (1.023). All dogs responded to DDAVP therapy. Six of 20 dogs developed neurologic signs ataxia, tremors, seizures 2 wks to 5 mos after diagnosis of CDI. CT or necropsy was performed in 9 of 20 dogs. A mass in the pituitary region was identified by CT in 4 of 5 dogs and in 4 additional dogs by necropsy. Five of these 9 dogs had neurologic signs. Necropsy of 4 dogs revealed adenoma (1), adenocarcinoma (1) and cyst (1) of the pars nervosa, and inflammation (1) of the pars nervosa of the pituitary.

MAGNETIC RESONANCE (MR) IMAGING OF THE BRAIN IN DOGS WITH PITUITARY-DEPENDENT HYPERADRENOCORTICISM (PDH): ONE YEAR FOLLOW-UP. E Bertoy, E Feldman, R Nelson, University of California, Davis.

The purpose of this project was to examine the growth rate of pituitary tumors (PT) in dogs with PDH. 21 dogs with untreated PDH underwent MR imaging of the brain within one month of diagnosis. None of the dogs had clinical signs suggestive of an intracranial mass. 11 of these 21 dogs had a visible PT (size: 4-12 mm). 20/21 dogs were treated with Lysodren. Each dog was monitored for 1 year or until death. 3/11 dogs with a visible PT died within the year; 2 of these 3 dogs developed clinical signs consistent with PT (2 of the 3 largest PT in the group of 11 [size: 10 mm @ 12 mm]). 8/11 dogs with a visible mass underwent repeat MR imaging at 1 year. 4/8 dogs had no apparent increase in PT size (pre: 7-9 mm; 1 year: 7-9 mm). 4/8 dogs had an increase in size of PT (pre: 5 mm, 6 mm, 8 mm, 11 mm; 1 year: 10 mm, 9 mm, 11 mm, 14 mm respectively); 2 of these 4 dogs developed neurologic signs (PT size: 11 mm @ 14 mm) and were treated with cobalt irradiation. 5/10 dogs without a visible mass died during the year. 5/10 dogs had repeat MR imaging; 2 of these 5 dogs had a visible PT (6 mm @ 7 mm). Conclusions: 1) 31% of dogs with PDH develop neurologic signs. 2) 4/5 dogs developed neurologic signs. 3) Lysodren treatment is not consistently associated with growth of PT in dogs with PDH. 4) Cobalt irradiation should be considered in dogs with PT $>$ 8 mm; cobalt irradiation is recommended in dogs with PT $>$ 10 mm.

GLYCOSYLATED HEMOGLOBIN CONCENTRATIONS IN DIABETIC CATS. D. Ellis, E. Feldman, L. Neal. University of California, Davis, CA.

Blood glycylated hemoglobin (GHb) was evaluated as a parameter of glycemic control in diabetic cats. GHb was measured by affinity chromatography. Mean (±SD) GHb was significantly higher in 22 previously untreated diabetic cats vs 59 healthy cats (3.0±0.8 vs 1.6±0.5%, respectively; P<0.001). Mean GHb was significantly lower (1.9±0.7 vs 2.6±0.8%, P<0.01) when glycemic control was good vs poor (ie, mean fasting blood glucose (FBG), 146±55 mg/dl, MBG, 293±59 mg/dl; mean glycemic control was better vs worse (1.8±0.2% vs 3.2±0.7%, P<0.01). Dogs treated with insulin showed a lower mean GHb than the untreated controls (1.3±0.6% vs 2.6±0.8%, P<0.01). 9 of 22 diabetic cats with a poor control showed a transient increase in GHb. The range (mean) for GHb during treatment of CDI was: pre-tinting, 1.001-1.016 (1.006); post-dehydration, 1.001-1.023 (1.017-1.036 (1.023). All dogs responded to DDAVP therapy. Six of 20 dogs developed neurologic signs ataxia, tremors, seizures 2 wks to 5 mos after diagnosis of CDI. CT or necropsy was performed in 9 of 20 dogs. A mass in the pituitary region was identified by CT in 4 of 5 dogs and in 4 additional dogs by necropsy. Five of these 9 dogs had neurologic signs. Necropsy of 4 dogs revealed adenoma (1), adenocarcinoma (1) and cyst (1) of the pars nervosa, and inflammation (1) of the pars nervosa of the pituitary.

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The objective of the study was to determine how soon after the onset of hyperglycemia elevated levels of glycated hemoglobin (GHB) and fructosamine are to be expected in dogs and cats. Since maintaining blood glucose concentrations at prescribed elevated levels over a prolonged period of time is difficult in vivo, the kinetics of glycolisation were investigated by analyzing pooled canine and feline blood samples in vitro. Both the dog and cat erythrocyte and serum samples were divided into 3 fractions resp., which by means of exogenous glucose were adjusted to glucose concentrations of 100 mg/dl, 200 mg/dl and 400 mg/dl.

It was possible to demonstrate that GHB as well as fructosamine formation depend on both the amount of time that has elapsed and on the degree of hyperglycemia. No increase of GHB content was seen in samples with a glucose concentration of 100 mg/dl. In the dog sample with a glucose concentration of 200 mg/dl GHB increased from 1.7% to 2.4%, in the sample with 400 mg/dl GHB was 2.7% after 156 hours. In the cat samples the initial GHB content was 0.9%. After 156 hours GHB was 1.4% in the sample with a glucose level of 400 mg/dl, whereas no increase was seen in the sample with a glucose concentration of 200 mg/dl. Correspondingly, fructosamine concentrations did not change in serum samples with a glucose content of 100 mg/dl. The greatest increase was measured in the samples with the highest glucose level (400 mg/dl). The initial fructosamine concentration of 297 umol/l (dog) and 345 umol/l (cat) increased during the course of 100 hours to 353 umol/l and 345 umol/l resp. In the serum samples with a glucose level of 200 mg/dl fructosamine had risen to a level of 305 umol/l; in the corresponding dog sample there was no increase in the level of fructosamine.

If the results obtained here are transferred directly to in vivo conditions, it may be assumed that GHB and fructosamine concentrations exceeding the respective reference ranges are an indication of there having been pronounced hyperglycemia for at least 6 resp. 4 days.
ACVM ABSTRACTS

A RETROSPECTIVE STUDY OF PITUITARY AND ADRENAL NEOPLASIA AND THE INCIDENCE OF HYPERADRENOCORTICISM IN A GERIATRIC BEAGLE COLONY

D. Bruyette, Dept. Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS. William Ruehl, Deprenyl Animal Health, Inc., Overland Park, KS.

A population of 318 Beagle dogs was studied to determine the incidence of pituitary and adrenal neoplasia as well as the occurrence of hyperadrenocorticism. Only dogs that lived to at least 6 years of age in the time period from 1963 to 1991 were included. Dogs ranged in age from 6-17 years. The group included 158 females and 160 males. Two-hundred and thirty-seven of the dogs had been exposed to radiomulides and 81 had served as controls. Pituitary or adrenal neoplasia occurred in 85 dogs (27%). Eight dogs had both pituitary and adrenal neoplasia. Pituitary tumors (31 adenomas, 1 carcinoma, 1 hemangiosarcoma) were found in 33 of the 318 dogs (10%). In the radionuclide group (8%) and 21 of the radionuclide group (7%). Adrenal neoplasia (43 adenomas, 7 carcinomas, 3 pheochromocytoma and 12 in the control group (15%). Adrenal neoplasia (43% (31 adenomas, 1 carcinoma, 1 hemangiosarcoma) were found in 60 of the 318 dogs (19%). The incidence of adrenal adenomas, 2 carcinoma, and 1 lymphoma) was found in 60 of the 318 dogs (19%). Adrenal neoplasia (43% (31 adenomas, 1 carcinoma, 1 hemangiosarcoma, and 1 lymphoma) was found in 60 of the 318 dogs (19%) and 15 in the control group (19%). Forty-three of the 85 dogs (51%) with morphologic evidence of pituitary and or adrenal neoplasia were felt to have hyperadrenocorticism. The diagnosis of hyperadrenocorticism was based on a triad of appropriate morphologic, clinical pathologic, and historical clinical signs. Hyperadrenocorticism (14%) and pituitary and adrenal neoplasia (27%) were common findings in this colony of geriatric beagle dogs and these findings may have implications for the geriatric pet dog population.

APROTINI PRESERVES IMMUNOREACTIVE ACTH FROM CANINE PLASMA

P. E. Kemppainen, T. F. Clark, M. E. Peterson. Auburn University College of Veterinary Medicine, Auburn, AL and the Animal Medical Center, New York, NY.

The susceptibility of adrenocorticotropic (ACTH) in canine blood and plasma to enzymatic degradation has limited the availability of endogenous ACTH assay for veterinary use. This study examined if a proteinase (enzyme) inhibitor, aprotinin, mixed with blood at the time of collection, would limit the loss of immunoreactive (IR) ACTH from canine plasma stored at various temperatures. Blood was collected from laboratory-maintained dogs or dogs with hyperadrenocorticism and placed into EDTA-containing tubes in the presence or absence of aprotinin. Plasma obtained was stored for 4 days at temperatures ranging from -86°C to room temperature (22°C). Results showed that addition of aprotinin preserved IR-ACTH in plasma stored for 4 days at temperatures ≤ 4°C, or in unfrozen plasma stored inside insulated shipping containers containing frozen refrigerant packs. Plasma collected with aprotinin and stored at 22°C showed a slight (17-23%) but significant (P < 0.05) decline in IR-ACTH. Unfrozen plasma collected without aprotinin showed significant (P < 0.05) loss of IR-ACTH during storage under identical conditions. Aprotinin has a profound preservative effect upon canine plasma IR-ACTH and that it may be possible to submit unfrozen samples collected with this inhibitor to appropriate reference laboratories for analysis of IR-ACTH.

EFFECTS OF CHRONIC TREATMENT WITH THE MONOMINE OXIDASE INHIBITOR (L-DEPRENYL) ON CRH STIMULATION TESTING IN GERIATRIC BEAGLE DOGS

David Bruyette, Dept. Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS. William Ruehl, Deprenyl Animal Health, Inc., Overland Park, KS, Bruce Hoggogen, Inhalation Toxicology Research Institute, Albuquerque, NM.

Dopamine plays a role in regulating anterior pituitary function and we have previously reported the efficacy of 1-deprenyl therapy in the management of canine pituitary dependent hyperadrenocorticism (PHD). Canine PHD may represent a neurodegenerative disorder affecting aged dogs secondary to the loss of dopaminergic neurons and dopamine has been shown to effect CRH mediated ACTH release in vitro. We examined the effects of 1-deprenyl therapy on CRH mediated ACTH and cortisol secretion in matched (age, sex) pairs of geriatric beagle dogs (6-17 yrs). One member of each pair had been treated orally with 1 mg/kg of 1-deprenyl daily for one year. CRH stimulation tests were performed on 58 animals (29 pairs). Plasma ACTH and cortisol concentrations were determined at times 0, 15, 30, 45, 60, 120, and 180 minutes following the IV administration of 1 ug/kg (1 mg/kg). Statistical analysis was performed with ANOVA and AUC’s for cortisol and ACTH secretion were determined. Plasma cortisol concentrations were significantly lower in the 1-deprenyl treated group at 120 and 180 minutes (p < 0.02). No differences in plasma ACTH concentration between the placebo and 1-deprenyl group were detected at any time point. The AUC for cortisol was significantly lower for the 1-deprenyl treated group when compared to placebo (p < 0.05). No difference in AUC for ACTH was detected. Treatment with 1 mg/kg of 1-deprenyl for one year results in a decreased cortisol response to CRH administration in geriatric beagle dogs.

A SIMPLIFIED GLUCOSE TOLERANCE TEST FOR USE IN CATS

K.R.J. Link, J.S. Rand, I.K. Hendrika; CAMS, UEL of Queensland, QLD, Australia

A standard iv glucose tolerance test (GTT) was compared with a simplified GTT in healthy cats. Glucose was measured with the Cobas Mira (Boehringer Mannheim; glucose oxidase method). Ten healthy cats (25 kg) were fasted for 18-22 h. The simplified GTT used 2 cephalic catheters and a 3 h wait after catheter placement. The standard GTT used a cephalic catheter, and a jugular catheter placed under general anaesthesia 24 h prior to the test. In both tests, glucose measurement was with the Cobas and Accutrend, a glucose dose of 0.5 g/kg BW was given, and blood glucose was collected at 0,5,10,15,30,45,60, and 120 min. ANOVA and MANOVA repeated measures tests were used. The Tw (min) and Kp (min) (% disappearance/min) values were calculated from the linear regression of the log, glucose concentration (conc) on time, between 30-60 min after injection. P values ≤0.05 were considered significant.

The Tw, Kp, and glucose conc versus time, were not significantly different between the simplified and the standard GTTs. For both the Cobas and Accutrend, peak glucose conc in simultaneously collected samples, was significantly higher in jugular compared to cephalic blood. For the same blood sample, there was no significant difference between the Tw, Kp, and glucose conc versus time, between the Cobas and Accutrend. For the Accutrend, there was no significant difference between 2 consecutive estimations of glucose from the same blood sample. Fasting glucose conc was normal 3 hours after injection. P values ≤0.05 were considered significant.

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Conclusions: 1. The simplified GTT with glucose measurement by the Accutrend meter can be used to calculate Tw and Kp from log glucose conc between 30 and 60 min. Results are similar to those from a standard GTT with glucose measurement by a Cobas Mira. 2 A 3 h wait after cephalic catheter placement is adequate to avoid stress hyperglycaemia. 3. One reading per sample on the Accutrend is sufficient.
The occurrence of pancreatic amyloid deposition was investigated in 83 random-source Australian cats (1.5-10 yrs old) and compared to values reported from a different gene pool (American cats). Formalin fixed tissue samples from the pancreas' left and right limb and middle segments were used. Histological sections were stained with Congo Red, and in 18 cats also with an immunohistochemical amylin stain ("IHS"; Peninsula, modified PAP technique). Amyloid was quantified with a semi-quantitative point-counting stereological method. In 17 cats, glucose tolerance test results were available.

More than 80% of cats had minor deposits of pancreatic islet amyloid (<20% of islet volume). In 4% of cats, pancreatic islet amyloid was absent. Amyloid deposition exceeded 50% in 10% of cats and comprised 80-90% of islet volume in 2 cats. The median for all cats was 9% islet amyloid. The relative number of islets affected with amyloid increased with the amount of amyloid per islet (p<0.001).

There was a highly significant positive correlation between amyloid deposition and the age of the cats (p<0.001). The amount of pancreatic amyloid was not different between the different pancreatic segments (p>0.9).

Results for extracellular amylin deposition determined by IHS were similar and positively correlated (p<0.001) with those obtained by Congo Red staining for amyloid. Extracellular amylin deposits stained in a homogeneous way whereas intracellular amylin-immunoreactivity had a granular pattern. Amylin-containing cells were predominantly located in the islet periphery. Amyloid deposition was positively correlated with age and glucose half-life.

Conclusions: 1) Similar to American cats, deposition of pancreatic amyloid is frequent in Australian cats. Only 4% of cats had no amyloid.

2) In most cats, amyloid deposition is <20% of islet volume. 3) Amyloid deposition is correlated with age and glucose half-life.

4) Distribution of islet amyloid is similar between different pancreatic segments. 5) IHS for extracellular amylin yields similar results to Congo Red stain for amyloid. 6) Islet amyloid mainly consists of amylin. 7) Amyloid deposition begins in the islet periphery.

**EVALUATION OF ARTERIAL BLOOD PRESSURE (BP) AND URINE PROTEIN CREATININE RATIO (UP/C) IN DOGS WITH CANINE CUSHING'S SYNDROME (CCS).**

T. Ortegan, P. Feldman, L. Cowgill, R. Nelson, M. Feldman. School of Veterinary Medicine, University of CA, Davis, CA

Systemic hypertension and proteinuria are recognized features of dogs with CCS; however, the incidence and magnitude of these abnormalities have not been well documented. The purpose of this study was to determine the prevalence of systemic hypertension (systolic BP [SBP] ≥ 160 mmHg & diastolic BP [DBP] ≥ 100 mmHg) and abnormal urine protein loss (UP/C > 1.0) in dogs with untreated CCS (PDI or ATH). For inclusion in this study, each dog must have had a history of CCS (5-dogs) significant improvement of arterial BP on enteral insulin absorption in dogs. Porcine zinc and linoleic acid (NM) have been shown to increase insulin absorption from the gastrointestinal tract in rats. The purpose of this study was to investigate the effect of NM on enteral insulin absorption in dogs. Porcine zinc insulin (10 U/kg) was administered endoscopically into the jejunum of 5 dogs in the presence and absence of NM, blood glucose and insulin concentrations were measured for 120 minutes following insulin administration. To establish absolute bioavailability insulin (0.2 U/kg) was also administered intravenously to each dog. The concentration-time profile of plasma immunoreactive insulin following IV injection was best described by a 2-compartment model with a mean distribution half-life of 1.12 ± 0.56 minutes, and a mean elimination half-life of 6.64 ± 1.92 minutes. Maximum hypoglycemia occurred at 15 ± 4 minutes after injection. The maximum decrease in blood glucose concentration from baseline was 58 ± 5 mg/dl. Intravenous administration of insulin alone (2 dogs) resulted in minimal insulin absorption or hypoglycemia with an insulin bioavailability of only 0.059 ± 0.018%. Administration of NM (5-dogs) significantly improved enteral insulin absorption resulting in a mean absolute bioavailability of 5.2 ± 1.25%. Maximum hypoglycemia occurred at 39 ± 4 minutes after insulin administration with a BQmax of 39 ± 5 mg/dl. The incorporation of bile salt/fatty acid mixed micelles markedly enhanced the enteral absorption of insulin in dogs. However, bioavailability appears to be much lower than has been observed in rats in previous studies.

**PANCREATIC AMYLOID IN NORMAL CATS - T.A. Leitz**

86 and J.S. Rand, University of Queensland, Brisbane, Australia

The occurrence of pancreatic amyloid deposition was investigated in 83 random-source Australian cats (1.5-10 yrs old) and compared to values reported from a different gene pool (American cats). Formalin fixed tissue samples from the pancreas' left and right limb and middle segments were used. Histological sections were stained with Congo Red, and in 18 cats also with an immunohistochemical amylin stain ("IHS"; Peninsula, modified PAP technique). Amyloid was quantified with a semi-quantitative point-counting stereological method. In 17 cats, glucose tolerance test results were available.

More than 80% of cats had minor deposits of pancreatic islet amyloid (<20% of islet volume). In 4% of cats, pancreatic islet amyloid was absent. Amyloid deposition exceeded 50% in 10% of cats and comprised 80-90% of islet volume in 2 cats. The median for all cats was 9% islet amyloid. The relative number of islets affected with amyloid increased with the amount of amyloid per islet (p<0.001).

There was a highly significant positive correlation between amyloid deposition and the age of the cats (p<0.001). The amount of pancreatic amyloid was not different between the different pancreatic segments (p>0.9).

Results for extracellular amylin deposition determined by IHS were similar and positively correlated (p<0.001) with those obtained by Congo Red staining for amyloid. Extracellular amylin deposits stained in a homogeneous way whereas intracellular amylin-immunoreactivity had a granular pattern. Amylin-containing cells were predominantly located in the islet periphery. Amyloid deposition was positively correlated with age and glucose half-life.

Conclusions: 1) Similar to American cats, deposition of pancreatic amyloid is frequent in Australian cats. Only 4% of cats had no amyloid.

2) In most cats, amyloid deposition is <20% of islet volume. 3) Amyloid deposition is correlated with age and glucose half-life.

4) Distribution of islet amyloid is similar between different pancreatic segments. 5) IHS for extracellular amylin yields similar results to Congo Red stain for amyloid. 6) Islet amyloid mainly consists of amylin. 7) Amyloid deposition begins in the islet periphery.
Dietary insoluble fiber and glycemic control in diabetic cats. R. Nelson, C. Scott-Mommaerts, S. Devries, D. Davenport, L. Neill. University of California, Davis, CA. Purdue University, W. Lafayette, IN, and Mark Norris Associates, Topeka, KS.

The effect of a high insoluble fiber (HIF; 12% dry matter) versus a low fiber (LF; 1% dry matter) canned diet on glycemic control was evaluated in 23 diabetic cats. The study consisted of two 18 week feeding trials with a 1 month "adaptation" period before each trial. Cats were randomly assigned to 1 of 2 diet sequences. Caloric intake was adjusted to keep body weight constant. Cats were treated by the owner. Glycemic control was assessed every 6 weeks during each feeding trial. Insulin dosage was adjusted during the adaptation period and after each 6 week evaluation.

The 9 cats that completed the study. The HIF diet improved glycemic control in 9 of 13 cats. In these 9 cats, there was no significant difference in mean (±SD) body weight (5.8±1.3 vs 5.4±1.3 kg) or mean daily insulin dosage (1.0±0.6 vs 1.20.7 U/kg/24h) between HIF and LF diets. There was a significant decrease in mean daily caloric intake 74±21 kcal/kg/24h (P<0.02), mean fasting blood glucose (191±118 vs 118±113 mg/dl, P<0.001), mean blood glucose/12 hours (182±99 vs 266±131 mg/dl, P<0.01), and mean glycooxylated hemoglobin concentration (2.1±0.4 vs 2.7±0.8 %, P<0.001) with the HIF vs LF diet, respectively. The HIF diet did not improve glycemic control in 4 cats. These results would support feeding a diet containing increased insoluble fiber to diabetic cats.

Single injection iohexol measurement of glomerular filtration rate (GFR) in dogs. DP Elmoohy, SA Brown, JA Barsanti. College of Veterinary Medicine, The University of Georgia, Athens, GA.

The Renalyzer is an apparatus designed to determine GFR in humans following a single IV dose of the radiocontrast agent iohexol. The apparatus is programmed to compute GFR from plasma decay of iohexol alone (IOCl), or from plasma and urine iohexol measurements (IOP). We evaluated the Renalyzer for GFR measurement in 7 dogs with chronic renal failure. Each dog received a single IV dose of iohexol (1 ml/kg body weight) and blood was obtained at intervals thereafter. During plasma decay of iohexol, GFR was measured by exogenous creatinine clearance (CRCL). In addition, plasma and urine iohexol measurements were used to calculate iohexol clearance (IIOCl) using the standard clearance formula. Values for GFR (ml/min) by the 4 methods were 12.5±4.2, 11.0±3.5, 12.7±3.9, and 13.3±4.4 for CRCl, IIOCl, IOP, and IOPU, respectively. Using CRCl as a valid measure of GFR, the IOCl, IOP, and IOPU data were each compared to CRCl by paired t-test. The CRCl method was not significantly different from IOP (P=0.60), but CRCl was significantly different from IOCl (P=0.003) and IOP (P=0.005). Good correlation existed between CRCl and IOCl (R2=0.986). CRCl and IOP (R2=0.933), and CRCl and IOPU (R2=0.97). We conclude that the Renalyzer provides a reasonable clinical estimate of GFR in dogs, and avoids urine collections with the IOP mode.

ALTERATIONS OF T LYMPHOCYTES IN DOGS WITH CHRONIC RENAL FAILURE TREATED WITH STANOZOLOL. FL Davis, LW Taylor, PA Brown, SA Brown, RA Johnson, SW McVey, SA Brown, R McLaughlin. Kansas State University, University of Georgia.

The purpose of this study was to determine the effect of stanozolol and chronic renal failure on peripheral blood T lymphocytes. Heparinized blood was collected from 22 male beagles initially (Time 1), 3 months after 15/16 nephrectomy and castration (Time 2), and during the last week of each 6 week treatment period with stanozolol or placebo (blinded cross-over design). The percent (%), and absolute number (A) of CD4+, CD8+, and MHCII+ lymphocytes were determined by flow cytometry and total lymphocyte count. A stimulation index (SI) was calculated from PHA-induced lymphocyte blastogenesis. Exogenous creatinine clearances (Ccr) were measured. The SI, MHCII+ A, MHCII+ % were weakly correlated with Ccr. There was a significant correlation of the lymphocyte count with CD4+, CD8+, and MHCII+. The lymphocyte count was not correlated with CD4+, CD8+, or SI. When compared to Time 1, the CD8+ % at Time 2 was significantly increased, resulting in a decreased CD4+/CD8+ ratio. Stanozolol administration significantly increased the ratio CD4+/CD8+ and decreased CD8+ % (ns). There was no significant effect of stanozolol on CD4+, CD8+, CD8A, MHCII+, or MHCII+ %.

In conclusion, in comparison to baseline, castrated dogs with chronic renal failure had decreased CD4+/CD8+ and decreased activation and blastogenesis of peripheral blood lymphocytes. In these dogs, treatment with stanozolol significantly increased the CD4+/CD8+ ratio.

RELIABILITY OF SINGLE URINE AND SERUM SAMPLES FOR TESTS OF 24-HOUR URINARY URIC ACID EXCRETION. P. Barretes, CA Osborne, LJ Felice, LK Unger, KA Bird, LA Koehler, M Chen. College of Veterinary Medicine, University of Minnesota.

Urine uric acid: urine creatinine (UUA:UC) ratios, urine uric acid concentrations, urine uric acid concentrations corrected for glomerular filtration rate (UUA-GFR), and urinary uric acid fractional excretions (FEua) were compared to 24-hour urinary uric acid excretions by 6 healthy adult female beagles. Comparisons using correlation analysis were made when dogs consumed a 10.4% protein (dry weight), casein-based diet and a 31.4% protein (dry weight), meat-based diet. UUA:UC ratios were determined in samples collected 2, 4, 6, 8, and 24 hours after initiation of collection; UUA-GFR, and FEua were determined in samples collected 8 hours after initiation of collection.

UUA:UC ratios, UUA-GFR, and FEua were not reliable estimates of 24-hour urinary uric acid excretions. Urine uric acid concentrations in samples collected 2, 4, 6, and 24 hours after initiation of collection correlated with 24-hour urinary uric acid concentrations when dogs consumed the casein-based diet; no correlation was found at any time interval when dogs consumed the meat-based diet.

These results indicate that caution should be used when "spot" urine samples are utilized for diagnostic and therapeutic tests.
COMPARISON OF TWO SALINE LOADING PROTOCOLS FOR PREVENTING NEPHROTOXICOSIS ASSOCIATED WITH HIGH-DOSE CISPLATIN. E.A. Fallin, S.D. Forrestier, G.K. Saunders, G.C. Troy, J.R. Wilcke. Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute, Blacksburg, VA.

This study was performed to compare efficacy of hypertonic saline with normal saline at preventing nephrotoxicosis associated with high-dose cisplatin (90 mg/m²). Twelve adult dogs were acclimated for 3 weeks. Dogs were included on the basis of normal findings on physical examination and routine laboratory evaluation. Dogs were randomly assigned to 1 of 2 groups with 6 dogs each. On day 0, both groups received 0.9% saline IV (25 ml/kg/hr) for 3 hr. Afterwards, cisplatin was mixed in 8.3 ml/kg of 7% saline for group 1 dogs and 0.9% saline for group 2 dogs and administered IV over 20 min. After completion of cisplatin infusion, 0.9% saline was continued (25 ml/kg/hr) for 1 hr in both groups. Exogenous creatinine clearances (ml/min/kg) were measured in all dogs on days 0, 5, 12, and 21. Complete blood platelet counts, and serum concentrations of magnesium, calcium, creatinine, and urea nitrogen were measured on day 0 and every 3 days after cisplatin infusion for 21 days. On day 21, all dogs were euthanized and necropsies were done.

Mean values for exogenous creatinine clearances on days 0, 5, 12, and 21 were not significantly different when groups 1 and 2 were compared; however, there was a trend for increased values in group 1 dogs. It is possible that hypertonic saline may be associated with less nephrotoxicosis; however, this needs to be evaluated in a larger number of dogs and after multiple doses of cisplatin.

USE OF EXTRACORPOREAL SHOCK-WAVE LITHOTRIPSY FOR TREATMENT OF SPONTANEOUS Nephrolithiasis IN DOGS. B. Block, L. G. Adams, W. R. Widmer and J. E. Lingeman.* School of Veterinary Medicine, Purdue University, West Lafayette, IN and Methodist Hospital Institute for Kidney Stone Disease,* Indianapolis, IN.

Extracorporeal Shockwave Lithotripsy (ESWL) is the treatment of choice for over 90% of humans with nephrolithiasis. We evaluated the safety and efficacy of ESWL for the treatment of spontaneous canine nephrolithiasis.

Five dogs were treated with ESWL. Body weight of the dogs ranged from 3 to 10 kg. Mean age of the dogs was 11 years (range 9-13 years). Four of five dogs had bilateral nephroliths. Urolith composition was confirmed as calcium oxalate in 4 of 5 dogs.

All lithotripsy treatments were performed under general anesthesia using an unmodified Dornier HM3 lithotripter. Each kidney received between 400 and 2000 shocks per treatment, at an energy level of 15 to 17 kilovolts. In dogs with bilateral nephroliths, both kidneys were treated during the same anesthetic episode, except for one dog in which treatments were staggered. Dogs received between 1 and 3 treatments (mean 1.8 treatments). Average treatment time was 28 minutes.

No significant complications occurred during or following treatment except for one dog that developed ureteroliths which partially obstructed the ureter. Follow-up serum chemistry profiles and urinalyses have not revealed decreased renal function compared to pretreatment evaluation. Four of five dogs have either been freed completely of their nephroliths or have had a sufficient decrease in stone burden and associated clinical signs so as to not warrant additional therapy. One dog is currently being evaluated following treatment.

ESWL appears to be a safe and effective means of treating canine nephrolithiasis. This form of therapy appears to be superior to nephrotomy with regard to renal parenchymal damage and subsequent renal function. More animals must be treated and extended follow-up will be necessary before specific treatment protocols can be designed and urolith recurrence rates identified.

URETHRAL PRESSURE RESPONSE TO SMOOTH MUSCLE RELAXANTS IN MALE CATS WITH NATURALLY OCCURRING URETHRAL OBSTRUCTION. L.M. Stracey-Knowlen, S.L. Marks, R.C. Speth, and G.G. Knowlen.* School of Veterinary Medicine, Washington State University, Pullman, WA. *Deceased

The effects of the skeletal muscle relaxing drug dantrolene sodium alone, and in combination with the α1-adrenergic antagonist prazosin, on the urethral pressure profile (UPP) were investigated in male cats with obstructive lower urinary tract disease. Decreases in segmental intraurethral pressure induced by the intravenous (IV) administration of dantrolene (1 mg/kg; n=3) or dantrolene in combination with prazosin (0.03 mg/kg; n=3) were evaluated statistically using a paired design (baseline vs treatment).

The administration of dantrolene alone decreased postprostatic/penile pressures significantly (p<0.05). Dantrolene in combination with prazosin caused a 20% pressure decrease in the prostatic segment (p=0.055). Preprostatic urethral pressure was not significantly affected by either treatment regimen.

These results demonstrate that dantrolene is effective in relaxing urethral striated muscle in male cats clinically affected with obstructive lower urinary tract disease. The results also suggest that prazosin in combination with dantrolene is useful for affecting relaxation of the prostatic segment of intravesical musculature. Therefore, dantrolene should facilitate urethral catheterization and treatment of feline, male lower urinary tract obstruction. The combination of prazosin and dantrolene may be more effective than dantrolene alone in the acute management of feline obstructive lower urinary tract disease.

ANTIGENICITY OF RECOMBINANT HUMAN ERYTHROPOIETIN (r-HuEPO) IN NORMAL DOGS. L.D. Corsell, L. Neal, J. Egie, J. Browne, A. Miller. School of Veterinary Medicine, University of California, Davis, CA and Amgen, Thousand Oaks, CA.

r-HuEPO has biologic efficacy in normal and uremic dogs, but its potential antigenicity in this species has not been defined. To examine this issue, 2 groups containing 16 healthy dogs were given r-HuEPO at 100 units/kg 3 times weekly for 12 weeks by intravenous (IV) or subcutaneous (SQ) routes. HCT was measured weekly during and for 8 weeks following treatment. Anti-r-HuEPO antibodies were assessed by a specific binding assay every 2 weeks, and M:E ratio was determined monthly on marrow aspirates.

Five IV and 8 SQ dogs developed low (<1:50) antibody titers but had biological responses identical to 7 IV and 5 SQ dogs with negative titers. Collectively in these dogs, HCT increased from 45.3 ± 4.8% to 65.6 ± 5.5% (P<0.001) in IV and from 42.7 ± 4.8% to 65.0 ± 11.1% (P<0.001) in SQ by week 12. There were no differences in response between IV and SQ. In contrast, 4 IV and 3 SQ dogs developed high titers (mean, 1:354 at week 12), and correspondingly HCT fell from a peak of 53.1 ± 5.6% (P<0.001 vs preRx) at week 3 to a nadir of 26.3 ± 6.2% (P=0.01 vs preRx) at week 10. With cessation of r-HuEPO, HCT returned to preRx at week 12 concomitant with antibody disappearance.

M:E ratio paralleled the temporal changes in antibody titer.

In conclusion, r-HuEPO is variably antigenic for normal dogs. Low titers do not alter biologic efficacy, while high titers reversibly impair erythropoiesis. IV and SQ dosing are equipotent and do not influence the antigenic outcome. M:E ratio correlates with antibody appearance/disappearance and r-HuEPO resistance.

ERYTHROPOIETIN (r-HuEPO) IN NORMAL DOGS. J. D. Corsell, L. Neal, J. Egie, J. Browne, A. Miller. School of Veterinary Medicine, University of California, Davis, CA and Amgen, Thousand Oaks, CA.

r-HuEPO has biologic efficacy in normal and uremic dogs, but its potential antigenicity in this species has not been defined. To examine this issue, 2 groups containing 16 healthy dogs were given r-HuEPO at 100 units/kg 3 times weekly for 12 weeks by intravenous (IV) or subcutaneous (SQ) routes. HCT was measured weekly during and for 8 weeks following treatment. Anti-r-HuEPO antibodies were assessed by a specific binding assay every 2 weeks, and M:E ratio was determined monthly on marrow aspirates.

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THE USE OF PLASMA IOHEXOL CLEARANCE TO ESTIMATE GLOMERULAR FILTRATION RATE (GFR) IN CATS. GA Brown, DR Finco, and St. Yarver, Coli Vet Med, Univ GA, Athens, GA.

EFFECTS OF POLYUNSATURATED FATTY ACIDS ON INDICES OF CANINE RENAL FUNCTION. D.Zoran, J. Harta, D.Senior, and J.Bauer. Texas A&M University, College Station, TX and Waltham Centre for Pet Nutrition, UK.

SERUM LIPIDS AND LIPOPROTEINS OF DOGS FED DIETARY N-6 AND N-3 FATTY ACID SUPPLEMENTS. K. McAlister, J. Harre, J. Bauer, Texas A&M University, College Station, TX and Waltham Centre for Pet Nutrition, UK.

PREVALENCE OF CANINE PROSTATIC CYSTS IN ADULT LARGE BREED DOGS. G. Marquez; T. Nyland; G.V. Ling; T. Baker. University of California, Davis.

The prevalence of prostatic cysts was evaluated in 85 adult large breed dogs (greater than 16 kg body weight and older than 3 years), who were presented to the clinic for problems unrelated to the prostate gland. Urine culture and prostatic evaluation by ultrasonography were performed in all dogs. Ultrasonographic imaging was performed with an ATL ultramark 8 scanner. Prostatic parenchymal echogenicity, presence of cysts, cyst number as well as their location, size, and echogenicity were recorded. Prostatic cysts were aspirated and cultured. Prostatic cysts were identified in 12 of the 85 dogs (14%). Cultures of prostatic cysts were positive in 5 of the 12 dogs (41%). Bacteria involved were hemolytic E.coli (2 dogs), Streptococcus viridans (2 dogs), Mycoplasma sp. (2 dogs), and Pasteurella multocida (1 dog). One dog had a mixed infection with P. multocida, S. xiridans, and Mycoplasma sp. Urine cultures correlated with prostatic cyst cultures in 4 of 5 dogs. In 1 dog, Mycoplasma sp. was isolated only from the cyst.

Results of this study indicate that the prevalence of prostatic cysts in adult intact large breed dogs is approximately 14% and that about half of them (74%) are infected. Urine culture may be helpful in identifying the bacteria present within the cyst.
CARBOXYL FRAGMENT INTERFERENCE IN ASSAY OF PLASMA PARATHYROID HORMONE

P. J. Bartke, P. J. Elliott, and R. J. Corcoran. Royal Veterinary College, London, UK.

Accurate measurement of plasma parathyroid hormone (PTH) concentration is essential to assess the severity of secondary renal hyperparathyroidism. Protelysis of PTH produces inactive carboxyl terminal fragments, which accumulate under conditions of reduced glomerular filtration rate. The purpose of the present study was to determine if such fragments could lead to misinterpretation of the PTH status of cats with renal failure.

PTH was measured using a two-site immunoradiometric assay (Allegro intact PTH, Nichols Institute Diagnostics) in cats with biochemical evidence of renal insufficiency. Mean plasma PTH was 146.2 ± 24.9 pg/ml (mean ± SE; n=60), compared to 10.9 ± 0.8 pg/ml (n=40) for normal cats. Plasma samples were diluted up to ninefold with human PTH depleted serum and assayed. The measured concentration was corrected for the dilution factor and compared to the undiluted value. Eight samples diluted in a predictable manner, but non-parallel dilution was demonstrated in 17 samples from cats with varying degrees of renal dysfunction; measured PTH concentration being underestimated by up to 48% (mean 27%) of that calculated from the diluted sample. A greater degree of interference was associated with higher concentrations of carboxyl fragment PTH, as measured by radioimmunoassay. To further test this hypothesis increasing concentrations of synthetic carboxyl fragment PTH were added to samples which had previously diluted in a parallel fashion. A concentration dependent decrease in measured intact PTH was demonstrated (carboxyl fragment PTH concentration 0.5 pg/ml, reduction in recovery of 86 ± 4%).

In conclusion, the valid interpretation of PTH results from this assay, in cases of renal insufficiency, requires the inclusion of a dilution to prevent underestimation of the true PTH concentration due to carboxyl fragment interference.

EFFECTS OF CHRONIC GLUCOCORTICOID THERAPY ON URINE PROTEIN:CREATININE RATIO AND RENAL MORPHOLOGY IN THE DOG

C. B. Waters, L. G. Adams, J. C. Scott-Moncrieff, D. B. DeNicola, P. W. Snyder, M. R. White and M. Gasparini.* School of Veterinary Medicine and Department of Statistics, Purdue University, West Lafayette, IN.

Glomerulosclerosis in the dog has been associated with exogenous glucocorticoid administration and spontaneous hyperadrenocorticism. The purpose of this study was to determine the effects of chronic glucocorticoid therapy on urine protein to creatinine (UP/C) ratios and renal morphology.

Nine young adult, male beagles were determined to be healthy and have normal renal function as assessed by physical examination, CBC, serum biochemistry profile, Knot's test for Proteinuria, urinary culture, endogenous creatinine clearance, 24-hour urinary protein excretion and UP/C ratio. Dogs were given oral prednisone (2.2 mg/kg q 12 h) for 6 weeks. Urinalysis and UP/C ratios were repeated at the end of weeks 1, 2, 3, 4 and 6. After the 6 week evaluation, dogs were euthanized and necropsy examinations were performed. Renal morphology was examined by light microscopy using H&E, PAS and Trichrome stains.

Mean UP/C ratio at baseline evaluation was 0.29 (SD = 0.10). Mean UP/C ratio progressively increased to a maximum of 1.27 (SD = 1.02) at the end of week 4. Mean UP/C ratio at the end of week 6 decreased slightly (0.92 ± 0.56), but remained significantly increased above baseline values. The most consistent finding, by light microscopy, was the presence of hypercellular glomerular tufts which were presumed to be due to mesangial cell proliferation. Some dogs had adhesions of the glomerular tufts to Bowman's capsule and thickening of Bowman's capsule. Immunofluorescence and electron microscopic examinations of the glomeruli are pending. We concluded that chronic glucocorticoid therapy in the dog can result in proteinuria and glomerular pathology.

ESTIMATION OF QUANTITATIVE ENZYMURIA IN CATS USING URINE ENZYME TO CREATINE RATIO ANALYSIS

R.C. Davis, P. J. Elliott, D. F. Blainey, J. A. Johnson, and R. J. Corcoran. Royal Veterinary College, London, UK.

Urine enzyme excretion is considered to be a sensitive indicator of nephrotoxicity. A number of methods have been described to determine urinary enzyme excretion. Urine enzyme to creatinine ratios (UP/C) have been used as an index of urinary enzyme excretion. This study was designed to examine the effect of dietary conditioning on renal function as assessed by physical examination, CBC, serum biochemistry profile, protein:creatinine ratio, and urine enzyme excretion in dogs with chronic allopurinol administration.

Each group was fed a different level of protein for 21 days. Urine enzyme excretion was calculated by radioimmunoassay of human crystallizable fragments. Glomerulosclerosis in the dog has been associated with exogenous glucocorticoid administration and spontaneous hyperadrenocorticism. The purpose of this study was to determine the effects of chronic glucocorticoid therapy on urine protein to creatinine (UP/C) ratios and renal morphology.

Nine young adult, male beagles were determined to be healthy and have normal renal function as assessed by physical examination, CBC, serum biochemistry profile, Knot's test for Proteinuria, urinary culture, endogenous creatinine clearance, 24-hour urinary protein excretion and UP/C ratio. Dogs were given oral prednisone (2.2 mg/kg q 12 h) for 6 weeks. Urinalysis and UP/C ratios were repeated at the end of weeks 1, 2, 3, 4 and 6. After the 6 week evaluation, dogs were euthanized and necropsy examinations were performed. Renal morphology was examined by light microscopy using H&E, PAS and Trichrome stains.

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INFLUENCE OF CHRONIC ALLOPURINOL ADMINISTRATION ON URINE ACTIVITY PRODUCT RATIOS OF URIC ACID, SODIUM URATE, AMMONIUM URATE, AND XANTHINE

J. C. Scott-Moncrieff, J. R. Adams, W. T. M. Clay, C. D. Grimes, J. C. Wilson, and S. M. D. Osburne. College of Veterinary Medicine, University of Minnesota.

This study of 6 healthy female beagles was designed to determine the influence of orally administered allopurinol for 8 weeks on urine saturation with uric acid, sodium urate, ammonium urate, and xanthine. Urine activity product ratios of uric acid (APRUA), sodium urate (APRUA), ammonium urate (APRXAN), and xanthine (APRXAN) were determined in 24-hour samples collected after 4 weeks of consumption of a 10% protein (dry weight), casein-based diet (baseline), and repeated after 4 and 8 weeks of consumption of this diet combined with oral administration of allopurinol (15 mg/kg q 12h).

Compared to baseline data, urine APRUA and APRXAN were reduced 50% and APRUA were reduced 75% in dogs given allopurinol. Compared to baseline data, significantly higher APRXAN were observed when dogs were given allopurinol. Differences in APRUA, APRUA, APRUA, and APRXAN were not observed between weeks 4 and 8 of allopurinol administration. These findings indicate that administration of allopurinol with a low protein diet effectively lowers urine saturation with uric acid, sodium urate, and ammonium urate; however, urine saturation with xanthine increases.
PROSTAGLANDIN E2 TREATMENT OF EXPERIMENTALLY INDUCED FELINE LOWER URINARY TRACT DISEASE. L.G., Adams, D.B. DeNicola, M.R. White, and M. Gasparini,* School of Veterinary Medicine and Department of Statistics,* Purdue University, West Lafayette, IN.

In humans, cyclophosphamide-induced cystitis is a severe, bacteriologically sterile, hemorrhagic cystitis which is refractory to treatment. Recently, intravesical instillation of prostaglandin E2 resolved hemorrhagic cystitis within 1 to 7 days. Therefore, we hypothesized that intravesical instillation of prostaglandin E2 would be effective for the treatment of idiopathic feline lower urinary tract disease (FLUTD).

The purpose of this study was to determine if intravesical instillation of prostaglandin E2 is effective for the treatment of experimentally induced FLUTD. Ten young adult, female cats were studied in a cross-over design. An experimental model of FLUTD was induced using an intravesical instillation of 0.1% salicilate. One group of 5 cats received daily intravesical instillations of prostaglandin E2 in 0.9% sterile saline for 3 days. The other group of 5 cats received daily intravesical instillations of 0.9% sterile saline. Intravesical instillations were performed via intermittent urethral catheterization with cats under general anesthesia. Serial urinalyses and clinical signs of lower urinary tract disease were monitored daily until the clinical signs and hematuria resolved. On days 10 and 21, urine was collected by cystocentesis for urinalysis and urine culture. Following a washout period of 2 weeks, the treatment groups were reversed and protocol was repeated. Cats were humanely euthanized and necropsy examinations were performed after data collection on day 22 of the second treatment cycle.

There was no significant difference in the duration of microscopic hematuria, pyuria, gross hematuria, or dysuria/pollakiuria following treatment with prostaglandin E2 versus saline. The duration of clinical signs of lower urinary tract disease was highly variable ranging from 1 to 21 days. Urinary tract infection was not detected in any of the cats. Necropsy findings were similar in cats treated with prostaglandin E2 versus saline. In this model, intravesical instillation of prostaglandin E2 was not effective for the treatment of experimentally induced FLUTD.

RED CELL BIOTINYLATION AS A NON-RADIOACTIVE METHOD OF ERYTHROCYTE LABELLING. Jörg Bucheler, Susan M. Cotter, Tufts University School of Veterinary Medicine, North Grafton, MA

Historically, the determination of erythrocyte life span required the labelling of erythrocytes with radioactive markers such as 51Cr or 11C. Disadvantages included the exposure of personnel and animals to radioactivity, short half lives of certain isotopes and rapid isotope elution from erythrocytes in some species. The present studies were performed to introduce a new, non-radioactive and inert label with high binding efficiency, to veterinary medicine. The vitamin and enzyme cofactor biotin, coupled to N-hydroxysuccinimide, was bound to biotin-residues on erythrocyte membranes. Streptavidin, coupled to a fluorescent marker, strongly bound biotin molecules on the membrane, and was sensitively recognized, counted, and retrieved by flow cytometry and avidin-coated petri dishes. Our studies show that canine and feline erythrocytes can be biotinylated without effects on erythrocyte metabolism. Clinical safety studies showed no adverse effects to dogs and cats after long term monitoring and repeated biotinylations. The life span of biotinylated canine and feline erythrocytes was similar to that using carbon or iron isotopes. We will report preliminary experiences with biotinylination in clinical settings, such as in FeLV-infected cats and heartworm infected dogs. In conclusion, erythrocyte biotinylation offers a new, sensitive, and highly reliable method of membrane labelling for various purposes without any clinically recognizable adverse effects or influences on metabolic or immunologic functions.

CYSTOSCOPIC IDENTIFICATION OF GLOMERULATIONS IN CATS. S. Osborn, DJ Chew, CA Buffington, M. Kendall, B. Woodward and T. McCarthy. The Ohio State University College of Veterinary Medicine, Columbus, Ohio.

Most cats that present for signs of lower urinary tract disease (LUTD) have no identifiable cause. Cats with idiopathic LUTD (i-LUTD) meet many of the objective NIH criteria for the diagnosis of interstitial cystitis (IC), a disease that predominantly affects women. The NIH criteria include chronic irritative voiding patterns, sterile urine, characteristic cystoscopic findings, and an inability to find an objective explanation for the clinical signs.

The characteristic cystoscopic findings required for the diagnosis of IC include prominent vascularity and glomerulations. Glomerulations are submucosal petechial hemorrhages observed through the cystoscope during bladder distension at 80 cm of water pressure. A similar lesion observed by one of us (TMcC) prompted futher urinary endoscopy of cats with i-LUTD.

We have conducted urethro-cystoscopy in 17 female cats and 5 male cats with perineal urethrostomy presented for treatment of i-LUTD. 8 normal female cats were examined in a similar way for comparison. Observations were made at low (5 cm H2O) and high (80 cm H2O for several minutes) pressures. One normal cat displayed a single glomerulation at low pressure; no glomerulations were seen in the others at either low or high pressure. Glomerulations were documented in 19/22 cats with i-LUTD. Glomerulations were visible in 14 cats at low pressure; 8 of these worsened at high pressure. Glomerulations were observed only at high pressure in 5 cats.

We conclude: Glomerulations occur frequently in cats with i-LUTD. They may develop only at high pressure in some, and worsen at high pressure in others. The appearance of glomerulations in cats with i-LUTD is similar to those seen in IC.

FELINE BLOOD COMPONENT THERAPY. IMI Hanson, AT Kristensen, PJ Armstrong and J Parrow, College of Veterinary Medicine, University of Minnesota, St. Paul, MN

The medical records for cats receiving blood component therapy were reviewed to determine the average benefit per unit transfused and the incidence of transfusion reactions. Over a 5.5 year period, 133 cats received 246 blood components: 82 whole blood (WB), 81 packed red blood cells (PRBC), 55 fresh frozen plasma (FFP). The average rise in PCV one hour post-transfusion from one unit of WB or PRBC was 6.25%. No adverse reactions were associated with the plasma transfusions. Transfusion reactions were associated with 12 (8.3%) of 131 cellular components administered. Transfusion reactions consisted of transient pyrexia (4), facial edema (1), circulatory overload (2), hemolysis over 2 days (3), acute hemolysis with pyrexia (1), and death (1). Of the 12 cats with transfusion reactions, 10 had a compatible pre-transfusion crossmatch and six had been previously transfused.

The results of 367 feline crossmatches were also reviewed. Major and minor crossmatches were performed at 37°C according to standard technique. Incompatible crossmatches were repeated with additional donors including a type B cat. Incompatibilities were found in 53 (14.4%) of the major crossmatches and 31 (8.4%) of the minor crossmatches. Almost all recipients incompatible with one type A donor were compatible with a different type A donor. Only 2 type B recipients were identified.
Natural killer (NK) cells are sometimes considered phagocytic cells. Moreover, because of their ability to kill tumor cells they have been suspected of producing reactive oxygen species (ROS). Neutrophils and monocytes are well-known for their ability to produce ROS during the oxidative burst. Previous attempts to measure this ability in NK cells have failed to detect ROS or chemiluminescence. To increase the sensitivity of the measurement system, we utilized 2 fluorochromes, 2',7'-dichlorofluorescein diacetate (DCDFH-DA) and hydroethidine (HE) which measure intracellular hydrogen peroxide (H₂O₂) and superoxide anion (O₂⁻) respectively. NK cells were isolated by ficoll-hypaque and percoll gradient centrifugation and labeled with anti-canine CD4 and CD8 monoclonal antibodies. The primary antibodies were labelled with fluorescein isothiocyanate (FITC) and phycoerythrin (PE) respectively for two-color flow cytometric analysis. The null cells (CD4⁺/CD8⁺) were isolated by fluorescence-activated sterile cell sorting. After sorting, the null cells were labelled with DCDFH-DA and PHA and phorbol 12-myristate 13-acetate (PMA), N-formyl-l-methionyl-l-leucyl-l-phenylalanine (FMLP), or Con A. Null cells stimulated with FMLP exhibited a 108% increase in mean channel DCF fluorescence. In comparison to null cells, the neutrophil produced approximately 10 times the quantity of H₂O₂.

These results indicate that the production of H₂O₂ in null cells following stimulation with PMA and thus suggest a new pathway for NK cell-mediated cytotoxicity.

**EFFECT OF ORAL CYCLOSPORINE (CS) IN DOGS WITH 109 REFRACTORY IMMUNE-MEDIATED ANEMIA (IMA) OR THROMBOCYTOPENIA (ITP).**

AK Cook, RVMS, EH Berto, DVM, CR Gregory, DVM, University of California, Davis; AP Stewart, DVM, Special Veterinary Services, California.

This study evaluated oral CS in dogs with refractory or relapsing IMA or ITP. All dogs had received immunosuppressive drugs for at least 4 weeks prior to enrollment in the study. CS was initially administered at 12-17 mg/kg/day, and the dose was then adjusted to achieve trough blood levels of 400-600 ng/ml.

Three dogs with IMA were studied. Duration of illness prior to receiving CS ranged from 6 weeks to 5 months, and mean packed cell volume (PCV) was 20.3 ±6.2%. Two dogs (67%) responded, with normal PCVs within 6 weeks (mean, 43.7 ±1.9%). The third dog died of toxicity after 15 days.

Four dogs with ITP were evaluated. All had received prednisone for 5-12 months prior to starting CS, and mean platelet count was 25,000 ±20,000/μl. Three dogs (75%) responded, with normal platelet counts after 3-5 weeks (mean, 290,000 ±59,000/μl). However, one dog died of systemic aspergillosis while still taking CS and immunosuppressive doses of glucocorticoids.

Immune-mediated hemolytic diseases may be difficult to manage and carry a guarded prognosis. Patients may die from the primary disease or succumb to complications such as sepsis, gastric ulceration or thromboembolism. We conclude that oral CS may be effective in dogs with refractory IMA or ITP, and warrants further investigation.
Low automated platelet counts (<150,000/μl) have been observed in Cavalier King Charles Spaniels (CKCS) referred for investigation of a variety of diseases. Examination of blood smears observed in CKCS were different in number and size from those of other breeds. Samples obtained from a group of 10 clinically normal CKCS and 18 dogs of other breeds were submitted to automated haematologic analysis and manual determination of platelet number and diameter. Manual platelet counts were similar in CKCS and non-CKCS. Platelet counts were lower than manual counts in both CKCS and non-CKCS (P<0.01), but the difference was much greater in CKCS than non-CKCS (P<0.001). Platelets from CKCS were larger in diameter (median 2.5-3.75μm) than those from non-CKCS (median 1.25-2.5μm; P < 0.001), with some platelets as large as erythrocytes. 80% of platelets in non-CKCS had a median diameter of 1.25-2.5μm. Frequency distribution of platelet diameters in CKCS was broader and bimodal, with 44.5% of platelets in size range 1.25-2.5 μm and 30% from 3.75-5.0 μm. The numbers of erythrocytes, and leukocytes, MCV, MCH, MCHC in samples from CKCS and non-CKCS were within reference ranges. No clinical evidence of platelet dysfunction was detected and buccal mucosal bleeding times in two CKCS were within normal limits. These findings indicate that CKCS may have large platelets which could lead to the erroneous diagnosis of thrombocytopaenia or autoimmune haematologic analysis. The cause and functional significance of the macrothrombocytosis is unclear.

There is almost no passage of maternal antibodies through the feline placenta making transfer of collostral antibodies to the neonatal kitten important for protection against disease, but also a risk factor for neonatal isoerythelysis (NI). To determine the amount and the time period in which intestinal absorption of immunoglobulins (Ig) takes place is the neonatal kitten, IgG, IgA, and IgM concentrations were quantitated in colostrum, milk, and serum of 11 queens and in the serum of 42 kittens before ingestion of colostum, but IgM was present in 11 of 19 cases tested (58%) and IgG in 0-186 mg/dl, and IgM from 0-535 mg/dl. Five queens had no detectable concentrations of IgM in their milk. There was no correlation between maternal serum and colostral/milk Ig concentrations. No IgG or IgA was detected in any of the serum samples obtained from kittens before ingestion of colostum, but IgM was present in 5 kittens at birth. Orally absorbed IgG peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days). Serum IgA peaked in the serum at 22.2 hours, after which it rapidly dropped (apparent t1/2=5.44 days), serum IgA peaked at 17.1 hours and disappeared within 5-7 days (t1/2=1.95 days), while serum IgM increased steadily from birth or peaked at 32 days, followed by a steady decrease until day 7 (t1/2=3.01 days).
REACTI0NS TO INTRADEMAL INJECTIONS OF HOUSE DUST AND HOUSE DUST MITES IN HEALTHY DOGS AND DOGS SUSPECTED OF BEING ATOPIC.

D.C. Lewis, J.K. Meyers, M.B. Callan, J. Boucheler, and U. Giger. College of Veterinary Medicine, Washington State University, Pullman, WA, and School of Veterinary Medicine, Pennsylvania, Philadelphia, PA.

This study determined the percentage of false positive reactions to house dust (HD) and house dust mites (HDM) using concentrations recommended by the manufacturer for intradermal (ID) allergy testing.

Fifty dogs were tested. Twelve dogs (group I) were healthy dogs obtained from a pound; 12 dogs (group II) were healthy, privately owned dogs; 15 dogs (group III) were atopic and had multiple positive ID reactions to inhalant allergens; and 11 dogs (group IV) were suspected of being atopic but had positive ID reactions limited to HDM, HD, and flea antigen. The dilution of HDM (1:5000 w/v) and HD (100 PNU/ml, currently recommended for ID allergy testing, resulted in false positive reactions in 58% and 50% of healthy dogs tested, respectively. No significant difference in number of positive reactions to HDM or HD was observed between any group of dogs, or between healthy dogs (groups I and II) and allergic dogs (groups III and IV). Therefore, the clinical significance of positive ID reactions to HDM or HD was uncertain in the allergic dogs.

Threshold concentrations for ID allergy testing were determined in 24 healthy dogs by ID testing with 5 dilutions of HD (1:1000 w/v, 1:5000 w/v, 1:10,000 w/v, 1:50,000 w/v, and 1:100,000 w/v) and 5 dilutions of HD (500 PNU/ml, 100 PNU/ml, 50 PNU/ml, 20 PNU/ml, 10 PNU/ml). Threshold concentrations for the commercial extracts used in this study were 31,500 PNU/ml of HD and 20 PNU/ml of HD. The threshold concentration for HDM determined in another study was 31 PNU/ml; however, this value is difficult to compare with the present study because of different units of measure.

Threshold concentrations are recommended for ID allergy testing to avoid false positive reactions and should be determined for each manufacturer's allergens.

DETECTION OF PLATELET-BIND AND SERUM PLATELET-BINDABLE ANTIBODIES IN THE DIAGNOSIS OF CANINE ITP.

D.C. Lewis, J.K. Meyers, M.B. Callan, J. Boucheler, and U. Giger. College of Veterinary Medicine, Washington State University, Pullman, WA; School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA; and School of Veterinary Medicine, Tufts University, North Grafton, MA.

The purpose of this study was to investigate the sensitivity and specificity of two antibody tests in dogs with idiopathic thrombocytopenic purpura (ITP).

ITP was diagnosed based on exclusion of other etiologies for thrombocytopenia and platelet counts greater than 100,000 w/v. ELISA tests were developed using staphylococcal protein A to detect platelet-bound antibodies (direct ELISA) and serum platelet-bindable antibodies (indirect ELISA).

The direct ELISA was positive in 32 of 34 dogs with ITP (sensitivity 94%) and negative in 13 of 21 dogs with other etiologies for thrombocytopenia (specificity 62%). The indirect ELISA was positive in 11 of 32 dogs with ITP (sensitivity 35%) and negative in 12 of 15 dogs with other etiologies for thrombocytopenia (specificity 86%).

Positive tests were also obtained in dogs with concurrent monocytic and lymphocytic leukemia, lymphoma, chronic lymphocytic leukemia, and chronic idiopathic thrombocytopenia. Detection of platelet-bound antibodies was more sensitive than detection of serum platelet-bindable antibodies in dogs with ITP. Therefore, a negative test for platelet-bound antibodies in dogs with thrombocytopenia is helpful in excluding ITP as an etiology. A positive test, however, is not specific for ITP.

STORAGE OF FELINE AND CANINE WHOLE BLOOD IN CPDA-1 AND DETERMINATION OF THE POSTTRANSFUSION VIABILITY.

Jörg Bischel, Susan M. Cotter. Tufts University School of Veterinary Medicine, North Grafton, MA.

CPDA-1, a blood storage solution, extends the shelf life for human blood to 35 days. Plastic bags equipped with CPDA-1 anticoagulant are widely used for the storage of blood products in veterinary medicine. Unfortunately, information about storage lesions and posttransfusion viability of erythrocytes is scant, and, to our knowledge, the shelf life of feline blood stored in CPDA-1 is still unknown. The goal of our studies was to investigate the posttransfusion viability of feline and canine erythrocytes as determined by the biotinylation method. Five healthy beagles and five healthy domestic short-haired cats were used as blood donors. Fresh whole blood was collected in CPDA-1 under standard blood bank conditions and stored at 4°C for 35 days. After storage the erythrocytes were biotinylated and returned to the donor. Periodic blood samples were collected and processed for flow cytometry. Posttransfusion viability was expressed as percentage of biotinylated cells remaining in the circulation after 24 hours. Aliquots of stored blood were put aside for hematologic and biochemical analysis. The 24-hour posttransfusion viability after 35 days of storage in CPDA-1 was 82.2% for canine erythrocytes and 84.8% for feline erythrocytes. According to standards of the American Association of Blood Banks, the reported posttransfusion viabilities are within the range of tolerance, and we conclude that feline and canine blood can be stored in CPDA-1 for 35 days with satisfactory erythrocyte survival.
DEMONSTRATION OF TOXOPLASMA GONDII-SPECIFIC IGA IN THE AQUEOUS HUMOR OF CATS. M.R. Launin, D.P. Burney, S.L. Hill, M.J. Chavkin. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

The purpose of this study was to evaluate measurement of T. gondii-specific Iga in the aqueous humor (AH) of cats as aid in the diagnosis of ocular toxoplasmosis.

Age-matched SPF cats (n = 4) were orally inoculated with T. gondii tissue cysts. Serum and AH were collected sequentially from 0-20 weeks post-inoculation (PI). Serum and AH samples from 29 cats with endogenous cysts were assessed. Each serum and AH sample was assayed with ELISA for T. gondii-specific IgM, IgG, and IgA, and with ELISA for calicivirus-specific IgG or total IgG. Aqueous antibody coefficients were calculated.

IgM, IgG, or IgA Cc-value (naturally infected cats) = T. gondii IgM, IgG, or IgA AH/saerum X calicivirus IgG serum/AH
IgM, IgG, or IgA Cc-value (experimental cats) = T. gondii IgM, IgG, or IgA AH/saerum X total IgG serum/AH

A Cc-value or C-value > 1 was considered evidence of antibody production in AH; values < 1 were considered evidence of leakage.

All 4 experimental cats developed IgG C-values > 1 (first detectable 4-8 weeks PI, undetectable by week 16 PI). Three of four cats developed IgA C-values > 1 (first detectable 4-6 weeks PI, undetectable in 1 cat on week 20 PI). IgG and IgA C-values > 1 were detected concurrently in 6 samples.

Toxoplasma gondii IgM was not detected in AH.

IgM or IgG Cc-values > 1 were detected in 16/29 (55.2%) AH samples from naturally-infected cats with cysts. IgA Cc-values > 1 were detected in the AH of 7/24 (29.2%) cats serum positive for IgA; IgM and IgG were undetectable in the AH of 2. Overall, IgM Cc-values, IgG Cc-values, or IgA Cc-values > 1 were detected in 18/29 (62.1%) AH samples.

Toxoplasma gondii-specific IgA is produced in the aqueous humor of some cats and may aid diagnosis of ocular toxoplasmosis.

TOXOPLASMA GONDII-SPECIFIC IMMUNOGLOBULIN A SEROLOGIC RESPONSES IN CATS. D.P. Burney, M.R. Lappin, and M.M. Spilker. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

The purpose of this study was to develop and evaluate an ELISA for detection of T. gondii-specific immunoglobulin A (IgA) in feline serum.

An indirect double sandwich ELISA for the detection of T. gondii-specific IgA was developed using T. gondii RH strain soluble antigens, goat anti-cat IgA, peroxidase-labeled rabbit anti-goat IgA, and chromagen. Optical dilutions were determined by checkerboard titration. Age-matched, SPF cats (n = 7) were orally inoculated with T. gondii tissue cysts. Serum was collected sequentially from 0-34 weeks post-inoculation (PI). Serum samples from 175 naturally exposed cats with suspected toxoplasmosis were obtained. Each serum sample was assayed with ELISA for T. gondii-specific immunoglobulin M (IgM), immunoglobulin G (IgG), and IgA. Select IgM or IgG positive serum samples were grouped by ocular (n = 45) or non-ocular (n = 30) clinical signs.

Toxoplasma gondii-specific IgA was detected in serum from all experimentally inoculated cats at some time PI. Immunoglobulin A was initially detected weeks 2-6 PI, peak levels were detected weeks 12-26 PI, and 4/6 cats tested week 34 PI had detectable IgA. In naturally infected cats, the seroprevalence of IgM or IgG was 67.4% (118/175); the seroprevalence of IgM, IgG, or IgA was 72% (126/175). Immunoglobulin A was detected more frequently in the serum of cats with ocular disease than in cats with non-ocular disease (X² = 7.6923, P < 0.01). Immunoglobulin A was associated with IgM more frequently in cats with ocular disease than in cats with non-ocular disease (X² = 12.463, P < 0.001). Toxoplasma gondii-specific IgA develops in the serum of some cats with toxoplasmosis and may be associated with ocular disease.

EVALUATION OF THE FIELD EFFICACY OF A TEMPERATURE-SENSITIVE FELINE INFECTIOUS PERITONITIS VACCINE. NP Reeves, MJ Coyne, JG Herman Exton, Pennsylvania

The objective of this study was to determine the efficacy of a temperature-sensitive Feline Infectious Peritonitis (FIP) vaccine against a natural exposure challenge. All healthy cats, 16 weeks of age or older, entering a large, non-euthanasia shelter were entered into the study. Cats were vaccinated with two doses of either vaccine or placebo, administered intranasally, 4 weeks apart. This was a double-blinded study. Cats were then placed in the main colony and monitored for signs of illness until the time of their death or completion of the study. Complete necropsies with their death or completion of the study. Complete necropsies with

The ability of Petaluma strain FIV to cause injury by infection of cultured feline astroglia was examined via vital fluorescence assays with a Meridian™ ACAS 570 Interactive Laser Cytometer. We previously determined that FIV disrupts electrical potential-dependent partitioning of rhodamine 123 into mitochondria, gap junction mediated intercellular communication, and calcium homeostasis in astroglia. In the present study, plasma membrane permeability decreased coincident with increased plasma membrane lipid mobility and FIV affected intracellular glutathione (GSH) levels in a dose dependent fashion. With a low viral inoculum there was minimal CPE and a slow decrease in intracellular GSH over 10 days. With a high dose of virus there was rapid CPE and cell death with an increase in intracellular GSH in surviving cells by 4 days postinfection. These experiments have identified several cellular processes altered in FIV-infected astroglia and these findings suggest that FIV-infection of feline astroglia affects cellular membranes, both structurally and functionally. Because of the importance of astroglia in maintenance of the CNS environment, it will be important to make a formal connection between altered astroglia membrane functions and the CNS symptomatology observed in lentiviral infected cats and people.

FELINE IMMUNODEFICIENCY VIRUS-INDUCED INJURY OF ASTROGLIA EXAMINED VIA VITAL FLUORESCENCE ASSAYS. E Zenger, R Barhoumi, E Collisson, R C Burghardt, E Tiffany-Castiglioni. Texas A&M University, College Station, TX.
THE PLACENTA IS AN EFFECTIVE BARRIER TO IN UTERO TRANSMISSION OF NCSU-FIV. Rance Sellon, Suzanne Kennedy-Stoskopf, Elizabeth Hardie, Wayne Tompkins. North Carolina State University College of Veterinary Medicine, Raleigh, NC.

We have previously reported the transmission of feline immunodeficiency virus (FIV) via milk during acuate maternal infection. We have extended studies of vertical transmission of FIV by addressing the hypothesis that FIV is transmitted in utero.

Eight specific pathogen free cats were bred and inoculated intravenously with $1 \times 10^7$ TCID$_{50}$ of FIV-NCSU,1 at 16-19 days gestation (n=3) and at 36-42 days gestation (n=5). Fetal tissues were obtained at 56-58 days gestation and examined for FIV by amplification of FIV-gag by polymerase chain reaction (PCR). Supernatants from cell cultures of fetal liver, spleen, thymus and bone marrow were examined for p24 antigen by commercial ELISA. Placental trophoblast cultures were established from infected and uninfected cats and evaluated for evidence of, or susceptibility to in vitro FIV infection, respectively, by immunocytochemistry. Last, cell cultures from unexposed fetal tissues were inoculated with FIV in vitro and p24 was measured in the supernatant to determine susceptibility to infection.

Of 36 fetuses examined, none had evidence of productive FIV infection. Three fetuses from one mother had FIV-gag detected by PCR in fetal tissues and cell cultures, but cell cultures were consistently negative for p24 antigen. There was no evidence of FIV infection of the placenta from infected cats, and trophoblast cultures were resistant to in vitro infection. Fetal peripheral blood lymphocytes, and splenic and thymic cells were, however, highly susceptible to FIV infection. We conclude that the placenta is an effective barrier to in utero infection with this isolate of FIV.

The purpose of this study was to analyze cat semen for evidence of feline immunodeficiency virus (FIV) infection. Intact male specific pathogen free cats were obtained from a group of cats that had been orally exposed to NCSU-FIV at birth. At 11-12 months of age, semen samples were obtained by electroejaculation of 7 FIV-infected cats and 1 uninfected control cat. Diluted whole semen and whole blood samples were analyzed for the presence of an FIV gag segment by polymerase chain reaction (PCR) using a single set of primers and/or nested primers. Seminal fluid was co-cultured with CD4+ cells, a CD4+ lymphocyte cell line previously developed in our lab. Co-cultures were monitored for syncytia formation, an indication of active FIV infection, for up to 4 weeks, then analyzed by PCR.

Four of 7 whole semen samples from infected cats were positive for virus by nested PCR. Syncytia formation was observed in seminal fluid co-cultures from 4/7 infected cats. Five of 7 co-cultures were positive for FIV by PCR. Whole blood samples from all 7 infected cats were positive for FIV by PCR. None of the samples from the control cat were positive for virus.

These results indicate that infectious FIV is present in semen and suggest that, like human immunodeficiency virus, FIV may potentially be transmitted sexually.

The effectiveness of commercially available temperature sensitive-feline infectious peritonitis vaccine for preventing feline infectious peritonitis (FIP) in young kittens was examined. One group of 20 kittens was vaccinated intranasally from the same commercial serial on days 0 and 21 days; a second group of 20 kittens served as age-matched, nonvaccinated controls. All kittens were challenged orally 28 days after the second vaccination with $10^7$ TCID$_{50}$ of DF2 strain of FIP virus. Following challenge, kittens were monitored daily for appetite, depression, evidence of enteric disease, rectal temperature, and body weight. Eight weeks after challenge, all surviving kittens were sacrificed and necropsied. Histopathologic evaluations were performed for all kittens. All vaccinated kittens developed anti-coronavirus antibody titers following intranasal vaccination. Nineteen of 20 (95%) vaccinated cats survived the challenge study. One vaccinated developed clinically apparent FIP and was euthanized 6 weeks after challenge. Fifteen of 20 (75%) controls survived challenge. The 5 controls that developed clinical FIP were euthanized at postchallenge days 11, 17, 25, 35, and 54. Vaccinates looked well-kempted and more healthy appearing than did the controls during postchallenge observation. The DF2 challenge did not cause high death losses in either vaccinated and control groups. Histopathology results revealed that 6 of 20 (30%) vaccinated and 12 of 20 (60%) controls had lesions characteristic of FIP. All cats with clinically apparent FIP (one vaccinates and 5 controls) had histopathology positive for FIP. Results of this study indicate that temperature sensitive-feline infectious coronavirus vaccine induced humoral responses in all vaccinated kittens and has merit in protecting cats from clinical FIP.
EVALUATION OF AN FIV ANTIBODY TEST KIT
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DESIGNED FOR IN-OFFICE USE WITH BLOOD AND SALIVA. J.K. Levy, R.K. Selkon, D.J. Anderson, W.A. Tompkins, M.B. Tompkins. College of Veterinary Medicine, North Carolina State University.

Cats infected with FIV seroconvert and remain antibody positive unless the terminal stages of disease or death. Because blood-borne viral antigen titer is low, the measurement of circulating specific antibody has become the most practical method of screening cats for FIV infection. Thus, we developed an ELISA (ASSURE/FIV, Synbiotics, San Diego, CA) in development for clinical use with saliva, whole blood, serum, or plasma. The test detects antibodies against transmembrane gp46 protein of FIV and can be performed by lay personnel in less than 20 minutes. Saliva and heparinized whole blood were collected from 158 cats, 72 of which had experimental or natural FIV infections confirmed by western blot or PCR. All but 13 infected cats were seropositive for more than a year at the time of test evaluation. The tests were performed by an investigator blinded to the true status of the cats. Results were:

|                | Blood | Saliva |
|----------------|-------|--------|
| Sensitivity    | 0.99  | 0.81   |
| Specificity    | 1.0   | 1.0    |
| Predictive value (+ test) | 1.0 | 0.99 |
| Predictive value (- test) | 0.99 | 0.86 |

Maximum performance was obtained with blood. Sensitivity with saliva was increased by extending incubation of substrate/enzyme from 5' to 60' min. Special attention must be paid to the wash step and in avoiding carryover among the test solutions to limit nonspecific color development and false positive results. Interpretation of test results should be made in the context of the clinical history and the suspected prevalence of FIV in the population tested.

EFFECTIVENESS OF FENBENDAZOLE AGAINST GIARDIASIS IN DOGS
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S.G. Barr, D.D. Bowman, R.L. Heller. School of Veterinary Medicine, Cornell University, Ithaca, NY.

*Giardia canis* is a protozoan parasite commonly found in the small intestine of dogs. Giardiasis is important because of its prevalence, seriousness as a disease entity, possible zoonotic potential, and poor efficacy or serious side effects of drugs commonly used in therapy. Metronidazole (the most commonly used drug) is only 67% effective, occasionally causes neurologic effects, disease entity, possible zoonotic potential, and poor efficacy.

Eighteen dogs (12 Giardia-infected dogs (identified using the zinc sulfated sedimentation technique - ZSCT) were randomly allocated to 3 groups (6 dogs/group). Group 1 dogs were treated with fenbendazole (Panacur™, Hoechst-Roussel Agri-Ve Co., Somerville, NJ) at 50 mg/kg, PO, daily for 3 consecutive days; Group 2 dogs were treated with fenbendazole at 50 mg/kg, PO, q 8 h, for 3 consecutive days; Group 3 dogs were untreated controls. Three fecal samples were examined using the ZSCT from each dog of each group within 5 days of the last fenbendazole treatment; at least 24 hours elapsed between sample collections. Dogs were considered to have giardiasis if 1 or more ZSCT were positive. All 3 posttreatment ZSCT were negative in all dogs in both Groups 1 and 2. In the untreated control group, 1 dog had negative results for all 3 tests; 5 dogs were remained positive. There was a significant (P < 0.01) difference between dogs treated with fenbendazole at both dose levels and untreated controls. No signs of toxicity were seen in any dog. It was concluded that fenbendazole at 50 mg/kg, PO, q 24 h for 3 doses (the current registered dosage regime for other parasites in dogs) is effective and safe for treating *Giardia* infection in dogs.

BLUETONGUE VIRUS (ORBIVIRUS) INFECTION IN DOGS ASSOCIATED WITH A BLUETONGUE VIRUS CONTAMINATED CANINE VACCINE. G.Y. Akita, M. Ianoucensu, R.T. Greene, N.J. MacLachlan, and B.I. Oasburn. Dept. of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, Davis, CA., and Southwest Veterinary Diagnostics Inc., Phoenix, AZ.

Bleuetongue virus (BTV) is an arthropod-borne orbivirus known to infect most domestic and wild ruminants. In these species, clinical signs associated with BTV infections can range from subclinical to death. BTV infection in carnivores has never been documented, although there is evidence that another orbivirus, African horse sickness virus, can infect canines. This report describes two sibling female Australian Shepherd dogs that were vaccinated during the last week of pregnancy with a commercial, canine, multivalent, modified live vaccine. Both bitches aborted 7-9 days after receiving the vaccines, and died, with signs of heart failure and respiratory distress 48-72 hours after the abortion. Histopathology of necropy tissues from one of the dogs revealed pulmonary congestion with multifocal myocarditis. Polymerase chain reaction (PCR) detected BTV in the vaccine and spleen of the necropsied dog. BTV serotype 11 was isolated from the vaccine by sheep inoculation. Anecdotal evidence from a few practicing veterinarians has suggested similar, or other reactions, to this vaccine.

SEROPREVALENCE OF RICKETTSIA HENSELAE IN CATS
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THROUGHOUT NORTH AMERICA. PERRY H. JAMESON, CRAIG E. GREENE AND RUSSELL L. REGNERY. COLLEGE OF VETERINARY MEDICINE, UNIVERSITY OF GEORGIA, ATHENS, GA AND CENTERS FOR DISEASE CONTROL, ATLANTA, GA.*

The purpose of this study was to determine the prevalence of elevated IgG antibodies to *R. henselae* in pet cats throughout North America. *R. henselae* has been shown to be the causative agent of both Cat Scratch- Disease and bacillary angiomatisms in humans. Epidemiologic studies have demonstrated cat exposure to be a significant predisposing factor in the development of these conditions in people.

Serum samples were obtained from 10 commercial diagnostic laboratories throughout North America. Samples were selected based on the next 20-25 submissions and not on the clinical status of the cat. A total of 577 samples from 35 areas were obtained from July 1990 - December 1993. Antibody titers were determined with an IFA test. An IgG titer of 1:54 or greater was considered positive.

Cats living in the Southeast had a high seroprevalence with 60% (46/77) having a positive IgG titer. Along the Pacific coast of California 40% (32/80) were seropositive. In the Pacific Northwest and South Central Plains 34% (24/70 and 27/80, respectively) had positive antibody titers. Cats in the Northeastern United States were 33% (18/54) positive. In the Midwest only 7% (4/56) had positive antibody titers. The Rocky Mountains, Great Basin, and Northern Great Plains also had a low seroprevalence of 4% (5/125). Hawaii had a high seroprevalence with 53% (10/19) of the cats tested showing positive titers. Alaska had one of the lowest prevalence rates with only 2% (1/26) being positive. Of all the cats tested 26% (163/577) had a positive titer.

It was concluded from the data that there is a high seroprevalence to *R. henselae* in the pet cat population throughout North America. Geographic areas with warm, humid climates had a higher prevalence than cold, dry areas. This would support a theory that an arthropod vector is involved in transmission.
ENDOCARDITIS IN A DOG DUE TO INFECTION WITH 133 A BARTONELLA SPECIES. E.B. Breitschwerdt, D.L. Kordick, D. Malarky, B. Keene, and K. Wilson, College of Veterinary Medicine, North Carolina State University, Raleigh, NC, and the Veterinary Administration Hospital, Duke Medical Center, Durham, NC.

Congestive heart failure due to vegetative valvar endocarditis involving the mitral and aortic valves was diagnosed clinically, radiographically, and echocardiographically in a 3-year-old spayed female Labrador retriever. Historically, the dog had been treated with tetracycline hydrochloride and prednisolone for positive seroreactivity to Ehrlichia canis and antinuclear antigens. Three aerobic and anaerobic blood cultures failed to grow bacteria. Blood cultured simultaneously using the lysis centrifugation technique grew a fastidious aerobic organism. Primers for polymerase chain reaction (PCR) were designed to target the 16S rRNA genes of Bartonella species.

We conclude that the dog was infected with Bartonella canis and is doing well on amoxicillin, clavulanate-potentiated amoxicillin, digoxin, and enalapril the owner elected euthanasia 17 days later. Necropsy confirmed acute and viral valvar endocarditis. Bacteria, conformationally similar to Bartonella species were visualized in the heart valve by electron microscopy. Using polymerase chain reaction, Bartonella DNA was amplified from frozen heart valve. To determine the relationship of this isolate to other members of the genus Bartonella, the 16S rRNA genes are being sequenced.

We conclude that a member of the genus Bartonella can induce endocarditis in dogs.

SUCCESSFUL MANAGEMENT OF GASTROINTESTINAL PYTHOSIS WITH ITRACONAZOLE IN TWO DOGS. J. Taboada, B. E. Werner, A. M. Legendre. School of Veterinary Medicine, Louisiana State University (IT, BW) and College of Veterinary Medicine, University of Tennessee (AL).

An 18-month-old male Labrador retriever (dog 1) and a 28-month-old female spayed Labrador retriever (dog 2) were treated with itraconazole (10 mg/kg daily) for severe pyogranulomatous eosinophilic gastroenteritis (dog 1) and enterocolitis (dog 2) caused by the protozoan organism, Pythium insidiosum. Dog 1 had a 6-week history of vomiting, anorexia, and weight loss. A mural lesion involving the pyloric antrum and proximal duodenum, a second lesion involving the proximal jejunum, and mesenteric lymphadenopathy were identified by abdominal ultrasound and subsequent celiotomy. Pythium organism were positively identified by indirect immunoperoxidase staining and culture from biopsy specimens. The dog was treated with itraconazole, cimetidine, and metoclopramide. He gained 29 pounds over 3 months and the mural lesions and lymphadenopathy, as measured by ultrasound, resolved over 6 months of treatment. There has been no recurrence over 27 months. Dog 2 had a 3-week history of bloody diarrhea, anorexia, and weight loss. An abdominal mass was evident on physical examination and mural thickening was noted on rectal examination. Celiotomy revealed mesenteric lymphadenopathy and diffuse intramural thickening of the distal small intestine and colon with partial colonic obstruction. The diseased tissue was not resectable but a partial colectomy was performed to relieve the obstruction. Pythium was identified. The palpable mass and rectal thickening resolved over 8 months. The dog was treated with itraconazole for 13 months at which time a second mass was identified. Exploratory celiotomy revealed a resectable Pythium mass at the ileocolic anastomosis site. The mass was resected and the dog is doing well 14 months after surgery.

POLYMERASE CHAIN REACTION DETECTION OF FELINE LEUKEMIA VIRUS IN NATURALLY INFECTED CATS. E.H. Kremer and J. P. Thompson. College of Veterinary Medicine, University of Florida, Gainesville, FL.

The aims of this study were (1) to compare enzyme immunoassay (EIA) detection of FeLV infection to polymerase chain reaction (PCR) detection of a 770 base pair (bp) region within the p15e gene of FeLV and (2) to identify restriction endonuclease patterns of PCR-amplified FeLV DNA. Cats examined for FeLV-related illness or for routine EIA testing comprised the study population. Blood was collected in EDTA and immediately between FeLV detection by EIA and PCR and suggests PCR amplification may reveal latent FeLV infection and genetic variability among FeLV field strains.

FINAL EFFICACY RESULTS OF IMMITICIDE® USED TO TREAT DOGS WITH SEVERE HEARTWORM DISEASE. F.A. Tannor and D.M. Kistler. Rhone Merieux, Inc., Athens, GA.

The purpose of this study was to investigate the efficacy of melarsomine dihydrochloride (Immiticide®) given to client owned, severely affected, heartworm infected dogs. Previous studies had indicated that an alternate dose regimen for Immiticide® had potential to reduce the incidence of life-threatening thromboembolic disease (TE). For most dogs, the alternative posology reduced the infected dogs’ worm burden with the first treatment (1 injection) and eliminated the worms with the second treatment (2 injections). A multi-centered clinical field trial recruiting 44 client owned, class 3 heartworm infected dogs was performed using this alternative dose regimen during April 1992 through March 1993. Efficacy was evaluated qualitatively by in-house heartworm antigen test results and quantitatively by heartworm antigen level (Diromal®). Treatment success was also judged clinically by objective and subjective parameters. Final results demonstrate an efficacy rate of 89.2% for treatment as detected in patients’ serum by a commercial antigen test kit (Assure/CHtm). Average antigen concentration fell from an average of 0.801 ± 0.147μg/ml pretreatment to 0.022 ± 0.007μg/ml. Mortality due to TE was 10%. Clinical response was good to excellent. Immiticide®, in this study, appears to reduce post-treatment TE associated mortality when patients are managed on an out patient basis, and appears to be effective in reducing or eliminating worm burden.
CRYPTOSPORIDIUM IN DOGS AND CATS. S.C. Bar, W.G. Guiledt, G.F. Lamont, W.E. Horbucks, D.D. Bowman. School of Veterinary Medicine, Cornell University, Ithaca, NY, and Dept. Veterinary Clinical Sciences, Massey University, Palmerston North, New Zealand.

Cryptosporidiosis is a protozoan parasite affecting a wide range of hosts including cats and dogs. Although infection in cats and dogs is usually subclinical, severe disease (manifested by diarrhea, weight loss, and anorexia) can occur when these hosts are immunosuppressed. Cryptosporidiosis is a major cause of death in patients with AIDS, although the exact potential of species in dogs and cats is unknown. Of the many agents tested to treat cryptosporidiosis only paromomycin (a broad spectrum antimonial that is poorly absorbed from the gastrointestinal tract) has shown effective anticytosporidial activity in calves, mice, and human beings with AIDS. Because of this effectiveness, and low toxicity in mice, the purpose of this study was to assess the effectiveness of paromomycin to treat cryptosporidiosis in 3 cats and 2 dogs, and to subjectively assess the toxicity of the drug.

Three cats and 2 dogs (of varying age, sex, and breed) with signs of diarrhea were diagnosed with cryptosporidiosis on the basis of demonstrating Cryptosporidium cysts in the feces. All animals were treated with paromomycin (Humantin™, Parke-Davis, Morris Plains, NJ) at a dose of 125 mg/kg and 165 mg/kg body weight, PO, q 12 h for 5 days. Cryptosporidium cysts were absent from the feces within 1 day of the last dose of drug in all animals. The diarrhea had resolved within 5 days after finishing treatment in the 2 dogs and 2 cats, and within 30 days in the 3rd cat. No signs of toxicity were seen in any animal. We conclude that paromomycin may be effective in treating cryptosporidiosis in cats and dogs, and that further controlled studies should be performed to determine efficacy, and a minimum effective dose.

CEREBROSPINAL FLUID (CSF) ANALYSIS: A VITAL DIAGNOSTIC PROCEDURE IN THE INVESTIGATION OF NEUROLOGIC DISEASE. M. C. Weeks, NL Christopher, CL Chrisman, AL Hopkins, and BH Homer. College of Veterinary Medicine, University of Florida, Gainesville, FL

Cerebrospinal fluid (CSF) analysis is a vital diagnostic procedure in the investigation of neurologic disease. In humans, significant biochemical and cytological differences exist between neonatal and adult CSF. CSF from infants less than 3 months of age has a higher white blood cell (WBC) count and protein levels than adult CSF. The most accepted explanation for these differences is greater permeability of the neonatal blood-brain-barrier. There are no recent studies that compare CSF values in puppies and adult dogs. Protein concentrations and cytological profiles were evaluated in spinal fluid collected from the cerebellomacular cisterns of 10 normal puppies at four, six, eight, and ten weeks of age.

There was a statistical difference between WBC counts and protein levels of puppies four weeks of age and puppies ten weeks of age. Mean WBC counts were 7.5 +/- 3.2/μl and 2.8 +/- 0.6/μl at 4 and 10 weeks, respectively. Mean total protein levels were 33.8 +/- 3.4 mg/dl and 21.14 +/- 0.6 mg/dl at 4 and 10 weeks, respectively. A declining trend was seen in the 4 and 8 weeks of age groups. Cytological differences included reactive lymphocytes, vacuolated macrophages, and mitotic figures. The results of this pilot study suggest the need for further evaluation of the maturation of canine CSF.

NEURAL GENERATOR OF THE INITIAL COMPONENT OF THE CANINE FLASH EVOKED POTENTIAL. P.A. March, S.U. Walkley and C.E. Schroeder, Albert Einstein College of Medicine, Bronx, NY.

The neural generator of the first component of the canine flash visual evoked potential (VEP) was investigated in studies of 12 normal Beagles, 9-12 months of age. For surface mapping, dogs were anesthetized with intramuscular xylazine (4mg/kg) and ketamine (6mg/kg). VEPs were recorded with subdural needle electrodes at 1.0 cm spacings over one hemisphere, utilizing both monopolar and bipolar derivations. For intracranial recordings, anesthesia was supplemented with sodium pentobarbital (25 mg/kg intravenously) and craniotomies were made at appropriate locations. Depth profiles of VEP, current source density (CSD) and multunit activity (MUA) were recorded from cortical and subcortical structures using linear array multicontact electrodes. Surface recordings demonstrated that the least active monopolar reference site was the distal tip of the pinna. Referencing to sites near the eye led to contamination from the electroretinogram (ERG). The initial VEP component was a positivity (P1) with average onset and peak latencies of 12.5 and 17.5 ms, respectively. P1 amplitude was maximal at a midline location approximately 2 cm caudal to vertex. ERG signal obscured P1 at rostrolateral recording sites. Intracranial studies revealed that P1 had a maximum laminar voltage gradient (including polarity inversion) with a concomitant source over the sensorimotor cortex. Increase in MUA immediately above Lamina IV. The earliest activity in cortex was observed as a region of current sink and MUA increase in Lamina IV. Recordings from optic tract, lateral geniculate and optic radiations ruled out prominent subcortical contributions. The combined measures indicate that P1 arises mainly from primary visual cortex, specifically, from activation of supragranular pyramidal cell ensembles, secondary to activation of the major thalamoreceptor zone, Lamina IV.

EFFECTS OF POLYLACTIC ACID POLYMER WITH AND WITHOUT CISPLATIN ON BRAIN TISSUE OF DOGS. M. O. Smith, J. Kirpensteijn, M. Cooper, B. Powers, D. Brown, S. J. Withrow. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. 80523.

A biodegradable polymer, open-cell polyactic acid polymer (OPLA) was used as a carrier for local delivery of the chemotherapeutic agent cisplatin (P1) to the brain in seven purpose-bred mongrel dogs. OPLA-P1 (0.5% to 2% of 100mg/m²) and OPLA alone were implanted into the left and right cerebral hemispheres respectively of five dogs using sterile surgical technique. Three dogs were controls. Venous blood and cerebrospinal fluid were collected before surgery and at regular intervals following surgery. Dogs were monitored daily for physical and neurologic abnormalities. Five dogs were euthanized on day 21, one on day 35 and one was not euthanized. Seizures occurred in four dogs, resolving without therapy in two dogs and resulting in euthanasia of two dogs. Dogs that received OPLA-P1 were blind in the contralateral eye after surgery. Histopathological examination of brain tissue after necropsy revealed moderate gliosis and vacuolar change in the cerebral cortex surrounding the OPLA implants to a depth of approximately 0.5mm, similar to findings in the sham surgery control. Massive hemorrhage, malacia, vascular necrosis and thrombosis, and perivascular cuffing by mononuclear cells surrounded the OPLA-P1 implants to a depth of 2-3mm. We conclude that OPLA is a satisfactory carrier for the direct delivery of drugs to intrathecal sites. At these doses the neurotoxicity of cisplatin makes it an unsuitable drug for administration by this route.
TREATMENT OF GERIATRIC-ONSET INAPPROPRIATE URINE

CLINICAL EFFECTS OF SURGICAL DIVISION OF THE CORPUS CALLOSUM IN NORMAL BEAGLES. R.S. Bagley, R.D. Keegan, M.L. Harrington, S.A. Greene, M.P. Moore. College of Veterinary Medicine, Washington State University, Pullman, WA

Surgical division of the corpus callosum (callustomy), was performed in clinically normal dogs to determine surgical morbidity prior to a study of this procedure as a treatment for seizures in dogs with idiopathic epilepsy. Normal physical and neurological examinations and normal CBC, serum biochemical profile, urinalysis and cerebrospinal fluid analyses were used. Each dog was anesthetized with isoflurane and prepared for intracranial surgery. The corpus callosum was approached via a dorsal craniectomy and bluntly divided along mid-line. After surgery, dogs were monitored daily by physical examination for 30 days. Neurological examinations were performed on days 1, 3, 5, 7, 14, 21, and 28 after surgery. All dogs recovered from anesthesia and were alive throughout the study period. Four of six had mild forebrain dysfunction for 7 and 14 days after surgery. Five of six were clinically normal by day 14 after surgery. One dog had mild residual forebrain signs throughout the study period. All dogs were euthanized 30 days after surgery and the brains examined histologically. Complete corpus callosum division was found in three dogs. In the remaining three, only a small portion of the of the rostral corpus remained intact. We conclude that corpus callustomy can be performed with minimal morbidity and mortality in clinically normal dogs. Further study is necessary to determine the efficacy of this procedure as an alternate seizure treatment in dogs with idiopathic epilepsy.

IDIOPATHIC POLYNEUROPATHY IN ALASKAN MALAMUTES

K.G. Brandt, C.T. Lowrie, A. Shores, S.M. Cochran, M.P. Moore, H.S. Steinberg, J.E. Steiss, R.D. Keegan. Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, Alabama

Inappropriate elimination of urine in the absence of urinary tract dysfunction occurs in elderly people, for example in those with dementia. A similar phenomenon occurs in elderly dogs. The purpose of this open label pilot clinical trial was to evaluate the safety and efficacy of 1-deprenyl for treatment of inappropriate urine elimination, defined as complete voiding in an inappropriate location, with or without intercurrent urine dribbling. Nineteen dogs exhibiting inappropriate urine elimination in conjunction with lack of evidence of PU/PD or debilitating organic disease (based on physical and neurologic examinations, CBC and chemistry profile results) were evaluated. One of the dogs also exhibited urine dribbling; none of the dogs exhibited other signs of uregonaic tract disease. Owners assessed their dogs via questionnaire at enrollment and monthly for 3 months with respect to urine elimination pattern and 14 additional parameters of behavior and cognition. No dogs experienced serious drug related adverse events. After one month of 1-deprenyl therapy at 0.5 mg/kg p o SID there was complete cessation of inappropriate urine elimination in 7 (37%) dogs, while an additional 9 (47%) exhibited partial response. The improvements were generally maintained at months 2 and 3. We conclude that 1-deprenyl deserves further study for treatment of urine inappropriate elimination, and perhaps for urine dribbling. Follow-up continues and expanded trials are being conducted.

HISTOCHEMICAL AND MORPHOMETRIC STUDY OF FIBER TYPES IN TEN SKELETAL MUSCLES OF HEALTHY YOUNG ADULT CATS. K.G. Brandt, K.A. Amling, J.R. Mehta, J.E. Steiss, C. Scholz. Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Auburn, Alabama

A histochemical and morphometric study of fiber types in a variety of skeletal muscles of healthy young adult cats was undertaken to provide normative data not available previously. Such data are needed to facilitate interspecies comparative studies and provide a framework against which fiber type alterations due to normal development, disease, aging, or experimental manipulations can be compared. Using a standardized system of nomenclature, type 1, 2A, 2B and 2C fibers were identified in most cat muscles on the basis of myosin adenosine triphosphatase (ATPase) staining at pH 4.45. Type 2M fibers were present in temporalis (TEM) and masseter (MAS) muscles. Type 1 fibers predominated in medial head of triceps (MHT) and soleus (SOL) muscles. Type 2B fibers were dominant in biceps femoris (BF), lateral head of gastrocnemius (LGA), cranial tibial (CT), long head of triceps (LHT), and superficial digital flexor (SDF) muscles; type 2A fibers were dominant in buccinator (BUC) muscle samples; and type 2M fibers were dominant in TEM and MAS muscles. Numbers of type 2C fibers did not exceed 2-3% of the myofiber population in any muscle. In CT and LHT muscles, a gradient of fiber type distribution was noted, with significant increase (p<0.05) in numbers of type 1 and type 2A fibers in deeper regions of the muscles. The distribution of fiber types was compartmentalized in MHT and MAS samples. Type 2B fibers were significantly larger (p<0.05) than type 1 and type 2A fibers in BF, LGA, CT, LHT, and superficial MHT. Type 2M fibers were significantly larger (p<0.05) than type 1 fibers in TEM and MAS muscles. SOL type 1 muscle fibers were the largest fibers encountered in any muscle. In MHT, fiber diameter of type 1 and 2A fibers varied significantly (p<0.05) in oxidative and glycolytic compartments. Variability coefficients were <200 in all muscles. Muscle spindles were not observed in MAS, TEM, or BUC muscle samples. In every muscle sample, the number of fibers with internal nuclei was ≤ 2 per cent.
PRETREATMENT CHARACTERIZATION OF BEHAVIORAL AND 145 COGNITIVE PROBLEMS IN ELDERLY DOGS. A.E. Buahidi, A. Buahidi, and S.J. Fluharty. School of Veterinary Medicine, University of Pennsylvania, PA

The central actions of angiotensin II (AngII) are involved in the regulation of cardiovascular homeostasis. Relatively little is known about the biochemical and molecular properties of neuronal AngII receptors, in part because they are located in small, restricted brain regions. Multiple subtypes exist, and at least one subtype is unique to the nervous system. The use of p-chloromercuri-phenylsulfonic acid (PCMS) to amplify weak AngII binding in rat brain was investigated. Binding assays and displacement studies with AngII analogs in the presence and absence of PCMS were performed. [125I]AngII binding to membrane bound AngII receptors was dramatically increased in the presence of PCMS in a dose response fashion. The highest concentrations of these receptors were in the olfactory bulb and thalamus/hypothalamus. [125I]AngII binding in the cerebellum and brain stem was not PCMS sensitive suggesting that these same receptors are not in these regions. It was concluded that PCMS was capable of increasing [125I]AngII binding in certain rat brain regions. Further specificity studies with AngII analogs should allow us to determine if PCMS sensitive AngII receptors represent a unique subpopulation of receptors in the brain. Regional sensitivity of cerebral AngII receptors to PCMS suggests an even greater degree of heterogeneity of these proteins in rat brain than previously was known.

GENUS-SPECIFIC DETECTION OF SALMONELLAR IN 147 EQUINE FECES BY THE POLYMERASE CHAIN REACTION (PCR). N.D. Cohen,1 H. L. Neibergs,2 D.E. Wallis,1 R. B. Simpson,1 E.D. McGruder,1 and B.M. Hargis.1 College of Veterinary Medicine, Texas A&M University, College Station, TX1 and National Animal Disease Center, Ames, IA2

Detection of Salmonella in feces from horses using the polymerase chain reaction (PCR) and genus-specific oligonucleotide primers was investigated. Feces from healthy horses were determined to be negative for Salmonella by microbiologic culture. Fecal samples were inoculated with known numbers of colony forming units (cfu) of Salmonella enteritidis (SE). DNA was extracted from fecal samples and amplified by the PCR using genus-specific primers. Five separate replications of the experiment were performed.

The sensitivity of the assay extended to 10^2 cfu of SE/g feces; the sensitivity of microbiologic culture with enrichment extended to 10^4 cfu of SE/g feces. Feces that were not inoculated with Salmonella were negative by the PCR. Detection of salmonellae in feces was possible using the PCR within 10 to 12 hours from the time of submission of samples. Results indicate that the technique may be useful for rapid screening of equine feces. Faster identification of salmonellae in feces would enable earlier implementation of appropriate strategies for treatment, control, and prevention.

AMPLIFICATION OF ANGIOTENSIN II RECEPTOR 146 BINDING IN RAT BRAIN. C.H. Ytje, J.R. Slenens, and S.J. Fluharty. School of Veterinary Medicine, University of Pennsylvania, PA

DEVELOPMENT OF PARASITE-SPECIFIC rDNA PROBE FOR SARCOCYSTIS NEURONA ASSOCIATED WITH EQUINE PROTOZOAL MYELOENCEPHALITIS. A.E. Marsh, BC Barr, IE Madigan, PA Conrad University of California, Davis and CVDLS.

Sarcocystis neurona is the etiologic agent of equine protozoal myeloencephalitis (EPM) was isolated and described in 1991. To date however, there are limited means available for antemortem detection of this protozoan in horses, and the life cycle, mode of transmission and pathogenesis of this disease remain unknown. Ribosomal DNA (rDNA) is present in multiple copy number and is highly conserved between protozoan species. Ribosomal DNA probes for S. neurona would allow antemortem detection and could be useful in elucidating the life cycle and pathogenesis of the parasite. The purpose of this study was to develop parasite specific rDNA probes for S. neurona. We obtained an isolate of S. neurona by in vitro cultivation of homogenized neural tissue from a horse with EPM and prepared DNA from culture-derived merozoites. Using primers for a highly conserved region of the rDNA gene partial sequences for the merozoite rRNA (1.8 kb) and equine rRNA (0.2 kb) genes, we amplified rDNA by the polymerase chain reaction (PCR) and used these to identify parasite-specific sequences. Protozoan-specific oligonucleotide primers were then synthesized and used to amplify the rDNA sequence in multiple protozoan parasites (Sarcocystis spp., Toxoplasma gondii spp., and Neospora spp.). A S. neurona amplification product was distinguished from the other parasites using a parasite-specific internal probe for S. neurona DNA. Preliminary data will be presented evaluating these probes on clinical material. Supported by a grant from The Equine Research Laboratory, University of California Davis.
CHARACTERIZATION OF CASES OF BOVINE SEVERE, ACUTE COLIFORM MASTITIS. C.K. Cebra, F.B. Garry, R.P. Simmerm, College of Veterinary Medicine, Colorado State University, Fort Collins, CO.

Clinical presentation and clinical pathology data were studied on 29 adult cows with severe, acute coliform mastitis. Diagnosis was confirmed by a positive milk culture for Escherichia coli on all cases. The cattle were grouped by stage of lactation and survival. Cattle within the first twelve weeks of lactation, compared to those further into lactation, maintained higher median blood band cell count (600 vs 100/µl) and neutrophil (800 vs 270/µl) levels and were more likely to die or be euthanized (26% vs 9%). When survivors and nonsurvivors from both groups were compared, nonsurvivors were less likely to be neutropenic, had higher median blood neutrophil levels (1000 vs 210/µl), packed cell volume (39.5 vs 34) and anion gap (24 vs 20), and lower serum protein (6.6 vs 6.9 gm/dl) and total CO2 (19.8 vs 24.7 mg/dl). Though these median values were significantly different (P > 0.05) between groups, many values lay within the physiologically normal ranges.

Bacteriologic blood cultures were performed on 21 of the 29 cattle studied. E. coli was isolated from the blood in 4 of the 21 (19%) cattle. Clinical presentation and clinical pathology data were compared in bactericemic versus nonbacteremic cows to evaluate these data as predictors of bacteremia. Median days in milk was significantly lower for the bactericemic cows (9.3 vs 78), but physical parameters and laboratory data for the two groups were almost identical. These findings suggest that bacteremic cases of coliform mastitis exist, especially early in lactation, and cannot be differentiated from nonbacteremic cases based on routine physical and laboratory evaluation.

PRELIMINARY INVESTIGATION OF AN EPIZOOTIC OF A NONCYTOPATHIC BOVINE VIRAL DIARRHEA VIRUS (BVDV) IN A BEEF RESEARCH HERD. SA Fleming, JW Scruge, WR Maslin and AM Groce

During a 3 month period of 1993, 8 calves 3.5 to 18 weeks old died or were euthanized. These calves came from 3 groups of a research herd representing 95 cow-calf pairs. The cows had received annual vaccination with a product containing killed cytopathic and noncytopathic strains of BVDV. Six of the affected calves were milked; 3 of the calves were Angus, 2 were Charolais, and 1 was crossed. The ages of the dams of affected calves were 4 years old (4), 6 years old (2), 9 years old (1) and 11 years old (1). Six of the calves presented with acute depression, weakness and diarrhea, and 2 calves exhibited a chronic illness. BVDV was identified on Buffy coat samples or immunofluorescence on tissues in 5 calves. Erythroid, myeloid and megakaryocytic necrosis was demonstrated on bone marrow samples. In two cases sub-physiologic osteoporosis-like lesions with retained physal cartilaginous necrosis and paucity of osteoclasts was found. BVDV serology and isolation of noncytopathic BVDV is pending on the dams. This appeared to be an outbreak of an unusual strain of BVDV with a particular tropism for the monocytic and megakaryocytic cell line, that included osteoclast destruction.

CLINICAL RESPONSE AND ANTIMICROBIAL RESIDUE TEST IN NON-ANTIBIOTIC TREATED COWS WITH INDUCED ACUTE COLIFORM MASTITIS. J.L. Stewufili, J. Nnvash, K. Leslie, C.L. Oyles, C.A. Mockie, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada

Fourteen early lactation Holstein cows were experimentally challenged by intramammary infusion of two teats to compare the virulence of strains of E. coli isolated from feces or from cases of bovine mastitis. Virulence was assessed by carefully monitoring clinical parameters and by collecting milk samples for SCC and bacterial isolation. The initial treatment protocol consisted of parenteral antibiotics and fluid therapy with the onset of high fever, significant systemic signs and local inflammation. Two cows treated with this protocol developed severe depression, dehydration, recumbency and were euthanized. Subsequently, the treatment protocol was revised to commence hourly stripping of the affected quarters plus injections of 30 IU of oxytacin once body temperature was ≥ 41°C. This was repeated at hourly intervals until the temperature was ≤ 39.5°C. All 12 cows treated with this protocol responded within 24 hours. Bacteria were cleared from all infected quarters within 96 hours. The presence of non-antibiotic inhibitory substances in milk of the infected and noninfected quarters was determined by the Brilliant Black Reduction Test (BRT), Delvotest® P (DTP) and Bacillus stearothermophilus Disc Assay (BSDA) residue test. False positive test results were found in at least one sample between 12 and 48 hours post-infection in 9, 5 and 7 cows using BRT, DTP and BSDA, respectively. These results indicate that non-antibiotic therapy involving stripping and oxytacin merits further study. In addition, acute coliform mastitis cases may represent a source of error in routine antibiotic residue testing programs.

LACTOFERRIN LEVELS IN COLOSTRUM FED TO NON-ANTIBIOTIC TREATED COWS WITH INDUCED ACUTE COLIFORM MASTITIS. H.R. Staemufli, J. Nnvash, K. Leslie, C.L. Oyles, C.A. Mockie, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada

Lactoferrin (LF), an iron binding protein that is present in colostrum, is believed to play an important role in the immune response to gram-negative bacterial infection. Previous studies have explored the importance of lactoferrin in conferring local immunity within the gut of the neonate. The purpose of this study was to establish normal serum LF levels in colostrum fed calves and try to correlate levels with colostral LF levels.

50 healthy Holstein calves were each fed 4 liters of dam's colostrum within 24 hrs of birth. Serum samples were collected on each calf 24 hrs later. First milking colostrum was collected from each dam. Colostrum and calf serum were analyzed for IgG, IgA, IgM, and LF. Immunoglobulin (lg) levels were determined by SRID. Serum LF levels were determined by SRID using a sandwich ELISA, while colostrum LF levels were determined by SRID using antibovine LF goat serum.

Mean serum LF was 4.9 ± 0.95 mg/L. No correlation was found between the dam's parity and any colostral proteins. Colostral LF was not significantly correlated with colostral IgG. Serum LF levels were significantly correlated with serum IgG (r= -0.42, p < .0024) and IgA (r= -0.28, p < .0464). The calf's Ig and LF absorption was independent of colostral concentration. Calves with adequate Ig absorption can be expected to have maximal LF absorption.
SURVIVAL AND REPLICATION OF RHODOCOCCUS EQUI IN MACROPHAGES. M. K. Hofland and D. M. Moser. School of Medicine, Temple University, Philadelphia, PA.

Though R. equi is accepted to be capable of survival within macrophages, the kinetics of bacterial intracellular growth have not been fully addressed, nor have intracellular survival differences between strains of R. equi been evaluated. We have studied the survival and replicative potential of R. equi in both equine alveolar macrophages and murine peritoneal macrophages in vitro, and we have compared two strains of R. equi, the avirulent type strain ATCC 6939 and a clinical isolate 238, with respect to intracellular growth. Rhodococcus-infected macrophage monolayers were fixed with methanol and then stained with polyclonal anti-rhodococcus antisera. Subsequent fluorescent microscopic examination then permitted visualization and enumeration of intracellular organisms. In addition, total fluorescence was quantitated using image analysis cytometry.

Results indicated that following an initial lag period of 6 to 12 hours, intracellular numbers of the clinical isolate 238 began to rise, often reaching macrophage compromising levels by 48 hours. These data were confirmed by quantitative fluorescent cytometry. In contrast to strain 238, the avirulent strain 6939 failed to efficiently replicate intracellularly; bacterial numbers remained relatively constant over the 48 hour observation period. Strain 238 and another virulent strain were shown to express a 17-kd virulence-associated plasmid protein, whereas the avirulent 6939 did not. These results suggest that plasmid-encoded bacterial virulence factors may be contributing to the ability of R. equi to replicate within its host cell, the macrophage.

Exposure to endophyte-infected (Acremonium coenophialum) tall fescue as a risk factor for laminitis in the horse: an aggregate risk study. B. W. Rohrbach, E. M. Green, J. W. Oliver, and J. F. Schneider. College of Veterinary Medicine, University of Tennessee, Knoxville, TN.

Loline and ergot alkaloids, found in endophyte-infected (Acremonium coenophialum) tall fescue (EITF) cause vasocstriction of equine vessels in vitro. An aggregate risk study was used to evaluate the association between horses exposed to EITF and incidence of laminitis. Veterinary teaching hospitals (VTHs) participating in the Veterinary Medical Data Base were grouped into high, moderate, or low risk of exposure groups. In total, 5,536 had a diagnosis of laminitis. Incidence rates in the high, moderate and low risk VTHs were 3.41, 3.04 and 2.00 cases of laminitis per 100 admissions, or fifteen percent of all admissions for laminitis to VTHs. Preliminary data support an association between horses exposed to EITF and increased risk of laminitis to VTHs in our data base. Preliminary data support an association between horses exposed to EITF and increased risk of laminitis, however, studies at the individual animal level are indicated to confirm this hypothesis.
157. EFFECT OF ENDOPHYTE-INFECTED TALL FESCUE ON EQUINE FETAL PULMONARY MATURITY

K.A. Smith Clare, E.M. Green, J.R. Strickland, J.W. Oliver, and F.M. Andrews (University of Tennessee College of Veterinary Medicine, Knoxville, TN); D.L. Cross, E.K. Atman, and D.K. Roach (Clemson University, Clemson, SC).

Indicators of fetal lung maturity were measured in amniotic fluid from mares grazing endophyte-infected tall fescue (EFF) and endophyte-free tall fescue (EFF). Eleven mares were divided into 2 groups, EFF (n=3) and EFF (n=8). Aminocentesis was performed on all mares at 14 days prior to expected date of parturition.

Thin layer chromatography was utilized to determine the presence of phosphatidylglycerol (PG), phosphatidylcholine (PL), and phosphatidylethanolamine (PE) in amniotic fluid. Lecithin (L) and sphingomyelin (S) were reported as percentages of total lipid content from which lecithin to sphingomyelin (L:S) ratios were calculated.

Student's t-Test was used to compare PG, PL, L, S, and L:S ratios between the 2 groups (p<0.05). Pulmonary phospholipids were often absent in amniotic fluid from mares grazing EFF. PG was detected in 1/3 EFF and 5/8 (62.5%) EFF mares. PL was detected in 3/3 EFF and 6/8 (75%) EFF mares. PE was different (p<0.000001) between groups, being present in 2/3 (66.7%) EFF and 1/8 (12.5%) EFF mares. The mean L:S ratios for EFF and EFF groups were 0.88 and 1.15, respectively.

These data suggest that ingestion of EFF during gestation may cause impaired equine fetal pulmonary maturity.
Effects of sodium bicarbonate administration on selected biochemical parameters in horses.

Six Standardbreds were administered sodium bicarbonate (50 mmol/kg IV) or a placebo on days 1, 2, 4, 6, and 8. Venous blood samples were collected at 2, 4, and 6 hours after sodium bicarbonate administration.

Results indicated that the CPK activity increased significantly after sodium bicarbonate administration compared to the placebo group. There were no significant changes in serum creatinine, blood urea nitrogen, or serum protein levels.

Conclusion: Sodium bicarbonate administration increased CPK activity in Standardbreds, indicating a potential for muscle toxicity. Further studies are needed to investigate the long-term effects of sodium bicarbonate on biochemical parameters in horses.

Pharmacokinetics of large-dose gentamicin in the horse. T. J. Doherty, M. J. Novotny, R. M. Desjardins, and S. A. Burton.

Once-daily aminoglycoside administration has been recommended based on reduced nephrotoxicity, enhanced concentration-dependent bactericidal killing, and prolonged postantibiotic effect associated with the high Cmin. This study determined the serum kinetics of gentamicin (8 mg/kg) following intravenous, intramuscular, and subcutaneous administration in three groups of healthy, adult Standardbreds. Venous blood samples were collected over 24 hours and serum gentamicin analysis was performed using an automated fluorescence polarization immunoassay (sensitivity 0.5 pg/ml). Data were analyzed using a non-compartmental approach and the results are presented below:

- IV (n=6): Cmax = 16.2 ± 3.4 pg/ml, T1/2 = 3.2 ± 0.8 hours, CL = 1.0 ± 0.2 ml/min/kg, Vd = 1.5 ± 0.3 l/kg
- IM (n=6): Cmax = 18.5 ± 3.9 pg/ml, T1/2 = 3.5 ± 0.9 hours, CL = 1.1 ± 0.2 ml/min/kg, Vd = 1.6 ± 0.4 l/kg
- SC (n=4): Cmax = 21.0 ± 4.2 pg/ml, T1/2 = 3.8 ± 1.0 hours, CL = 1.2 ± 0.3 ml/min/kg, Vd = 1.7 ± 0.5 l/kg

The hemodynamic effects of phenylbutazone in exercising horses. L.A. Mitten, K.W. Hinchcliff, and R.H. Burton.

Phenylbutazone is a drug widely used in performance horses, but little is reported on its effects on the physiologic responses to exercise. Therefore, we investigated the effects of phenylbutazone on hemodynamic variables in horses running on a high speed treadmill. Six Standardbred horses participated in each of 2 trials in a randomized, blinded, crossover design. Either phenylbutazone (8.8 mg/kg PO Q 24 h) or a placebo was given for 2 days prior to the exercise trial. One hour before each trial each mare received either phenylbutazone (4.4 mg/kg IV) or a similar volume of isotonic saline. Horses ran for 4 min at 4 m/s, 2 min at 7 m/s, 2 min at 9 m/s and until exhaustion at 10 m/s on a high speed treadmill at a 4° slope. Data was collected at rest, during the last 15 seconds of each speed, and at 5 and 15 minutes during recovery. Physiologic data collected included: heart rate; mean right atrial pressure; mean, systolic, and diastolic carotid and pulmonary arterial pressures and time to fatigue. There was no effect (P > 0.05) of treatment on mean, systolic or diastolic carotid or pulmonary arterial pressures or time to fatigue. Right atrial pressures increased with increasing speed in treated and untreated horses, but horses receiving phenylbutazone had higher (P < 0.05) right atrial pressures at 7 and 9 m/s than did untreated horses (29 ± 2.6 mmHg vs 22.7 ± 3.0 mmHg, mean ± SE at 9 m/s). Horses receiving phenylbutazone had higher heart rates (P < 0.05) at 4, 7 and 9 m/s than did untreated horses (308 ± 4 vs 193 ± 3 bpm at 9 m/s). We conclude that phenylbutazone administration alters the hemodynamic responses of horses running on a treadmill.
PHARMACOKINETICS OF GENTAMICIN IN GOATS. Peter Q. Ogunbiyi, Lanell Ogden, Emmanuel G. Mduvwa, B. A. Akinlosotu, R. Ram Purohit, and Robert Wilson. School of Veterinary Medicine, Tuskegee University, Tuskegee, AL, and College of Veterinary Medicine, Auburn University, Auburn, AL.

The pharmacokinetics of gentamicin were studied in healthy adult, female, nubian goats. Eight goats were given gentamicin sulfate (3 mg/kg) by intravenous (IV) and intramuscular (IM) routes to determine single dose kinetic parameters. Six other goats were given gentamicin sulfate (3 mg/kg), IM, twice a day for 5 days, to evaluate the peak and trough values. The serum gentamicin concentration-time curves were analyzed using a non-compartmental model based on the statistical moment theory.

The elimination half-lives after IV and IM administration, were (means ± SD): 88.24 ± 48.32 and 111.54 ± 47.43 minutes, respectively. Following IV administration, the mean residence time (MRT) was 86.69 ± 28.33 minutes, the apparent volume of distribution at steady state (Vss) was 0.254 ± 0.150 ml/kg and the total body clearance (Cl) was 2.25 ± 0.67 ml/min/kg. The bioavailability, after IM administration, was 96.52 ± 12.64%. Based on the pharmacokinetic data of this study, a dose of 3 mg/kg, IM, administration, were (means ± SD); 88.24 ± 0.67 ml/min/kg. The bioavailability, after IM administration, was 96.52 ± 12.64%. Based on the pharmacokinetic data of this study, a dose of 3 mg/kg, IM, every 12 hours provided adequate gentamicin levels in goat serum with a peak and a trough values (means SD) of 12.43 ± 2.27 and 0.65 ± 0.68 µg/ml, respectively.

ALLEVINATION OF THE EFFECTS OF ENDOTOXIN ADMINISTRATION IN HORSES BY PRETREATMENT WITH A MONOCLONAL ANTIBODY AGAINST EQUINE TUMOR NECROSIS FACTOR. J. Cargile and R. MacKay. LACS Dept. Univ. of Florida, College of Veterinary Medicine; Gainesville, FL 32610.

To determine the role TNF plays in E. coli endotoxemia, a murine anti-Eq TNF monoclonal antibody (mAb) was tested in horses given endotoxin (LPS). An IgG, isotype mAb with high titrated and specific anti-Eg TNF activity was produced against isolated native Eq TNF. Ten healthy young adult miniature horses were randomly sorted into 2 groups to receive either the anti-TNF mAb or an isotype-matched control mAb at 2 mg/kg IV, 10 minutes prior to IV bolus of 0.25 µg/kg LPS (E. coli O55:B5). Clinical signs and blood samples were taken 20 minutes prior and at intervals for 24 hours after LPS infusion. WBC, TP, and PCV were determined within an hour after sampling. Plasma was harvested immediately then stored at -80°C for later TNF, IL-6, and lactate analysis. Data were analyzed by 2-way ANOVA for significant (P<0.05) time by treatment interaction. Plasma TNF and IL-6 activities and lactate concentration were significantly reduced in anti-TNF treated horses with maximal values of 4.6 ± 1.8 µg/ml TNF, 59.2 ± 29.2 RU/ml IL-6, and 16.0 ± 1.8 mg/dl lactate vs 4.176 ± 2.425 RU/ml TNF, 68.4 ± 37.9 RU/ml IL-6, and 26.0 ± 1.03 mg/dl lactate in control horses. Anti-TNF treated horses also had significantly improved clinical scores, lower heart rates, and higher WBC counts vs control horses. We conclude that TNF neutralisation alleviates the response of horses to bolus LPS treatment and that its evaluation in clinical cases is warranted.

EFFECTS OF SPECIFIC TUMOR NECROSIS FACTOR BLOCKADE IN ENDOTOXIN TREATED CARPAL JOINTS IN THE HORSE. E. MacKay, D. Naviaux, and J. Cargile. LACS Dept., University of Florida, College of Veterinary Medicine, Gainesville, FL 32610.

Elucidation of the role of TNF in acute synovitis may provide a basis for new treatment strategies. In this study, synovial TNF was neutralized in joints of horses infused with endotoxin. An IgG, murine mononclonal antibody was produced against purified equine serum TNF. To facilitate frequent synovial fluid collection, indwelling catheters were secured in the palmarolateral portals of the antebrachial carpel joints of 6 horses. In each horse, 1 joint was injected with a mixture of anti-TNF mAb (5 mg) and endotoxin (1 µg; E. coli O55:B5) while the contralateral joint received 1 µg endotoxin plus isotype-matched control mAb. Subjective grading of joint swelling was performed by two investigators blinded to treatment. Data were subjected to ANOVA (continuous) or Wilcoxon Rank Pair Test (ordinal). Compared with control joints, there was significantly less (P = 0.043) swelling in anti-TNF-treated joints 5 and 8 hours after endotoxin. In control joints, maximal mean synovial activities for TNF (1019 ± 310 U/ml), IL-1 (173 ± 102 U/ml) and IL-6 (15.8 ± 2.1 x 10³ U/ml) were found at 2, 5 and 8 hours, respectively. No TNF was detected in anti-TNF-treated joints; however, significant reduction in IL-1 and IL-6 was not found. Maximal WBC counts for both control (15.6 ± 3.2 x 10⁶ cells/µl) and anti-TNF-treated (12.5 ± 3.3 x 10⁶ cells/µl) joints were found at 5 and 8 hours after endotoxin (not significant). The results of this study indicate that TNF may play a role, albeit minor, in the pathogenesis of endotoxin-induced synovitis.

CLASSIFICATION OF ADHESION MOLECULES COMPRISING CD18 SUBUNIT ON THE UNSTIMULATED EQUINE NEUTROPHIL. C.J. Savage, M.V. Crisman, J.R. Wicke. Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA.

The surface presentation of CD18-containing adhesion molecules on neutrophils was evaluated in six clinically normal horses twice at 7 to 30 day intervals. The monoclonal antibodies 60.3, 60.2#25 and #25 recognize CD18, which is part of heterodimeric integrins LFA-1, Mac-1 and p150, 95, which have crucial roles in neutrophil-endothelial adhesion and the complement cascade. Neutrophils were isolated from whole blood and incubated with primary monoclonal antibodies (60.3, #25 or #25) or balanced salt solution. Cells were then incubated with the secondary fluorescent monoclonal antibody [Fluorescein isothiocyanate (FITC) - conjugated AffiniPure F(ab'), fragment goat-antimouse (GAM) IgG], which acted as a fluorescent tag for fluorescence activated cell sorting. Cell viability measurements were performed pre- and post-incubation.

Results indicate that unstimulated equine neutrophils expressed CD18 cell surface adhesion molecules (p<0.05) using monoclonal antibodies 60.3, #25 and #25. Some autofluorescence was evident in neutrophils not incubated with primary monoclonal antibodies. However, non-selective fluorescence was minimized by use of a secondary fluorescent monoclonal antibody composed of F(ab'), which is part of heterodimeric integrins LFA-1, Mac-1 and #25. Viability pre- and post-incubation ranged from 94 to 100% and was not different, indicating that monoclonal antibody incubation did not adversely affect cells. It was concluded that unstimulated neutrophils from horses express important integrin adhesion molecules on their cell surface, which are crucial to the immune response. These modalities could be used to manipulate certain diseases (e.g. respiratory distress syndrome, ischemia/reperfusion diseases, degenerative joint disease).
CHANGES IN LYMPHOCYTE SUBPOPULATIONS FOLLOWING PROLONGED EXERCISE IN HORSES. M. T. Hines, A. Leroux, K. C. Schott, W. C. Davis, S. E. Blank. Washington State University, Pullman, WA.

Strenuous exercise represents a significant physiological stress that modifies the immune response and may result in increased susceptibility to disease. The effects of prolonged exercise on circulating lymphocyte subpopulations were investigated at a 50 mile endurance ride. Peripheral blood was collected from 3 horses immediately prior to and on completion of the ride. Absolute lymphocyte numbers were determined and numbers of T helper/inducer (CD4+) and T cytotoxic/suppressor cells (CD8+) were measured by flow cytometry using monoclonal antibodies HB61 and HT14 respectively.

In all cases there was a decrease in the total number of circulating lymphocytes immediately following the ride. The number of CD4+ cells declined, while there was little or no change in the number of CD8+ cells, resulting in a decrease in the CD4:CD8 ratio in all horses. These findings indicate that the stress of prolonged exercise alters the population of lymphocyte subsets in the circulation, which may affect cellular immune function and impair resistance to infection.

THE INTERRELATIONSHIP BETWEEN REACTIVE OXYGEN AND ARACHIDONIC ACID METABOLITES WITH NEUTROPHILIC INFLTRATION IN THE large INTESTINE IN A PONY MODEL OF ACUTE COLITIS. RS McConnico, MC Roberts, MB Poston. College of Veterinary Medicine, North Carolina State University, Raleigh, NC.

The pathologic mechanisms associated with massive secretory diarrhea in horses and ponies is unknown. Inflammatory mediators are important components of the gastrointestinal immune response but at the same time may play a critical role in the pathogenesis of acute colitis diarrhea. This study was undertaken to show that an increase in cecal and colonic mucosal tissue levels of reactive oxygen metabolites (ROM) and prostaglandin E2 (PGE2) coincides with early neutrophilic infiltration in acute stages of colitis while diminished levels are associated with resolution of diarrhea and restitution of the mucosa. Cecal and colonic tissues were harvested from 8 ponies (4 each at 12 and 24 hours) following single dose administration of castor oil (2.5ml/kg body weight via nasogastric intubation) and 4 ponies with naturally occurring acute colitis. Control samples were collected from age and weight matched normal animals. Mucosal tissues were analyzed for lipid peroxidation (reflection of ROM levels), PGE2 levels (radioluminamassay), myeloperoxidase activity (reflection of neutrophilic infiltration), and adjacent samples examined histologically. Myeloperoxidase activity, lipid peroxidation, and PGE2 levels were markedly elevated in cecal and colonic mucosal tissue in ponies and horses with castor oil-induced or naturally occurring acute colitis compared to normal control animals.

NECROTIZING ENTEROCOLITIS IN HORSES. W. J. Saville, K. W. Hirschcliff, B. E. Moore, C. W. Kohn, S. M. Reed, L. A. Mitten, L. J. Rivas. Department of Veterinary Clinical Sciences, The Ohio State University, Columbus, Ohio

Despite aggressive medical therapy and initial correction of electrolyte and acid-base abnormalities, horses dying of necrotic enterocolitis evidence severe abdominal pain and develop metabolic abnormalities refractory to treatment. Case records of 16 horses with histologically confirmed acute necrotizing enterocolitis were reviewed. Nine were intact males, 5 were females, and 2 were geldings; median age of 21 months (range 4 to 144 months). Horses presented with a history of diarrhea < 36 h duration (median 19, range < 5 to >36 h).

At initial examination horses were pyrexic (38.4°C, 33.8 to 40.6°C), tachycardic (93 bpm, 66 to 138), tachypneic (36 bpm, 16 to 80), dehydrated and had discolored mucous membranes (red to purple). Packed cell volume was elevated (> 45%) in 14 horses. Six horses were leukopenic (<5000 cells/µl); 12 were neutrophic (<2300 cells/µl) and 14 had >100 band neutrophils/µl (range 200 to 2700). Twelve horses were acidicotic (pH < 7.37, range 6.88 to 7.33). Venous bicarbonate concentration was low (<20 mEq/L) in 8 horses. Median anion gap in 15 horses was 31.5 mEq/L (normal=15 mEq/L). Abdominal fluid was examined in 12 horses; 4 had protein >2.5 g/dl and 6 had WBCC >5,000 and <10,000 cells/µl, none had WBCC >10,000 cells/µl. Eight of 12 samples revealed a neutrophilia (>50%), all were nondegenerate. No etiologic agents were seen. Abdominal fluid collected immediately before death in 4 horses was normal in 2 and showed suppurative inflammation in 2. Eight of 8 horses had low or nonexistent serum immunofluorescent antibody titers to E. risticii; 4 of 15 horses yielded Salmontilla sp. from feces or tissues. All 16 cases either died (3 of 16; 31%) or were euthanized. Median time to death was 45.5 hours (range 7 to 113 hours). Death was preceded by severe abdominal pain in 14 horses; exploratory laparotomy was performed on 2.

We conclude that fatal necrotizing enterocolitis of horses is characterized by a brief course, profound dehydration, electrolyte and acid-base abnormalities, minimal abdominal fluid abnormalities early in disease, and terminally, severe abdominal pain.

HYPERTONIC SALINE-DEXTRAN RESUSCITATION OF HYPOVOLIC DIARRHEAL CALVES

The effects of small volume hypertonic saline-dextran (HSD) solution were determined in dehydrated diarrheal calves. Sixteen healthy dairy calves aged 3-6 days were instrumented for thermocilium cardiac output determinations. Osmotic diarrhea and hypovolemia were induced by administering milk replacer (33 ml/kg) and isotonic sucrose (2 g/kg) solutions PO, q 8 h, and furosemide (2 mg/kg, IM) q 4-8h. Administration of milk replacer solution and furosemide was discontinued when calves became 6% dehydrated. Calves were then randomly allocated to one of 4 groups: CONTROL (no treatment); HSD solution (4 ml/kg, 2400 mOsm/L NaCl in 6% Dextran-70, administered over 30 minutes, IV); ORAL (isotonic electrolyte solution, 55 ml/kg, q 8h, PO); HSD-ORAL (combination of HSD and ORAL treatments), and monitored for 24 hours.

Changes produced by the osmotic diarrhea model included severe watery diarrhea, marked depression, a decrease in cardiac output (9.5 to 3.8 L/min) and plasma volume (4070 to 3050 ml), and an increase in lactate concentration (0.9 to 1.7 mM/L). CONTROL calves remained depressed and dehydrated, and became progressively tachycardic, acidemic, and hyperkalemic. A transient increase in cardiac output and plasma volume occurred in the HSD group; however, the response had waned by 2h. Cardiac output and plasma volume increased slowly in the ORAL group. An immediate and sustained increase in cardiac output and plasma volume was observed in the HSD-ORAL group, indicating that treatment of hypovolemic diarrheal calves with intravenous HSD solution and oral electrolyte solution is superior to administration of either solution alone.
The effect of three different drugs on myoelectric activity of the ileum, cecum, and proximal loop of the ascending colon (PLAC) was determined in four healthy Jersey cows implanted with 8 pairs of bipolar electrodes. A 4x4 Latin square design was used. The treatments included xylazine (0.04 mg/kg, IV), cisapride (0.08 mg/kg, IV), naloxone (0.05 mg/kg, IV), and 0.9% NaCl solution (20 ml, IV). Myoelectric activity was recorded for 4 hours following treatment.

Xylazine significantly (P<0.05) increased the duration of phase 1 of the first migrating myoelectric complex in the ileum. The number of propagated spike sequences in the cecum and PLAC was decreased for the first 2 hours, and the number of spikes/min and the duration of spike activity (% of recording time) were decreased for the first 3 hours following injection of xylazine. A significant difference in TNCCId was not found between control and either cisapride or naloxone. It was concluded that none of the tested drugs was suitable for medical treatment of cecal dilatation in cattle, where hypomotility of the cecum and PLAC has to be reversed.

The effect of allopurinol on postischemic reperfusion of the large colon of the horse.

The purpose of this study was to investigate the effect of allopurinol, a xanthine oxidase inhibitor, on post-ischemic reperfusion injury. Twelve adult horses were anesthetized and a reversible ischemic injury was created in the left dorsal and ventral colon. The horses were randomly assigned to one of two groups to receive either allopurinol prior to reperfusion after 90 minutes of ischemic injury or to be a control and receive an equivalent volume of an isotonic electrolyte solution.

Full thickness biopsies were taken from the left ventral and dorsal colon prior to creating the ischemic injury and then prior to restoration of the blood flow. Circulation was restored and subsequent tissue samples were taken at 30 minute intervals for two hours after reperfusion. Intestinal biopsies were evaluated by light microscopy for mucosal and submucosal pathologic changes. Numerical values were assigned to the observed changes and then analyzed for statistical difference between treated and control animals. There was not a statistical difference identified. Allopurinol did not appear to prevent reperfusion injury after an ischemic insult in the large colon of horses.
CYTOLOGIC PROFILE OF BRONCHOALVEOLAR LAVAGE FLUID IN STANDARDBRED RACEHORSES WITH REACTIVE AIRWAY DISEASE.

R. Moore, S Krakowka*, JM Cummins**, Kansas State University, Manhattan, KS. *The Ohio State University, Columbus, OH. **Amarillo Cell Culture, Amarillo, TX.

The purpose of this study was to characterize the cytologic profile of bronchoalveolar lavage fluid (BALF) obtained from horses with reactive airway disease. Reactive airway disease was identified in 32 Standardbred racehorses with poor exercise performance and high endoscopic examination scores of the upper and lower airway. Total and differential cell counts were determined in BALF from affected horses and six Standardbred racehorses with satisfactory exercise capability and low endoscopic scores. Lymphocyte sub-populations in BALF were identified using B cell, CD4+, CD5-, and CD8-like monoclonal antibodies. Sub-populations were expressed as a percentage of lymphocytes within the backgated population. Absolute neutrophil, macrophage, and lymphocyte counts and total cell counts were significantly higher in BALF of affected than control horses. Eosinophilia, greater than 25% of total cells in BALF occurred in 4 affected horses. BALF lymphocytes were primarily CD5+ cells (pan T) in affected and control horses. The percentage of B cells and CD4+ (helper T) cells was lower in affected than control horses.

Neutrophilia and eosinophilia in BALF are consistent with Type-III and Type-I hypersensitivity reactions, respectively, indicating the pathophysiology of reactive airway disease is multifactorial. Decreased B cell and CD4+ lymphocytes may reflect increased CD8 (suppressor T) activity.

CYTOLOGY AND BACTERIOLOGY OF TRANSTRACHEAL ASPIRATES FROM CLINICALLY NORMAL LLAMAS.

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To establish normal values, transtracheal aspirates (TTA) and pleural fluid were obtained from 17 adult llamas which were free of clinical signs of respiratory disease. Complete blood counts, fibrinogen levels, and thoracic radiographs obtained prior to sampling were within normal limits. Transtracheal aspirates and pleural fluid were collected as previously described using a 10 gauge through-the-needle 18 inch catheter and an 11 cm teat cannula, respectively. The llamas were sedated with xylazine HCl (0.1 mg/kg IM) to aid collection of samples. Cytologic evaluation of the TTAs revealed the majority of cells to be vacuolated macrophages, some with small amounts of cellular debris. Giant cells were not observed. The predominant cells found in non-blood contaminated pleural fluid samples were small lymphocytes. In 10 of 17 TTA's, neither aerobic nor anaerobic bacteria were recovered. Of 7 samples yielding low numbers of aerobic bacteria, 3 were composed of mixed bacteria likely due to pharyngeal contamination. Bacteria recovered in pure culture included Acinetobacter sp., and Bacillus sp. and Staphylococcus sp. The mean ± standard deviation (SD) for total cell counts in the pleural fluid was 576 ± 361/ul. Twelve of 17 refractometer assessed total protein concentrations were less than 2.7 g/dl, with the highest value 4.4 g/dl. Pleural glucose and lactate concentrations were compared to plasma concentrations. The mean ± SD for pleural and plasma glucose concentrations were 133 ± 9.02 and 29.68 ± 15.65 mg/dl, respectively. The mean 7 SD for pleural and plasma lactate concentrations were 2.95 ± 1.34 and 3.91 ± 1.91 mg/dl, respectively.
LUNG ABSCESSES IN FOALS AND ADULT HORSES: A REVIEW OF 40 CASES. J.P. Laverty, L. Fiset and S. Laverty. Faculté de Médecine Vétérinaire, Université de Montréal, ST-Hyacinthe, Québec, Canada.

A retrospective study of 40 horses with primary lung abscesses without pneumonia was performed. Lung abscesses occurred predominantly in young horses, usually in foals of 6 months of age or less (60%). The Standardbred breed was over-represented compared to the overall hospital population during the same period. Hyperbiatrionemia was present in all but 2 horses, and other common clinical and hematological findings were hyperthermia, tachycardia, and neutrophilic leucocytosis. The most common bacterial species isolated from trans-tracheal aspirates were S. zooepidemicus followed by R. equi.

Most horses discharged from the hospital, were long term survivors. Twelve of 19 horses for which an athletic follow-up was available, were trained or ran the race they were intended to. None of the parameters evaluated in this study could reliably predict the bacterial species involved or the outcome.

The results of this study highlight the importance of S. zooepidemicus as a causal agent of lung abscesses in horses of all age groups and indicate that successful athletic performance can be achieved following the successful treatment of lung abscesses.

PHENYL BUTAZONE INHIBITS THE DIURESIS INDUCED BY LOW INTENSITY EXERCISE IN HORSES. H.C. Schott II. College of Veterinary Medicine, Washington State University, Pullman, WA.

Low intensity exercise has been documented to result in an increase in urine flow (UF) in horses. The mechanism has not been established, but an increase in renal prostaglandin production during exercise is likely a contributing factor. To test this hypothesis, mares were exercised with (BUTE) and without (CONTROL) prior administration of phenylbutazone (4.4 mg/kg PO q 12 hr for 3 days). The exercise bout consisted of 2 hours of low intensity treadmill exercise (3.5 to 3.7 m/s at 0% slope) and elicited a mean heart rate of 101.4 beats/min. Urine was collected continuously during the studies via indwelling ureteral catheters. As detailed in the table, UF increased and urine osmolality (Uosm) decreased during the control exercise bout. However, no changes in these parameters were observed during exercise after treatment with phenylbutazone.

|          | CONTROL | BUTE |
|----------|---------|------|
| UF (ml/min) | rest   | 7.1 ± 0.9 | 6.9 ± 2.1 |
|           | exercise| 22.4 ± 4.2 | 6.1 ± 1.5 |
| Uosm (mosm/kg) | rest   | 959.5 ± 113.3 | 949.7 ± 349.8 |
|           | exercise| 556.4 ± 59.9 | 1024.6 ± 58.2 |

These data support a role for renal prostaglandins in the diuresis induced by low intensity exercise in horses.

URINARY INDICES IN LLAMAS FED TWO DIFFERENT DIETS. H.E. Laskey, E.B. Belknap, L.W. Johnson. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO

Many diagnostic procedures are used in human and veterinary medicine to accurately assess renal function, to prognosticate, and to institute prophylaxis (e.g., calculation of endogenous creatinine clearance as a measure of GFR, measurement of total and fractional excretion rates of protein and electrolytes as estimators of tubular function, determination of urine enzyme activity as a reflection of renal tubular cell damage). These measurements along with urine volume, serum and urine osmolality, and water intake can provide insight into renal health and function.

Normal values for many urinary indices have been reported for cattle, sheep, and horses, but none exist in llamas. In this project, several urinary indices were measured in healthy adult llamas over a 24 hour period while on two different diets. Endogenous creatinine clearance, total and fractional excretion rates of Na, K, Cl, P and protein, and urinary gamma-glutamyltranspeptidase and beta-acetylglucosaminidase activities were measured in 12 male llamas. Dietary intake and water consumption were quantitated over each 24 hour period. Llamas were kept in individual tie stalls and were fed alfalfa hay. Two months later the same study was done feeding grass hay. Each llama was fitted with a urinary collection device. For each trial, urine and blood samples were taken at hours 6, 12, and 24.

Our study revealed that methods used to measure specific urine electrolyte levels in other species, such as urinary K, are not reliable in llamas. The values for several urinary indices differ enough from other domestic species, including other ruminants, that establishing a normal reference range for llamas is warranted. Differences due to diet were observed in many parameters.
INTRAORBITAL NERVE BLOCK: A DIAGNOSTIC TOOL FOR HEADSHAKERS. P.A. Wilkins, N.G. Ducharme, P.R. Leser* Cornell University College of Veterinary Medicine; *The Equine Clinic at OakesCoff, Ravenna, NY.

Headshaking or headbanging behavior in horses is a diagnostic dilemma. Difficulty in diagnosing the condition may preclude successful management. Hearing with clinicians and owner. A comprehensive history combined with a surgical systemic diagnostic protocol will rule out some of the more common causes of headshaking. The use of bilateral infraorbital nerve blocks may limit further diagnostic and therapeutic efforts and allow recognition of potential candidates for infraorbital neuroectomy.

Eleven horses were examined over a twelve month period. All horses underwent a standardized diagnostic protocol that included physical examination, observation at exercise, skull radiographs, endoscopic evaluation of the upper respiratory tract and oral, ophthalmic and otic examinations.

Response to bilateral infraorbital nerve block using 10 ml mepivicaine over and within the infraorbital canal was evaluated in horses demonstrating headshaking behavior at the time of examination.

Six of eleven horses demonstrated greatly reduced frequency of headshaking following infraorbital nerve block. Three horses that improved following unilateral infraorbital nerve block underwent bilateral infraorbital neuroectomy. All three subsequently demonstrated much reduced headshaking behavior among their owners. One of the three required a second neuroectomy when the behavior reappeared two months after neuroectomy. This horse is still following from the second neuroectomy.

These data suggest that a large number of headshakers have lesions associated with the infraorbital nerve. Bilateral infraorbital nerve blocks appear to be useful in the evaluation of headshaking behavior in horses. Candidates for surgical intervention should demonstrate repeatable improvement following infraorbital nerve blocks. Pending more critical evaluation infraorbital neuroectomy should be considered a salvage procedure; however, it may allow certain horses to return to previous levels of performance.

SPINAL ACCESSORY NERVE BIOPSY AS AN ANTE MORTEM DIAGNOSTIC TEST FOR EQUINE MOTOR NEURON DISEASE. C. A. Jackson, A. de Lahunta, J. P. Cummis, T. J. Diver. College of Veterinary Medicine, Cornell University, Ithaca, N.Y.

The effectiveness of spinal accessory nerve branch biopsy evaluation as a means to confirm the diagnosis of equine motor neuron disease (EMND) was investigated. Sixteen horses with histories and clinical signs suggestive of EMND and sixteen control horses with neither histories nor clinical signs of any neurologic disorder were subjects of the study. Biopsy samples of the ventral branch of the spinal accessory nerve were obtained either surgically under general anesthesia or post mortem immediately after euthanasia. Evaluation of the spinal cord was done on all horses to serve as the definitive diagnostic indicator of EMND.

Results indicate that biopsy of the ventral branch of the spinal accessory nerve is a reliable ante mortem diagnostic test for EMND. Clinical and histologic evidence of the degeneration of myelinated axons is present in both acute and arrested cases. The ventral branch of the spinal accessory nerve is easy to access surgically and biopsy of the nerve causes no disfigurement of the sternocleidomastoid muscle. The use of thin Epon sections is an excellent method of sample preparation. Formalin fixation and routine paraffin embedment may prove more accessible and provide good quality preparations. Sensitivity and specificity reliability coefficients for spinal accessory nerve branch biopsy were 91% and 92% respectively. These factors make this technique an extremely valuable diagnostic tool for evaluation of the living horse suspected of having EMND.

CHARACTERIZATION OF CANINE AND EQUINE MESANGIAL CELLS IN CULTURE. Daniela Ennulet, and Scott A. Brown. College of Veterinary Medicine, Univ of Georgia, Athens, GA.

Mesangial cell contraction, proliferation, and matrix production play a central role in the pathophysiology of renal diseases in domestic species. Our goal was to establish techniques for the growth and characterization of canine and equine mesangial cells. Glomeruli were isolated from kidneys of normal dogs (n=25) and horses (n=14) using a differential sieving technique. Canine glomeruli were suspended in RPM1-1640 nutrient media with 20% fetal calf serum and seeded into tissue culture flasks for explant outgrowth. Equine glomeruli required collagenase digestion (30 minutes 750 U/ml collagenase type IV), followed by suspension in RPM1-1640 with 10% fetal calf serum prior to plating. Cellular outgrowth appeared as early as 5 days after seeding of glomeruli, and the cells reached confluency in 10-14 days. Serial passage produced an increasingly homogenous population of multilayered, spindle-shaped cells, and third through eighth passage cells were used in characterization studies. Canine mesangial cells grown using these conditions had a mean doubling time of 3.34 days, while equine mesangial cells doubled every 2.19 days. Immunohistochemistry and Western blotting techniques demonstrated the presence of actin, α-actinin, desmin, smooth muscle myosin, and vinculin in canine and equine mesangial cells. As expected, the cells did not express cytokeratin, leukocyte common antigen, or von Willebrand's Factor. Both canine and equine cells produced an extracellular matrix that contained chondroitin-6-sulfate, type IV collagen, fibronectin, and laminin, and the cells contracted in response to the calcium ionophore, A23187. We conclude that the culture of mesangial cells from canine and equine kidneys provides a model for the study of cellular mechanisms that regulate mesangial cell contraction, proliferation, and matrix production in these species.