## Index of Abstracts

| Abstract Number | Presenting Author | Abstract Title |
|-----------------|-------------------|----------------|
| **Small Animal—Endocrinology** | | |
| 1               | Rosenthal, K. L.  | Adrenal function in ferrets: plasma cortisol and corticosterone responses to synthetic ACTH administration |
| 2               | Rosenthal, K. L.  | Adrenocortical disease in 47 ferrets |
| 3               | Bertoy, E.        | Magnetic resonance (MR) imaging of the brain in dogs with recently diagnosed but untreated pituitary-dependent hyperadrenocorticism |
| 4               | Duesberg, C.      | The use of magnetic resonance (MR) imaging of the brain in dogs with pituitary-dependent hyperadrenocorticism (PDH) and central nervous system signs |
| 5               | Zerbe, C. A.      | Regulation of ACTH secretion from dog anterior pituitary in vitro |
| 6               | Dyer, K. R.       | Effects of phenobarbital administration on endogenous ACTH, ACTH response test, alkaline phosphatase isoenzymes, and bile acid metabolism |
| 7               | Behrend, E. N.    | Pharmacokinetics of exogenous ACTH in dogs with hyperadrenocorticism and in hospitalized dogs with non-adrenal illness |
| 8               | Greco, D. S.      | Dose-dependent dexamethasone pharmacokinetics in normal dogs |
| 9               | Nelson, R.        | Transient diabetes mellitus in the cat |
| 10              | Ford, S.          | Intensive evaluation of glipizide therapy in the management of feline diabetes mellitus |
| 11              | DeVries, S.       | Primary parathyroid gland hyperplasia in 6 dogs |
| 12              | Peterson, J. L.   | Humoral hypercalcemia of malignancy in dogs: serum parathyroid hormone-related protein |
| 13              | Post, G.          | Circulating parathyroid hormone-related peptide in dogs with malignancy-associated hypercalcemia |
| 14              | Finco, D. R.      | Fluctuation in canine plasma parathyroid hormone (PTH) concentration |
| 15              | Kintzer, P. P.    | Mineralocorticoid therapy of spontaneous primary hypoadrenocorticism in 176 dogs |
| **Small Animal—Cardiology** | | |
| 16              | O'Grady, M. R.    | Occult dilated cardiomyopathy: an echocardiographic and electrocardiographic study of 193 asymptomatic Doberman Pinschers |
| 17              | O'Grady, M. R.    | Myocardial myoglobin deficiency: an etiology for Doberman dilated cardiomyopathy? |
| 18              | Rishniw, M.       | Contrast enhanced ultra-fast computed tomography assessment of changes in myocardial perfusion in the dog |
| 19              | Lehmkuhl, L. B.   | Comparison of pressure gradients determined by Doppler echocardiography and cardiac catheterization in dogs with subaortic stenosis |
| 20              | Lehmkuhl, L. B.   | Therapeutic balloon valvuloplasty in dogs with subaortic stenosis |
| 21              | Ewey, P. D.       | Survival in treated and untreated dogs with congenital pulmonic stenosis |
| 22              | Beardow, A. W.    | The prevalence of mitral systolic murmurs in the Cavalier King Charles Spaniel (CKCS) |
Heart rate variability in veterinary species

Automatic implantable cardioverter defibrillators in German Shepherds with inherited sudden cardiac death

Plasma catecholamine concentrations and cardiac arrhythmias in dogs with severe noncardiac diseases

Morphologic features of ventricular arrhythmias in dogs with and without underlying cardiac diseases

Noninvasive assessment of hemodynamic changes caused by intravenous acepromazine-buprenorphine in healthy conscious dogs

Comparison of canine blood pressures and pulse rates obtained in clinic and at home by indirect oscillometry

Comparison of direct arterial and indirect oscillometric measurement of blood pressure in conscious dogs

Lability of blood pressure in genetically hypertensive dogs using 24-hour monitoring

Measurement and characterization of endothelin-1 in plasma of dogs

Respiratory distress syndrome in young Dalmatian dogs

Laryngeal paralysis in Dalmatians

Effect of chronic administration of phenobarbital on disposition of clorazepate in dogs

Osmotic opening of the blood-brain barrier to anti-tumor agents

Autonomic dysfunction in three dogs

Baer thresholds of clicks and various tone frequencies in Dalmatian puppies

Pattern electroretinograms (PERG) in dogs: response of transient PERG to alterations in spatial frequency

Tolerability of Lufenuron (CGA-184699) in normal dogs and cats

Effect of albumin and Tamm-Horsfall protein on struvite crystal growth in cat urine

Post-surgical recurrence of calcium oxalate uroliths in dogs

Effects of oral NaCl administration on urinary oxalate excretion

Non-invasive determination of canine effective renal plasma flow

Predictive value of urodynamic measurements in the management of ectopic ureters in the dog

Measurement of GFR in dogs using endogenous creatinine clearance

A new familial membrano-proliferative glomerulonephritis in Bernese Mountain Dogs

Experimental production of glomerulonephritis and the nephrotic syndrome (NS) in dogs

Effects of angiotension converting enzyme inhibition (ACEI) and calcium channel blockade (CaChB) on renovascular resistance in diabetic Beagles

Nephrotoxicity of Easter lily (lilium longiflorum) when ingested by the cat

Verapamil and quinine as modifiers of drug resistance in canine lymphoma

Feline leukemia virus detection in paraffin-embedded, formalin-fixed tissues by polymerase chain reaction and immunohistochemistry

An epidemiological evaluation of 1202 dogs with testicular neoplasia

An in vivo murine model to study multiple drug resistance

Preoperative irradiation of facial tumors in cats

The concentration of doxorubicin and its associated metabolites in canine urine following a single administered dose

Doxorubicin combined with liposomal-MTP

Antibodies bound to the surface of platelets from dogs with idiopathic thrombocytopenic purpura and anti-platelet autoantibodies
| Page | Author(s)          | Abstract                                                                 |
|------|-------------------|--------------------------------------------------------------------------|
| 58   | Rentko, V. T.     | Efficacy of an ultra-purified, polymerized hemoglobin based oxygen carrying solution |
| 59   | Grauer, G. F.     | Effects of low-dose aspirin and thromboxane synthetase inhibition on platelet function in dogs |
| 60   | Ford, S.          | Inherited erythrocyte pyruvate kinase (PK) deficiency causing hemolytic anemia in an Abyssinian cat |
| 61   | Klag, A.          | Immune-mediated hemolytic anemia in the dog: A retrospective study of 42 cases |
| 62   | Dial, S. M.       | Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome) in a Miniature Pinscher |
|      |                   | **Small Animal—Infectious Disease** |
| 63   | Davidson, A.      | Treatment of nasal aspergillosis with topical clotrimazole |
| 64   | Breitschwerdt, E. B. | Preliminary characterization of a novel infectious cause of thrombocytopenia in dogs |
| 65   | Lappin, M. R.     | Demonstration of Toxoplasma gondii-antigen containing immune complexes in the serum of cats |
| 66   | Sellon, Rance K.  | Evidence for perinatal transmission of feline immunodeficiency virus |
| 67   | Olsen, J. W.      | The use of liposomal amphotericin B in mycotic and algal diseases in the dog |
|      |                   | **Small Animal—Hepatology** |
| 68   | Hitt, M. E.       | Hepatocellular cytoprotection against the hepatotoxic effects of thiacetarsamide using dextrose and N-acetyl-L-cysteine in the dog |
| 69   | Hitt, M. E.       | Cytoprotection of NCTC 1469 mouse hepatoma cells against the toxic effects of thiacetarsamide using N-Acetyl-L-Cysteine |
| 70   | Boothe, D. M.     | Comparison of indocyanine green, caffeine and antipyrine disposition kinetics in dogs with experimentally induced progressive liver disease |
| 71   | Bunch, S. E.      | Iron status in 12 dogs with congenital portosystemic shunts |
| 72   | Levy, J. K.       | Congenital portosystemic vascular shunts in cats |
| 73   | Gartrell, C. L.   | Evaluation of fasting and postprandial bile acids as a diagnostic acid in detecting feline hepatic disease |
| 74   | Day, D. G.        | Serum bile acids in cats after a meal and after exogenous administration of cholecystokinin octapeptide |
| 75   | Hall, J. A.       | Lipid composition of liver and adipose tissues from normal cats and cats with hepatic lipidosis |
| 76   | Armstrong, P. J.  | L-carnitine reduces hepatic fat accumulation during rapid weight reduction in cats |
| 77   | Holste, L. C.     | Portal glucose delivery fails to alter the counterregulatory response to hypoglycemia |
|      |                   | **Small Animal—Gastroenterology** |
| 78   | Guilford, W. G.   | Development of a model of food allergy in the dog |
| 79   | Hoskins, J. D.    | Effectiveness of temperature sensitive feline infectious peritonitis virus vaccine against a feline enteric coronavirus |
| 80   | Simpson, K. W.    | The effect of subtotal nephrectomy on circulating trypsin-like immunoreactivity, amylase, lipase and gastrin in the dog |
| 81   | Williams, David A. | Evaluation of radioassay methods for analysis of canine serum cobalamin and folate |
| 82   | Matz, M. E.       | The use of misoprostol for prevention of gastroduodenal hemorrhage and ulceration associated with aspirin therapy |
| 83   | Leib, M. S.       | Comparison of diagnostic tests in dogs experimentally infected with Giardia |
| 84   | Barr, S. C.       | Evaluation of a fecal Elisa and peroral string tests for the diagnosis of canine Giardiasis |
| 85   | Westermarck, E.   | Development of pancreatic acinar atrophy (PAA) in a German Shepherd dog |
| 86   | Washabau, Robert J. | Serotonin (5-HT) mediates contraction of feline proximal and distal colonic smooth muscle |
| 87   | McCrackin, M. A.  | Endoscopic placement of a percutaneous gastroduodenostomy feeding tube in the dog |
|      |                   | **Small Animal—Nutrition/Metabolism** |
| 88   | Diehl, K. J.      | Evaluation of three enteral feeding formulas in cats |
| 89   | Hill, R. C.       | The effect of texturized vegetable protein (TVP) on apparent digestibility in the dog |
DHEA in the treatment of canine obesity
Hypercholesterolemia in Briards in the United Kingdom
Blood chemistry changes in dogs competing in a long distance sled race
Physiological alternations occurring during a long distance sled dog race

Large Animal—Gastroenterology

Duckett, W. M.
Nappert, G.
Koenig, G. J.
Murray, Michael J.

Cimetidine, aminophylline interaction in foals
Determination of extent of milk malabsorption in diarrheic calves
Influence of intravenous sodium propionate on abomasal emptying rate in dairy cattle
Application of gastric pHmetry in horses: Measurement of 24 hour gastric pH in horses fed, and treated with ranitidine

Large Animal—Hematology/Immunology

Robinson, J. A.
Durando, M. M.
Kohn, Catherine
Kehrli, M. E.

Interleukin-6 in sublethal intravenous endotoxin challenged neonatal foals
Evaluation of two potential treatments of equine endotoxemia
Myeloid hypoplasia in related Standardbreds
BLAD (bovine leukocyte adhesion deficiency): clinical immunology and symptoms
BLAD (bovine leukocyte adhesion deficiency): pathology and diagnostic tests

Large Animal—Infectious Disease

Coyne, C. P.
Edens, L. M.
Bertone, Joseph J.
Clabough, D. L.
Long, M. T.
Barratt-Boyes, S. M.
Davis, E. W.

Pharmacological neutralization of lipopolysaccharide-induced macrophage TNF-alpha synthesis
In vitro lysis of equine herpesvirus-1 infected target cells by equine peripheral blood mononuclear cells
Diarrhea associated with Rotavirus challenge in foals: clinical, virologic and serologic evaluation
Wild-type equine infectious anemia virus replicates predominantly in mature tissue macrophages, not in peripheral blood mononuclear cells
Preliminary investigations of the fetal infectivity of Ehrlichia risticii in broodmares
Interaction of bluetongue virus with bovine blood mononuclear cells
Use of autogenous bacterin-toxoid and toxoid to prevent Corynebacterium pseudotuberculosis infection in horses

Large Animal—Respiratory/Neurology

Traub-Dargatz, J. L.
Hormanski, C.
Harrison, G. D.
Rush Moore, B.
Furr, M. O.

Upper airway obstruction in four foals resulting from a polymyopathy suspected to be hyperkalemic periodic paralysis
Concentrations in equine amniotic fluid during the last third of gestation
Fiber type grouping in the laryngeal muscles of draft horse foals
Contrast-enhanced computed tomography in six horses with cervical stenotic myelopathy
Normal cerebrospinal fluid values in the foal: Birth to 42 days of age

Poster Sessions

Lutz, T. A.
Zerbe, C.
Monroe, W. E.
Sanders, N.
Sisson, David
Fox, P. R.

Comparison of five commercial insulin RIA kits for use in cats
Regulation of ACTH and MSH secretion from dog anterior and intermediate lobe pituitary cells in long term culture
Evaluation of C-peptide radioimmunoassay kits for use with feline and canine serum and urine
Effects of enalapril on healthy cats
Efficacy of enalapril in dogs with chronic heart failure
Comparison of plasma taurine, alpha-tocopherol, selenium, total triglycerides, cholesterol and retinol in healthy and heart failure cats
| 125 | Keyes, M. | Ventricular arrhythmias in dogs with splenic masses |
| 126 | Dye, J. A. | Pulmonary function in cats with bronchopulmonary disease and acute responses to IV bronchodilator challenge |
| 127 | Moore, M. P. | The effects of boron neutron capture therapy irradiation on quantitative electroencephalography in normal dogs |
| 128 | Sträter, J. M. | The effect of succinylcholine, diazepam and dantrolene on the urethral pressure profile of the anesthetized, healthy intact male cat |
| 129 | Callan, M. B. | Evaluation of the hemocue system for hemoglobin measurement in animals |
| 130 | Mackin, A. J. | Effects of vincristine sulfate on normal canine platelet number and function |
| 131 | Gelens, C. J. | Canine blood type frequencies and an acute hemolytic transfusion reaction |
| 132 | Codner, E. | Comparison of intradermal allergy test and enzyme linked immunosorbent assay |
| 133 | McDevitt, J. | Evaluation of lincomycin in healthy dogs using a non-infected and infected tissue cage model |
| 134 | Papasouliotis, K. | The effect of dietary fibre on oro caecal transit time in dogs |
| 135 | Kilborn, S. H. | Clinical utility of venous blood gas analysis in dogs. |
| 136 | Belknap, E. B. | Antibody response to bovine respiratory syncytial virus proteins in colostrum-fed calves |
| 137 | Gerros, T. C. | Effect of method of administration and dosage of endotoxin on clinical, hematologic and metabolic responses |
| 138 | Williams, A. | Comparison of amniotic and allantoic fluid in late gestational mares |
| 139 | Rossier, Y. | Variations in urinary GGT/urinary creatinine ratio in horses treated with gentamicin |
| 140 | Geor, R. J. | Hemorheologic effects of furosemide in the horse |
| 141 | Nappert, G. | Atresia coli in foals: 7 cases (1964–1990) |
| 142 | Gardner, S. Y. | Pharmacokinetics of cefotaxime in neonatal pony foals |
ADRENOCORTICAL DISEASE IN 47 FERRETS. K.L. Rosenthal, M.E. Peterson, K.E. Quesenberry, E.V. Hillyer, S.D. Moroff, N. Beoer, C.D. Lothrop. Animal Medical Center, New York, NY, Rutherford Animal Hospital, Rutherford, NJ, and College of Veterinary Medicine, University of Tennessee, Knoxville, TN.

Adrenocortical disease (hyperadrenocorticism) in pet ferrets (Mustela putorius furo) has recently been recognized, but only 3 cases had been previously reported. We report here 47 ferrets with hyperadrenocorticism-like disease, including clinical signs, diagnosis, and treatment. Thirty-three (70%) of the ferrets were female and 14 were male; only 1 female was sexually intact. The mean age of onset was 3.4 years. The most common clinical sign was vulvar enlargement, noted in 30 of the 33 females (91%). Alopecia, involving the tail, flanks, and trunk was present in 40 (85%) of the 47 ferrets. Other signs included pruritus in 18 (37%), and polyuria and polydipsia in 4 (8.5%). Physical examination revealed a mass at the cranial pole of the kidney in 15 ferrets (32%). Hematologic testing revealed anemia in 4 and thrombocytopenia in 2 ferrets. ACTH stimulation tests were normal in all 20 ferrets tested. Radiographs were unremarkable in all ferrets, whereas ultrasonography, performed in 36, identified an adrenal mass in 18 (50%). Surgical removal of the diseased adrenal gland was performed in 36 ferrets. Five ferrets died of complications in the immediate postoperative period. In the remaining 31 ferrets, resolution of vulvar swelling, alopecia, and pruritus was noted by 5 months. Complete necropsy was performed in the 11 ferrets not treated. Histopathological studies revealed adrenocortical adenoma, carcinoma, or nodular hyperplasia in all ferrets. Metastasis was not identified at time of surgery or at necropsy in any of the ferrets. These results indicate that adrenocortical disease (usually adrenal neoplasia) develops with some frequency in pet ferrets. In the broadest sense of the word, these ferrets do have hyperadrenocorticism but it should not be assumed that excessive production of cortisol is responsible for the syndrome since ACTH stimulation tests were normal.

Adrenal steroids other than cortisol are likely to be responsible for this disease in ferrets because clinical signs of vulvar enlargement, alopecia, and pruritus resolve after removal of the diseased adrenal gland.

3 MAGNETIC RESONANCE (MR) IMAGING OF THE BRAIN IN DOGS WITH RECENTLY DIAGNOSED BUT UNTREATED PITUITARY-DEPENDENT HYPERADRENOCORTICISM. E Bertoy, E Feldman, R Nelson, C Duesberg. Sch of Vet Med, University of California, Davis; M Reid, A Dublin. Diagnostic Radiological Imaging, Sacramento, CA

The purpose of this project was to determine the incidence of macro-sized (visible) pituitary tumors, using MR imaging, in dogs with newly diagnosed and untreated pituitary-dependent hyperadrenocorticism (PDH). Additionally, this study allows an assessment of MRI as a diagnostic aid in veterinary medicine. For inclusion in this study, each dog must have had clinical signs and routine data base (CBC, serum chemistry, UA) results consistent with a diagnosis of hyperadrenocorticism (HAC). Further, each dog must have had plasma cortisol concentrations post-ACTH or post low-dose dexamethasone administration consistent with HAC. PDH must have been confirmed with results of plasma endogenous ACTH concentrations and abdominal ultrasonography. No dog could have been treated for HAC and none could have clinical signs suggestive of a large intra-cranial mass. Eighteen dogs met these criteria and underwent MR imaging of the brain consisting of sagittal and coronal T1 weighted images before and following IV administration of gadopentetate dimeglumine (100mg/kg). Five dogs (42%) had normal scans and 7 (58%) had easily visualized masses in the pituitary ± suprasellar cistern. The masses were 4 to 12mm in diameter. In conclusion: MRI scans are informative, the incidence of macro-sized pituitary tumors in PDH is probably greater than previously appreciated; absence of clinically detectable neurologic signs does not rule out presence of a visible (large) pituitary tumor; the clinical significance of such large tumors is yet to be determined.

4 THE USE OF MAGNETIC RESONANCE (MR) IMAGING OF THE BRAIN IN DOGS WITH PITUITARY-DEPENDENT HYPERADRENOCORTICISM (PDH) AND CENTRAL NERVOUS SYSTEM SIGNS. C Duesberg, E Feldman, R Nelson. Sch Vet Med, Univ of CA, Davis; and M Reid, Diag Rad Imaging, Sacto, CA

The purpose of this project was to determine the value of brain MRI in the diagnostic evaluation of dogs that have PDH and have neurologic signs of a large intra-cranial mass. For inclusion in this study each dog must have had the previously mentioned signs as well as PDH, as determined from clinical signs, routine data base test results, and commonly performed endocrine test results (ACTH stimulation, low and high-dose dexamethasone, endogenous ACTH). Eight dogs, seen consecutively, met the criteria for inclusion. Their CNS signs included disorientation (6 dogs), inappetence (5), ataxia (4), pacing (3), circling (3), and seizures (3). MRI scanning, utilizing ketamine and diazepam sedation, consisted of 4mm sagittal and coronal sections through the brain, T1 and T2 weighted images obtained before and following the IV administration (100mg/kg) of gadopentetate dimeglumine. Each dog had a large (10 - 21mm diameter) easily visualized pituitary mass: 4 of 8 masses were enhanced by contrast. Other anatomical abnormalities visualized included compression of the hypothalamus and/or 3rd ventricle (3 of 8 dogs) and obstructive hydrocephalus (2 of 8 dogs). In conclusion, MRI scanning was considered safe, informative, & a valuable tool in the evaluation of each dog.
5 REGULATION OF ACTH SECRETION FROM DOG ANTERIOR PITUITARY IN VITRO. R. J. Kemppainen, T. P. Clark, J. L. Sartin and C. A. Zerbe. College of Veterinary Medicine, Auburn University, AL and University of Pennsylvania, Philadelphia, PA.

The major peptide regulators of ACTH release in most species are corticotropin-releasing hormone (CRH), arginine vasopressin (AVP), oxytocin (OT), and angiotensin II (AII). In the rat, CRH is much more potent than the other peptides in its ability to stimulate ACTH release in vitro, while AVP is the more potent secretagogue in the sheep. The purpose of the present study was to determine which of these hypothalamic peptides influenced ACTH release from pituitary cells obtained from healthy dogs.

Anterior pituitaries, collected from two healthy dogs, were enzymatically dispersed using 0.4% collagenase. Cells were plated into 48-well plates and incubated in Media 199 containing 10% fetal bovine serum. On day 4, cells were washed with serum free Media 199 and treated with various doses (0.01-100 nM) of ovine CRH, AVP, OT, or AII. After 3 hours of incubation the media was removed, centrifuged, and stored for ACTH radioimmunoassay. Of the four peptides, only CRH significantly increased ACTH secretion from dog pituitary cells and this peptide was effective at the lowest dose tested (0.01 nM, P < 0.01). To test for possible synergistic actions between CRH and the other peptides, ACTH secretion in response to 100 nM CRH, or CRH together with 100 nM AVP, OT, or AII was determined. Co-addition of these peptides with CRH did not increase ACTH secretion (P = 0.16) beyond that caused by addition of CRH alone. The results support a role for CRH in the physiologic regulation of ACTH secretion from the dog anterior pituitary, but do not support regulatory roles for AVP, OT, or AII.

6 EFFECTS OF PHENOBARBITAL ADMINISTRATION ON ENDOGENOUS ACTH, ACTH RESPONSE TEST, ALKALINE PHOSPHATASE ISOENZYMES, AND BILE ACID METABOLISM. R. R. Deor, W. E. Monroy, and S. D. Forrester. Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA.

The acute effects of phenobarbital administration were evaluated in 6 adult mixed breeds that received phenobarbital (6 mg/kg PO q 12h) for 8 consecutive weeks. Six additional dogs served as untreated controls. At 2-week intervals the following hematologic parameters were evaluated: endogenous adrenocorticotrophic hormone (ACTH), cortisol concentrations before and after two hours after receiving porcine aqueous ACTH (2.2 IU/kg IM), pre and postprandial bile acids, and alkaline phosphatase isoenzyme activities. Using a one way analysis of variance, no significance difference (p > 0.05) was detected in endogenous ACTH concentrations, cortisol concentrations before or after exogenous ACTH administration, or bile acid concentrations. However, using a repeated measures analysis of variance, 3 of the 6 dogs receiving phenobarbital developed significantly (p < 0.05) higher alkaline phosphatase activities after the second week of therapy. These activities returned to baseline within 2 weeks of discontinuing phenobarbital administration.

To evaluate the chronic effects of phenobarbital administration, serum and plasma was collected from 4 epileptic dogs that had received phenobarbital for > 1 year and had serum phenobarbital concentrations > 20 g/dl. Endogenous ACTH concentrations and ACTH response test results were within established normal ranges for all 4 dogs. Bile acid metabolism was considered normal in 3 dogs, but both fasting and postprandial bile acid concentrations were abnormal in the fourth. Alkaline phosphatase concentrations were elevated in 3 of the 4 dogs in this group. Results indicate that neither endogenous ACTH nor exogenous ACTH response cortisol concentrations are influenced by phenobarbital administration. However, variable increases in alkaline phosphatase activities may be seen within 2 weeks of initiating phenobarbital therapy. Bile acid metabolism is not affected by acute phenobarbital administration, but abnormally hepatic function may be associated with chronic phenobarbital administration.

7 PHARMACOKINETICS OF EXOGENOUS ACTH IN DOGS WITH HYPERADRENOCORTICISM AND IN HOSPITALIZED DOGS WITH NON-ADRENAL ILLNESS. E.N. Behrend, D.S. Greco and R.P. Gronman; College of Veterinary Medicine, Colorado State University, Fort Collins, CO.

The ACTH stimulation test is used to diagnose hyperadrenocorticism (HAC). However, the disposition of ACTH in dogs with HAC and in hospitalized dogs with suspected HAC (later proven to have non-adrenal illness) has not been studied. In order to study the pharmacokinetics of ACTH, four dogs documented to have HAC (3 with pituitary-dependent and 1 with an adrenal tumor), and six dogs with non-adrenal illness (NAI) were injected with 0.50 U/kg of ACTH intravenously. Plasma samples (EDTA) were collected prior to the injection and then six samples were drawn over a two hour period. Plasma concentration of ACTH was determined by a commercial RIA assay (Nichols Institute, San Juan Capistrano, CA) validated for use in the dog.

The pharmacokinetics of ACTH best fit a one-compartment open model in both groups. The harmonic mean of the half-life and the mean (± SEM) of the kinetic parameters are shown in the following table:

| Parameter | Value (± SEM) |
|-----------|--------------|
| k₀ (min⁻¹) | 0.0330 ± 0.0014 |
| t½ (min) | 21.02 ± 0.086 |
| C₀ (pg/ml) | 1.66 ± 0.086 |
| AUC (pg·min/ml) | 4.74 ± 0.234 |
| Cl₀ (L/min/kg) | 1.064 ± 0.055 |

**HAC**

| Parameter | Value (± SEM) |
|-----------|--------------|
| k₀ (min⁻¹) | 0.0283 ± 0.0017 |
| t½ (min) | 25.93 ± 0.115 |
| C₀ (pg/ml) | 1.61 ± 0.623 |
| AUC (pg·min/ml) | 6.23 ± 0.762 |
| Cl₀ (L/min/kg) | 0.840 ± 0.076 |

**NAI**

A significant difference (p < 0.05). AUC = Area under curve, C₀ = peak concentration, Cl₀ = clearance, k₀ = elimination rate constant.

In conclusion, plasma half-life of exogenous ACTH in dogs with hyperadrenocorticism was significantly shorter (p < 0.05) than that of dogs with non-adrenal illness while systemic clearance of exogenous ACTH appeared to be unaffected by the disease state (p = 0.084).

8 DOSE-DEPENDENT DEXAMETHASONE PHARMACOKINETICS IN NORMAL DOGS. D.S. Greco, S.A. Brown. College of Veterinary Medicine, Colorado State University, Ft. Collins, CO and College of Veterinary Medicine, Texas A&M University, College Station, TX.

Dexamethasone pharmacokinetics (PK) were studied in ten clinically healthy dogs receiving low-dose dexamethasone (LDD, 0.01 mg/kg IV) or high-dose dexamethasone (HDD, 0.1 mg/kg IV) alone or combined (HDDA) with ACTH (0.5 IU/kg IV) in an incomplete cross-over design. Samples were drawn at 0, 5, 10, 15, 20, 30, and 45 min, and at 1.5, 2, 3, 4, 6, 8, 12, 18, 24, 36, and 48 hrs following dexamethasone administration. Dexamethasone PK were adequately described by a 2-compartment first-order model; results are shown in the following table:

| Parameter | Value (± SEM) |
|-----------|--------------|
| AUC (min·ng/ml) | 3.7 ± 0.7 |
| MRT (min) | 192 ± 1 |
| β (1/0) | 5.4 ± 3.5 |
| Cl₀ (L/min/kg) | 6.4 ± 2.8 |
| Vdₐ (L/kg) | 1.9 ± 1.2 |

Harmonic mean, 1 °P < 0.025; AUC = area under the curve, MRT = mean residence time, Cl₀ = clearance, Vdₐ = volume of distribution, β = elimination rate constant, 1/0 = elimination half-life.

Comparison of pharmacokinetics for the LDD and HDD or HDDA protocols revealed dose-dependence; all parameters, except the distribution rate constant (ν), and distribution half-life (1/0), increased significantly when dexamethasone dosage increased. In conclusion, concurrent administration of ACTH did not have an effect on dexamethasone disposition. Furthermore, the dose-dependent increase in pharmacokinetic parameters for the HDD and HDDA protocols may be related to the detection of a terminal phase not observed at the lower dosage of dexamethasone.
Diabetes mellitus was diagnosed in 10 cats by clinical signs, persistent fasting hyperglycemia and glucosuria. Treatment included high fiber diet (6 cats), glipizide (7 cats), and protamine-zinc insulin (4 cats). Glipizide and insulin treatment was discontinued in all cats within 1.6 mos. (range, 1-3 mos.) because of resolution of clinical signs and hyperglycemia. Mean fasting blood glucose concentration and mean 8 hr blood glucose concentration [ie, mean of blood glucose concentrations measured q 2h for 8 hrs] at initial diagnosis, was 45±42 and 37±27 mg/dl; at the time of discontinuing treatment, 102±48 and 96±32 mg/dl; and 1 month later, 109±30 and 103±25 mg/dl, respectively. Results of glucagon tolerance testing revealed increased mean (+SD) baseline serum insulin concentration (15±9 vs 6±6 uU/ml), insulin peak response (47±74 vs 92±78 uU/ml), and total insulin secretion (101±132 vs 56±90 uU/ml/hr) after treatment was discontinued versus at initial presentation, respectively. Evaluation of pancreatic biopsies obtained in 4 cats after discontinuing therapy revealed decreased beta cell numbers (3 cats), beta cell hyperplasia (2 cats) islet vacuolar changes (1 cat), and positive immunocytochemical staining for insulin (3 cats). Hyperglycemia recurred in 1 cat after 6 mos. Hyperglycemia has not recurred in 9 cats 9 to 36 mos after resolution of diabetes. These findings support the existence of noninsulin-dependent diabetes mellitus and glucose toxicity in the cat.

Persistent hypercalcemia due to primary hyperparathyroidism was identified in 6 dogs. For inclusion in this study, each dog must have had parathyroid hyperplasia identified histologically on tissue removed at surgery and each dog must have had complete resolution of all clinical signs and chemistry abnormalities following surgery. Clinical signs included polydipsia (4 dogs), polyuria (4 dogs) and signs caused by cystic calculi (3 dogs). Abnormal laboratory findings included hypercalcemia (mean 13.6 ± 0.7 mg/dl), hypophosphatemia (mean 2.2 ± 0.5 mg/dl), increased SAP activity (mean 144 ± 72 IU/L) and isosthenuria (mean 1.012 ± 0.01). Serum PTH concentration was increased in 4 dogs (mean 23.2 ± 31.1 pmol/L).

At surgery, the number of enlarged parathyroid glands was variable, being limited to one gland in 3 dogs, 2 glands in 2 dogs and 4 glands in 1 dog. Serum calcium concentration decreased into or below the reference range within 72 hours of surgery in all dogs. Each dog was treated with vitamin D and calcium carbonate following surgery. The dog which had 4 parathyroid glands removed has remained eucalcemic with vitamin D therapy for more than 1 year. Vitamin D and calcium were discontinued 4 to 12 weeks after surgery in the remaining 5 dogs and these dogs remain eucalcemic. In conclusion, parathyroid hyperplasia is a potential cause for primary hyperparathyroidism in the dog and may involve more than 1 gland.

The purpose of this project was to closely monitor the effectiveness of oral glipizide medication in the management of cats with naturally occurring DM. For inclusion each cat must have had persistent fasting hyperglycemia, glucosuria, and typical clinical signs. Twenty cats with DM were randomly selected. Each cat was to have blood obtained for [glucose] and [insulin] every 2 hrs from 0800 - 1800 hr before and every 4 hrs after treatment began, unless it was taken off the project due to need for insulin therapy or persistent euglycemia. Treatment (5mg glipizide BID x 16 wk; phase 1) was followed by 16 wks with no therapy (phase 2) and then 16 wks of glipizide therapy (phase 3). During phase 1, 10 cats deteriorated, requiring exogenous insulin; 3 became hypoglycemic and then persistently euglycemic after discontinuing therapy; all 13 were dropped from the study. Body weight (kg) in the remaining 7 cats, before and following each phase was 4.6, 5.1, 4.8, and 5.3, respectively. Mean (+SD) blood glucose (mg/dl) before treatment was 381 ± 72. Mean (+SD) blood glucose of all samples during phase 1 from these 7 cats was 258 ± 120. During phase 2 it was 310 ± 128 and during phase 3 it was 266 ± 114. Mean insulin concentrations (uU/ml; ± SD) at these same intervals were: 6.7 ± 3.1 (pre); 12.7 ± 8.1 (phase 1); 8.6 ± 7.9 (phase 2); and 15.4 ± 14.7 (phase 3). In conclusion, as many as 50% of cats diagnosed as having DM may not require exogenous insulin to survive; 15% of cats with DM may have clinically transient DM, and as many as 35% of DM cats may be responsive to oral hypoglycemic therapy.

Humoral hypercalcemia of malignancy is a common clinical condition in dogs with lymphoma (LSA), anal sac adenocarcinoma (ASCa), and other miscellaneous (Misc) tumors. Parathyroid hormone-related protein (PTHrP) concentration was measured in dog serum or plasma by a N-terminal radioimmunoassay kit for human PTHrP (Inctar). Control dogs (8) had undetectable plasma levels (< 1.8 pM) of PTHrP. Serum PTHrP was detected in dogs with neoplasia as follows (means and ranges listed):

| Tumor          | Detectability | PTHrP (pM) |
|----------------|---------------|------------|
| Hypercal LSA   | 23/25         | 7.6 (1.8-16.7) |
| Normocal LSA   | 3/11          | 3.6 (1.8-14.5) |
| Hypercal ASCa  | 8/8           | 39 (5.4-99)   |
| Normocal ASCa  | 6/9           | 3.1 (1.8-7.6) |
| Hypercal Misc  | 6/7           | 12.9 (3.8-38) |
| Normocal Misc  | 4/8           | 1.7 (1.8-3.5) |

These data indicate that PTHrP can be detected in the serum of dogs and is increased in dogs with humoral hypercalcemia of malignancy, but is also detectable in some dogs with neoplasia and normocalcemia.
13 CIRCULATING PARATHYROID HORMONE-RELATED PEPTIDE IN DOGS WITH MALIGNANCY-ASSOCIATED HYPERCALCINEMIA. E. Weir, G. Post, R. Matus, K. Insogna, W. Burtis. Yale School of Medicine, New Haven, CT; VA Medical Center, West Haven, CT and The Animal Medical Center, New York, NY.

We and others have previously reported that hypercalcemia (HC) associated with lymphosarcoma (LSA) and apocrine cell adenocarcinoma of the anal sac (APO-AS) occurs via a humoral mechanism. The probable mediator is a parathyroid hormone-related peptide (PTHrP) which we have identified by bioactivity and Northern blot analysis in tumor tissues from HC dogs. To examine whether circulating levels of PTHrP are elevated in dogs with hypercalcemia of malignancy (HCM), we used a two-site immunoradiometric assay (IRMA) directed towards PTHrP amino acid sequence 1 to 74, to measure plasma levels of PTHrP. Nineteen normal dogs had low or undetectable plasma PTHrP (mean ± SD, 1.4 ± 0.9 pM; upper limit of normal 3.2 pM). 10 of 10 dogs with HCM, all had detectable plasma PTHrP ranging from 2.0 to 69.5 pM, and 9 had levels above the normal range. Mean plasma PTHrP was 16.5 ± 16.7 pM, 12 times the normal mean. By contrast, of 7 non-HC dogs with cancer 5 had undetectable plasma PTHrP, and all were within normal range (mean 1.0 ± 0.1 pM, range 1.0 to 1.2 pM). Finally, 3 animals with HC due to other causes had plasma PTHrP levels within the normal range.

We conclude that the two-site (1-74) IRMA detects circulating PTHrP in dogs, and that normal values approximate those in man. Dogs are elevated in most dogs with HCM, but not in non-HC dogs with cancer, or those with HC due to other causes. These data suggest that measurement of plasma PTHrP may be useful for the differential diagnosis of HC in dogs.

14 FLUCTUATION IN CANINE PLASMA PARATHYROID HORMONE(PTH) CONCENTRATION. DR Finco and SA Brown. College of Veterinary Medicine, The University of Georgia, Athens, GA.

A kit for assay of canine PTH recently was validated. We used this kit for measuring plasma PTH concentration in azotemic dogs and found considerable fluctuation between serial samples on the same dog. The fluctuation could lead to major misinterpretation of PTH status, so we attempted to determine its cause.

Dogs had stable plasma concentrations of creatinine, phosphorus, and ionised calcium. All samples for PTH assay were handled in an identical manner, and assayed strictly according to directions.

Technical errors in assay were eliminated as a source of the fluctuation. Time of blood sampling (6 AM vs 12 PM vs 6 PM vs 12 AM), source of blood (jugular vs saphenous veins), and time of feeding did not explain the fluctuation. When equal quantities of plasma samples from a dog were pooled, PTH concentration of the pool was equal to the mean of individual samples.

We conclude that plasma PTH concentration in azotemic dogs may vary by over 100% from day to day, for reasons not determined. We recommend that equal quantities of 3 daily plasma samples be pooled for the composite analysis, to obtain a value for PTH concentration that more accurately reflects the status of the dog's parathyroid glands.

15 MINERALOCORTICOID THERAPY OF SPONTANEOUS PRIMARY HYPOADRENOCORTICISM IN 176 DOGS. P. P. Kinzer and M. E. Peterson. Tufts University, North Grafton, MA, and The Animal Medical Center, New York, NY.

Primary hypoadrenocorticism (Addison's disease) is a well-recognized disorder in dogs, but there have been few reports of the response to long-term replacement treatment. The purpose of this study was to evaluate and compare the efficacy of oral fludrocortisone (Florinef®) and intramuscular desoxycorticosterone pivalate (DOCP) in dogs with adrenal insufficiency. Between 1979 and 1991, we treated 176 dogs in which hypoadrenocorticism was diagnosed on the basis of history, clinical signs, routine laboratory findings (ie, hyperkalemia and azotemia), and subnormal basal and ACTH-stimulated serum cortisol concentrations. In all 176 dogs, mineralocorticoid replacement was initially given as Florinef at the mean (±SD) daily dosage of 15.2 ± 7.8 µg/kg (median, 13.0 µg/kg). In 24 of these dogs, therapy was changed to DOCP because of adverse effects (usually polydipsia and polyuria), drug resistance, or financial considerations. The initial mean dosage of DOCP was 1.33 ± 0.35 mg/kg (median, 1.23 mg/kg; range, 0.85-2.0 mg/kg), initially administered at 25-30 day intervals. After a mean treatment time of 3.6 ± 2.5 years (median, 2.8 years; range, 0.7-9.7 years), the final mean dosage of DOCP required was 1.66 ± 0.46 mg/kg (median, 1.68 mg/kg; range, 0.93-2.77 mg/kg); only 3 dogs (12.5%) required ≥ 2.2 mg/kg. Administration of DOCP was required at intervals of 15, 21, and 30 days in 2, 7, and 15 (62.5%) of the dogs, respectively. In the remaining 152 dogs in which Florinef was administered as the initial therapy, DOCP daily dosages increased from 15.6 ± 8.1 µg/kg (median, 13.5 µg/kg) to 25.1 ± 13.4 µg/kg (median, 22 µg/kg) over a mean treatment time of 3.2 ± 2.3 years (median, 2.7 years; range, 0.03-11.8 years). Our results demonstrate considerable individual variation in the mineralocorticoid dose required for normalization of serum electrolyte concentrations. Over half of dogs can be expected to require a daily Florinef dosage of at least 20 µg/kg, and very few can be controlled on less than 10 µg/kg. Most dogs can be controlled on maintenance DOCP dosage of 1.4-1.8 mg/kg/dose, and few require < 1.0 mg/kg or > 2.2 mg/kg/dose.

16 OCCULT DILATED CARDIOMYOPATHY: AN ECHOCARDIOGRAPHIC AND ELECTROCARDIOGRAPHIC STUDY OF 193 ASYMPTOMATIC DOBERMAN PINCERS. M.R. O'Grady and R. Horne. Ontario Veterinary College, Univ of Guelph, Guelph, Ont, Canada.

193 Doberman Pinschers, noted to be free of symptoms of myocardial disease based on history, underwent M-mode echocardiography and routine electrocardiography to determine the presence of occult myocardial disease in the breed.

The study group consisted of 60 intact females, 39 spayed females, 60 intact males, and 34 neutered males. The mean body weight was 33.1 kg; the range was 18 to 52.2 kg. The mean age was 4.7 years; the range was 0.4 to 11 years. 27 dogs (14%) had a left ventricular internal diameter in diastole (LVID-D) of greater than 45 mm (3% were female, 12% were male). 62 dogs (32%) had a LVID-D of 40 to 45 mm. The largest LVID-D tended to occur in older dogs. The overall mean fractional shortening (FS) was 0.20; 88 dogs (46%) had a FS of < 0.20; (47 females, 41 males). There was a weak tendency for the older dogs to demonstrate a lower FS. The overall echocardiographic E point to septal separation (EPSS) value was 3.2 mm; 25 dogs (14%) had an EPSS of > 6 mm (15 females, 10 males). There was a tendency for the older dogs to demonstrate a higher EPSS. Overall 30 dogs (16%) demonstrated ectopy (16 females, 14 males). 14 females showed ventricular ectopy (VPCs); 12 males showed VPCs; 4 females showed supraventricular ectopy (SVPCs); and 7 males showed SVPCs. There was a tendency for the incidence of ectopic beats to increase with age. The overall incidence of minor morphologic aberrations on the QRS of the EKG (MIMI) was 23% (42 dogs); both sexes were equally affected. The presence of MIMI was not influenced by the age of the dog.

Occult myocardial disease appears to be very common in the Doberman breed. There does not appear to be a sex predilection.
17 MYOCARDIAL MYOGLOBIN DEFICIENCY: AN ETIOLOGY FOR DOBERMAN DILATED CARDIOMYOPATHY? M.R. O’Grady, J.L. McCutcheon, H. Shen, R. Horne, P.W. Armstrong, P.J. O’Brien. Ontario Veterinary College, Univ of Guelph, Guelph, Ont, and Div of Cardiology, St.Michael’s Hospital, Univ of Toronto, Toronto, Ont, Canada.

Myocardial myoglobin concentration ([Mb]) was determined in dogs with heart failure (HF) and in normal dogs to assess the effect of HF on the myocardial levels of this protein. [Mb] was determined from myocardial biopsy samples obtained just prior to euthanasia.

The heart failure group consisted 14 dogs in which HF was induced by rapid right ventricular pacing (RVP) and 9 Doberman Pinschers with spontaneously occurring HF. The control group consisted of 11 mongrel dogs and 5 asymptomatic Doberman Pinschers all determined to be free of heart disease based on history, and physical examination, and for the Dobermans only, a normal echocardiogram (fractional shortening and left ventricular internal diastolic dimension < 45mm).

[Mb] was determined from myocardial heart catheterization performed using a high-fidelity dual micromanometer catheter with simultaneous pressure measurements at cardiac catheterization. Left ventricular and aortic pressure traces, and the electrocardiogram, allowing a beat-to-beat comparison between techniques. In each dog, 5 sinus beats were measured after instrumentation, during the administration of the ultrashort-acting beta-blocker esmolol, and after balloon valvuloplasty. Additionally, 10 catheter-induced atrial or ventricular extrastoles or post-extrasystolic potentiated beats were measured. Doppler peak and mean gradients were calculated by application of the simplified Bernoulli equation to the velocity spectra.

Doppler peak and mean gradients were calculated by application of the simplified Bernoulli equation to the velocity spectra. Linear regression analysis demonstrated an excellent correlation for simultaneously maximal instantaneous Doppler and catheter gradients (r=0.979, n=123) and for Doppler and catheter mean gradients (r=0.980, n=123). For maximal instantaneous Doppler and peak to peak catheter gradients, the correlation was also linear (r= 0.981, n=123) but as expected the Doppler gradient consistently overestimated catheter peak to peak gradients. CW DE is a reliable alternative to cardiac catheterization for the measurement of subaortic stenosis pressure gradients in dogs.

18 CONTRAST ENHANCED ULTRA-FAST COMPUTED TOMOGRAPHY ASSESSMENT OF CHANGES IN MYOCARDIAL PERFUSION IN THE DOG. M.Rishopw, GG Knowles, P.Schrott, Dept of VCMS, Washington State University, Pullman, WA, *Real Time Diagnostics, Spokane, WA.

Changes in myocardial perfusion estimated by contrast enhanced ultra-fast computed tomography (UFCT) were examined in 6 dogs.

All dogs were anesthetized with thiamylal and halothane. Catheters were positioned in the right atrium and aortic root. Via a left lateral thoracotomy the left anterior descending (LAD) and the left circumflex (LC) coronary arteries were isolated. Transit-time Doppler flow probes and cuff occluders were placed on the proximal portion of each vessel. The ECG, aortic root pressures, LAD and LC flow were monitored and recorded. ECG-gated multi-slice UFCT images were collected during suspended respiration. The LAD and LC arteries were sequentially occluded to produce 50% and 100% reductions from baseline flows. Non-ionic contrast material was injected via the right atrial or aortic root catheters during image acquisition. Studies were repeated with adenosine enhanced coronary flow. UFCT images were analyzed using indicator dilution theory to estimate myocardial perfusion in ml/gm/min.

Significant changes (p<0.05) produced in measured LAD and LC flow were consistently and correctly tracked by similar changes in the estimates of myocardial perfusion produced by the contrast-enhanced UFCT images.

These results demonstrate that indicator dilution theory applied to gated contrast-enhanced UFCT images is capable of producing reliable and reproducible estimates of myocardial perfusion.

19 COMPARISON OF PRESSURE GRADIENTS DETERMINED BY DOPPLER ECHOCARDIOGRAPHY AND CARDIAC CATHETERIZATION IN DOGS WITH SUBAORTIC STENOSIS. L.B.Lehmkohl, J.D.Bonagura, E.L.Stepien, D.E.Jones. The Ohio State University College of Veterinary Medicine.

The purpose of this study was to compare pressure gradients obtained from continuous wave (CW) Doppler echocardiography (DE) with simultaneous pressure measurements at cardiac catheterization. Left heart catheterization was performed using a high-fidelity dual micromanometer pigtail catheter in 5 Newfoundland dogs. The RBC velocity spectra in the ascending aorta was interrogated from a Hewlett-Packard echiocardiograph with a 1.9 MHz CW transducer. Pressure signals were DC coupled to the echocardiograph superimposing simultaneous aortic velocity spectra, left ventricular and aortic pressure traces, and the electrocardiogram, allowing a beat-to-beat comparison between techniques. In each dog, 5 sinus beats were measured after instrumentation, during the administration of the ultrashort-acting beta-blocker esmolol, and after balloon valvuloplasty. Additionally, 10 catheter-induced atrial or ventricular extrastoles or post-extrasystolic potentiated beats were measured. Doppler peak and mean gradients were calculated by application of the simplified Bernoulli equation to the velocity spectra.

Linear regression analysis demonstrated an excellent correlation for simultaneously maximal instantaneous Doppler and catheter gradients (r=0.979, n=123) and for Doppler and catheter mean gradients (r=0.980, n=123). For maximal instantaneous Doppler and peak to peak catheter gradients, the correlation was also linear (r= 0.981, n=123) but as expected the Doppler gradient consistently overestimated catheter peak to peak gradients. CW DE is a reliable alternative to cardiac catheterization for the measurement of subaortic stenosis pressure gradients in dogs.
21 SURVIVAL IN TREATED AND UNTREATED DOGS WITH CONGENITAL PULMONIC STENOSIS. D.M. Emery, P.D. Flon, and D.W. Hird. School of Veterinary Medicine, University of California, Davis, CA.

The effect of four treatment regimens (no treatment [NT, n=72], valvulotomy [VX, n=12], patch graft [PG, n=18], and percutaneous balloon valvuloplasty [PBV, n=25]) upon survival time in dogs with congenital pulmonic stenosis (PS) were evaluated retrospectively. Among the intervention groups, mortality was significantly lower (P<0.001) in dogs treated by VX, PG, and PBV, respectively, died during or within 36 hours of surgery.

Cumulative percentages of dogs surviving to the end of the second year post-treatment were 94%, 65%, 52%, and 84 for PBV, NT, PG, and VX groups, respectively. Untreated dogs had a 2.1 times (95% CI 1.3 to 3.8) greater risk of dying within the first 2 years than did dogs treated by PBV. In dogs surviving >2 years, there was no significant difference in survival time in dogs treated by PBV, PG or VX. 9/12, 6/18, and 0/25 dogs treated by VX, PG, and PBV, respectively, died during or within the first 3 months of surgery.

22 THE PREVALENCE OF MITRAL SYSTOLIC MURMURS IN THE CAVALIER KING CHARLES SPANIEL (CKCS) A.W. Beadew and J.W. Buchanan. School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pa.

The aims of this study were to 1) examine a large number of young American bred CKCS dogs 2) determine the age specific prevalence rates of mitral regurgitant murmurs in these clinically normal CKCS's 3) determine the influence of sex and coat color on the frequency of murmurs.

Stethoscopic examination was performed on 226 CKCS's at the North-East regional specialty show (Nov 1990). All murmurs and thrills were classified according to location, grade (I-VI) and character. A questionnaire pertaining to medical and family histories was completed by each owner.

Of 225 dogs included in the analysis (1 had pre-diagnosed Pulmonic Stenosis) the overall prevalence rate for left apical systolic murmurs was 23.5%. In dogs aged 4 years and older the prevalence increased to 51%. There was no significant difference in the frequency of murmurs between the sexes or in relation to coat color.

It was concluded that systolic murmurs are detectable at an unusually early age in CKCS dogs and that the prevalence increases with age at a greater rate in other breeds.

23 HEART RATE VARIABILITY IN VETERINARY SPECIES. Elizabeth Settles, Allen W. Hahn, Karla S. Rugh and Benlu Jiang. College of Veterinary Medicine and the John M. Dalton Research Center, Univ. of Missouri, Columbia, MO 65211.

We examined the beat to beat changes that occur in the heart rate of several species of veterinary interest, e.g.; dogs, horses, cats, swine, and cattle. We collected telemetered electrocardiographic data with a portable personal computer (Macintosh) and, with an algorithm developed in our laboratory, computed instantaneous heart rate from each R-R interval. Animals were from hospitalized subjects without heart disease or from those used as blood donor or student examination animals. After receipt of the data in digital form, the R waves are identified and the time of occurrence of the R wave for computation of the R-R interval and then instantaneous heart rate. Further processing of the instantaneous heart rate in the frequency domain was used to identify respiratory components.

The coefficient of variation (mean / s.d * 100) was used as a measure of the heart rate variability (HRV). This coefficient varied from over 36 in a recumbent dog to as little as 3.8 in a standing horse. The data show that all species examined have significant variations in their instantaneous heart rate. Dogs, with their large sinus arrhythmia, have the largest coefficient of variation of the instantaneous rate but much of that can attributed to respiratory variation. Since it has been shown that HRV decreases just prior to serious events, we felt it well to present our data on normal HRV in veterinary species.

24 AUTOMATIC IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN GERMAN SHEPHERDS WITH INHERITED SUDDEN CARDIAC DEATH. H.S. Moise, E.S. Paine, J.A. Flanders, R. F. Gilmour Jr. NYSCVM, Cornell University, Ithaca, NY.

The feasibility of using the automatic implantable cardioverter defibrillator (ICD) was determined in German Shepherds at risk for sudden death because of ventricular arrhythmias. The ICD (Ventricor, Cadence	extsuperscript{m}t was implanted in 3 of these dogs (1M, 2P) at 5 months of age. A lateral thoracotomy was used for the implantation of the leads. The pulse generator was secured intraabdominally. After implantation the ICDs were interrogated weekly for delivery of therapy. Initially the ICDs were programmed for defibrillation using tachycardia detection (TD) of 210 ms for 20 intervals. The initial therapy for sequential shocks was (1) 400V, 450V, or 500V; (2) 550V; (3) 750V x 4. One female received inappropriate therapy that resulted in ventricular fibrillation (VF) and death. During the first 3 months inappropriate charges occurred in the male (2 delivered, 1 aborted) and female (2 delivered, 8 aborted). These charges were due to T-wave sensing and sinus tachycardia. High signal amplitude and sinus rate necessitated modification of ICD software. To decrease T-wave sensing the ICDs were programmed to deliver 1 million bigeminal rhythms. The TD was increased to 200 ms for 40 intervals. Programmed stimulation was used to determine the effective refractory periods and up to 3 premature stimuli were delivered without the induction of VF. VF was induced with pacing and successfully delivered by the ICDs. The voltage needed for defibrillation was greater than at implantation possibly because of growth of the heart and repositioning of the leads; therefore, the voltage was increased for the male dog (1) 550V, (2) 750, (3) 750 x 1 and for the female dog (1) 600, (2) 700V, (3) 750 x 1. Further followup revealed the ICDs to be well-tolerated. Thus, the properly programmed ICD is feasible in these dogs and will allow nonpharmacologic control of fatal arrhythmias and noninvasive programmed stimulation.
FLASMA CATECHOLAMINE CONCENTRATIONS AND CARDIAC ARRHYTHMIAS IN DOGS WITH SEVERE NONCARDIAC DISEASES

Julie Kopser, John E. Rush, Rajeek A. Agarwal, M.S.A. Kumar, Dept. of Medicine, Dept. of Anatomy and Cellular Biology, School of Veterinary Medicine, Tufts University, N. Grafton, MA.

Dogs diagnosed with GDV, trauma, neurologic disease, or splenic mass may develop ventricular arrhythmias (VPCs). Additionally, elevations in plasma catecholamine concentrations [CA] have been shown to cause myocardial lesions and arrhythmias. The purpose of this study was to determine whether plasma [CA] are significantly elevated in dogs with the above diseases and no clinical evidence of cardiac disease (i.e., cardiomyopathy, endocardiosis, etc.) and 40 had VPCs in association with GDV, trauma, pancreatitis, or other systemic disease.

Thoracic radiographs, 10 lead ECGs and echocardiograms were used to exclude primary cardiac disease in 20 dogs (multiple trauma [11], neurologic disease [7], splenic mass [4], GDV [2]). Continuous EKG monitoring was performed to search for VPCs. Serial plasma samples were assayed for CA using high performance liquid chromatography with electrochemical detection. Ten control dogs were similarly monitored. Nine of the study dogs and none of the control dogs developed VPCs.

Plasma [CA] were NS elevated in study dogs when compared to controls. The maximum number of VPCs per minute was not linearly related to plasma [CA]. Plasma [CA] did not significantly increase to cause arrhythmias in dogs. Therefore, it does not appear that plasma [CA] play a direct role in the development of VPCs in these dogs. From this study, we cannot exclude the possibility that local catecholamine concentrations contribute to the pathogenesis of such arrhythmias or that moderate elevations of CA predispose the myocardium to the adverse effects of ischemia or electrolyte imbalances.

MORPHOLOGIC FEATURES OF VENTRICULAR ARRHYTHMIAS IN DOGS WITH AND WITHOUT UNDERLYING CARDIAC DISEASES

J. Bucheler, J. Rush, Dept. of Medicine, School of Veterinary Medicine, Tufts University, N. Grafton, MA.

Electrocardiograms (ECGs) were obtained from dogs with ventricular arrhythmias (VPCs). Dogs were determined to have either underlying cardiac disease or a normal heart (with the exception of VPCs) on the basis of history, physical exam, thoracic radiographs and/or ECHO findings. Of 135 dogs, 95 had underlying cardiac disease (i.e., cardiomyopathy, endocardiosis, etc.) and 40 had VPCs in association with GDV, trauma, pancreatitis, or other systemic disease.

Lead II ECGs were measured for p wave duration (Pp), QRS duration (QRS), and QT interval (QT). VPC duration (QRSVPC), morphology, and ventricular pairing were evaluated in all available leads (usually ≥ 3 leads). The widest VPC was measured for QRSVPC and QTint. All leads with VPCs were evaluated for the presence of QRSVPC notching. When VPCs were present in pairs or runs, the shortest R-R interval between VPC's was measured.

Traditionaly, normal values for canine blood pressures have been established in either experimental or clinical settings. Yet, it is well documented in human patients that the anxiety associated with clinical environments can transiently elevate blood pressure and pulse measurements recording false diagnoses of hypertension. Although isolated VPCs were more common in dogs with underlying cardiac disease, when VPCs were paired they were much more likely to occur at shorter R-R intervals.

COMPARISON OF CANINE BLOOD PRESSURES AND PULSE RATES IN H VETERINARY PATIENTS CAUSED BY INTRAVENOUS ACEPROMAZINE

J. JD, Bednarski RM, Ruiz WM: Department of Veterinary Clinical Sciences, The Ohio State University.

The clinical use of tranquilizers, sedatives, and opioids is influenced by the cardiovascular (CV) effects of these drugs. The hemodynamic effects are usually studied by invasive techniques requiring anesthesia. To assess the feasibility of noninvasive estimates for evaluating hemodynamic changes of these drugs, we measured central hemodynamics and ventricular function invasively while simultaneously recording Doppler-echocardiographic (DE) estimates of CV function in 11 conscious, previously instrumented dogs. Acepromazine (0.1 mg/kg) and buprenorphine (0.004 mg/kg) were administered intravenously.

Blood pressure (BP) and left ventricular systolic (LVsys) function (LVdV/dt) were measured with micromanometer-tip catheters and cardiac output (CO) was measured by thermodilution. These invasive measures were compared to oscilometric and pulse wave estimations obtained in 11 dogs with and without clinical settings. Oscilometric measurements are comparable in both environments.

Noninvasive measurements of systolic function (LVdV/dt) were compared to invasive measures in 11 dogs with and without clinical settings. Oscilometric measurements are comparable in both environments.
COMPARISON OF DIRECT ARTERIAL AND INDIRECT OSCILLOSCOPE MEASUREMENT OF BLOOD PRESSURE IN CONSCIOUS DOGS. A.M. Kallet, Corte Madera CA; L.D. Cowgill, and Phil Kaab. Univ. of California, Davis CA.

Frequent comparisons have been reported between direct and indirect blood pressures recorded in anesthetized dogs. Depending on the methods and conditions under which the measurements were obtained, the two methods did not agree. For outpatient practice where routine anesthetics are not practical, the anxiety of the clinic environment and pain associated with the methods may produce clinically significant differences between the two methods. To investigate this issue, direct arterial blood pressure measurements were compared with oscillometric pressures obtained indirectly in normal conscious dogs in a clinical setting. Direct arterial pressure and pulse were recorded from the femoral artery in 15 laterally recumbent dogs with a CS-525 pressure monitor. The artery was punctured with a 22 gauge needle attached directly to a Bell and Howell Thrombomonitor. Oscillometric pressures were obtained from the femoral artery in the same recumbent animals using appropriately sized and fitted neonatal blood pressure cuffs connected to the Dinamap 8100 pressure monitor. Differences were analyzed by ANOVA and paired t-tests.

Direct systolic pressure was significantly higher than the comparable indirect measurements (168 ± 12 vs 137 ± 15 mmHg, respectively; P < 0.001). No differences were observed for direct and indirect diastolic pressure (P = 0.7 104 ± 13 mmHg, respectively). Reflecting the differences in systolic pressure, the true arterial pressure measured directly was higher than that measured by oscillometry (136 ± 25 vs 102 ± 13 mmHg, P = 0.01).

Intra- and interassay variation amounted to 8% and 5%, respectively.

In the post-mortem examination the lungs were wet, heavy, beefy and firm. Haemorrhages and oedema fluid were evident. Histologically intra-alveolar haemorrhages and macrophages with brown pigmented cytoplasm were also present in the alveolar walls. Eosinophilic hyaline membranes were seen throughout the lungfield, particularly in the caudal lobes.

Pneumomediastinum and gastro-oesophageal intussusception developed in the latter part of the disease. A mild leucocytosis with neutrophilia was the main haematological finding.

There was no response to therapy with antibiotics, corticosteroids, diuretics or oxygen.

In the post-mortem examination the lungs were wet, heavy, beefy and firm. Haemorrhages and oedema fluid were evident. Histologically alveolar oedema and fibrinous exudate were seen. Eosinophilic hyaline membranes were lining the alveolar walls. Haemorrhages and oedema fluid were evident. Histologically intra-alveolar haemorrhages and macrophages with brown pigmented cytoplasm were also present as well as pulmonary fibrosis in more longstanding cases. The changes are typical for adult respiratory distress syndrome (ARDS). Renal aplasia in two dogs and hydrocephalus in one dog were other incidental findings.

Etiology remained obscure. Trauma, paroxysmal toxicity, pulmonary infection and septicaemia which are the most common causes for ARDS could not be identified. Some hereditary defect was suspected as an initiating factor.
LARYNGEAL PARALYSIS IN DALMATIANS. K.G. Braun; A. Shores; N. Di Pinto; D. Forrester; L.O. Shell; S.M. Cochrane; I.M. Parent, Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University, Alabama.

Laryngeal paralysis (LP) is most commonly seen as an idiopathic, naturally-occurring condition in aging large or giant-breed dogs. A hereditary form, transmitted as an autosomal dominant, has been documented in young Bouvier des Flandres, and a presumed hereditary form has been reported in young Siberian Huskies, young Husky cross-breeds, and young bull terriers. Two years ago, we described the first cases of LP in 5 young Dalmatian dogs. Since that time we have encountered LP in an additional 11 Dalmatians (both male and female with a mean age of 11 months) from 9 litters (8 in the U.S.; 1 in Canada). Preliminary clinical and pathologic studies are reported here.

Clinical signs included inspiratory stridor, exercise intolerance, syncope episodes, cyanosis, dyspnea, dysphagia, and coughing or gagging when eating or after exercise. Megasoephagus was present in 8 dogs. LP typically was associated with a more generalized polymyopathy. Neurologic abnormalities included hyporeflexia, muscle atrophy/fasciculations, limb hyperextension, facial/lingual paralysis, and hypermetria. EMG abnormalities included fibrillation potentials in laryngeal, esophageal, facial and distal appendicular muscles.

Nerve conduction velocities were normal. Neurogenic atrophy was observed in intrinsic laryngeal and appendicular muscles. Changes in cranial and appendicular nerves were dominated by axonal neuropathy. The amount of ND present in circulation during each dose interval was significantly reduced. This study indicates that adequate seizure control may require increased dose rates for CLZP when it is co-administered with PB.

OSMOTIC OPENING OF THE BLOOD-BRAIN BARRIER TO ANTI-TUMORAGENTS. RA Kroll, DP O'Brien, MK Gumerlock, JC Lattimer, GC Johnson. University of Missouri, Columbia, MO

One problem associated with treatment of CNS neoplasia is drug delivery across the blood-brain barrier (BBB). The technique of osmotically disrupting the BBB allows investigation of anti-tumor agent delivery to brain of proven new approaches to the treatment of brain tumor patients. The purpose of this study was to evaluate, in dogs, the neurotoxicity of carboplatin when delivered across a modified BBB.

To effect reversible blood-brain barrier disruption (BBBD), mannitol (25%, 1.4 osm) was infused into the internal carotid artery at a rate of 1.5 ml/sec for 30 sec. Carboplatin (Paraplatin) was administered in a dose of 500 mg/m² was administered via the internal carotid artery, over a 15 minute period, beginning immediately after infusing the disrupting agent. Saline was used as the negative control for both disruption and chemotherapy.

Successful BBBD was achieved in 4 of 6 dogs in both BBBD groups. All four in group #1 died or required euthanasia within 4 days of treatment due to development of status epilepticus and/or seizures. Histologic findings included ipsilateral edema, hemorrhagic infarction, and uncal herniation. Two of the 4 disrupted dogs in group #2 developed seizures 15 and 18 days after treatment, respectively, and were euthanized. The other 2 survived the full four weeks of the study, with no neurologic abnormalities. Five of the 6 dogs in group #3 had trace BBBD. One died with severe nephrosis and one died with aspiration pneumonia. None had neurologic signs. Seven of the 12 dogs receiving carboplatin had some degree of nephrosis.

Carboplatin at 500 mg/m² following BBBD appears to be excessively neurotoxic. Since only 2 of 6 group #2 dogs (BBBD + NaCl) were positively disrupted, without complication, the technique of BBBD requires further study before it can be recommended as a treatment method.

EFFECT OF CHRONIC ADMINISTRATION OF PHENOBOBRITAL ON DISPOSITION OF CLORAZEPATE IN DOGS. SD Forrester, JR Wilcke, KR Dyer, JD Jacobson. VA-MD Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, Virginia.

Disposition of clorazepate (CLZP) (Tranxene,® Abbott), an anticonvulsant drug, was determined before and after chronic administration of phenobarbital (PB) to dogs.

Six adult dogs were given a single oral dose of CLZP (2 mg/kg) and blood samples were collected serially for 24 hours after administration. Then, CLZP was administered at the same dose q12h for 44 consecutive days; PB was administered concurrently (5 mg/kg PO q12h). On day 44, blood samples were collected serially for 24 hours after administration of CLZP and PB. Serum concentrations of nordiazepam (ND), the principal metabolite of CLZP, were determined by fluorescence polarization immunoassay.

Maximal ND concentrations ranging from 569.6 ng/ml to 1387.9 ng/ml (880.2 ± 248.9) occurred 0.28 to 2.19 hr (1.42 ± 0.61) after a single dose of CLZP. After PB administration, maximal ND concentrations were significantly lower (P < 0.001), ranging from 209.6 to 698.5 ng/ml (399.3 ± 155.6) and occurring 1.14 to 2.43 hr (1.55 ± 0.43) after dosing. Area under the curve (AUC) after PB administration (2771 ng-hr/ml ± 513) was less than AUC after a single dose (5618 ng-hr/ml ± 997) of CLZP (P < 0.001).

Chronic administration of PB altered disposition of CLZP such that amount of ND present in circulation during each dose interval was significantly reduced. This study indicates that adequate seizure control may require increased dose rates for CLZP when it is co-administered with PB.

AUTONOMIC DYSFUNCTION IN THREE DOGS. DP O'Brien, RA Kroll, GC Johnson. College of Veterinary Medicine, University of Missouri, Columbia, Missouri

Three dogs were diagnosed with autonomic dysfunction. Two of the cases presented with classic signs of dysautonomia. Case one (a four-month-old, female English bulldog) died of aspiration pneumonia prior to extensive diagnostic workup. In the second case (a three-year-old, male Doberman pinscher), neurologic exam and pharmacologic testing revealed evidence of diffuse, post-ganglionic loss of both sympathetic and parasympathetic systems. Both cases had typical histologic changes of dysautonomia at necropsy: loss of neurons in autonomic ganglia with no evidence of inflammatory response. The third case (a four-year-old, female, spayed Irish setter) had signs of somatic motor and sensory involvement as well as autonomic dysfunctions. Peroneal nerve biopsy revealed axonal degeneration and secondary demyelination. This case responded to corticosteroid therapy for six months, but eventually progressed. The dog was euthanized 9 months after admission, but she was not necropsied.

Dysautonomia in dogs is a rare disease of unknown etiology. It is characterized by degeneration of neurons within autonomic ganglia and signs of diffuse autonomic dysfunction. The prognosis in dysautonomia is grave and treatment palliative. Autonomic dysfunction can, however, occur as a component of a generalized peripheral neuropathy, which may be amenable to specific therapy.
Threshold levels of clicks, 1.2, and 4 KHz tones were determined in a linear study of 60 Dalmatian puppies from 4-8 weeks of age. The maturation of the BAER response was also evaluated. Clicks have a broad frequency spectrum and cannot be used to assess auditory thresholds at particular frequencies. Brief tone-pips were used to evaluate particular frequencies. Notched noise was used to mask the frequency spread of acoustic energy in the brief tone-pips in order to isolate the specific response areas in the cochlea.

A series of tones were evaluated at varying decibels until the threshold was reached in that particular frequency. The puppies were not sedated and usually fell asleep during the testing. The ear canals of the youngest puppies were too small to insert an earphone and a padded external earphone was used. The external earphone was better tolerated in the older puppies and gave more repeatable data.

The threshold level for the clicks was approximately 50 decibels per sound pressure level in all ages of puppies tested. The latency of the BAER response decreased markedly as the puppies matured. The latency of the waves were increased in the 4 week puppies as the decibels per sound pressure level were decreased. There was little change in latency in the 8 week puppies with change in decibels per sound pressure level. The threshold of 4KHz tones was approximately 40 decibels per sound pressure level. The thresholds of the other frequencies are currently being established.

Pattern electroretinograms (PERG) were recorded from anesthetized healthy mongrel dogs using square-wave vertical grating patterns at spatial frequencies of 0.015, 0.03, 0.06, 0.12, 0.24, 0.48, 0.96, and 1.92 cycles/degree. Patterns were presented on a 12-inch monitor at a distance of 20 cm from the cornea. Dogs were corrected for distance and refractive error using streak retinoscopy and then presented the stimuli at a rate 1.7/sec. Monocular PERG were recorded by a subconjunctival electrode referenced to a subcutaneous electrode placed just caudal to the lateral canthus. Two averaged PERG, each in response to 512 pattern reversals, were recorded with a time base of 500 msec and a vertical calibration of 0.61-1.21 uV/vertical division. Responses were recorded from each dog during 2 separate recording sessions approximately 1 week apart.

In response to low-frequency stimuli, PERG consisted of a small negative peak (N1), a larger positive peak (P1), followed by a much larger negative peak (N2). The peak times of N1, P1, and N2 ranged from 12.09-23.09, 33.1-40.8, and 82.1-114 msec, respectively. The amplitudes of P1 and N2 ranged from 0.34-1.66 and 1.04-4.88 uV, respectively. Increasing the spatial frequency of the stimulus caused a monotonic decrease (P<0.05) in the amplitudes of both positive and negative peaks. There was an increase (P<0.05) in the peak times of N1 and P1 across spatial frequencies, but a decrease (P<0.05) in the peak time of N2. There was considerable variation between dogs, but there was no difference (P>0.05) between trials for each dog. Using the protocol described in this study, dogs did not demonstrate the type of spatial tuning reported for PERG in some studies in human beings. The physiologic implications of luminance and spatial contrast components of PERG will be discussed.
POSTSURGICAL RECURRENT OF CALCIUM OXALATE UROLITHS IN DOGS
J. Lulich, L. Pertine, C. Osborne, L. Unger, University of Minnesota

Following surgical removal of calcium oxalate (CaOx) uroliths in dogs, preventative therapy to minimize urolith recurrence has been commonly recommended. However, the frequency with which CaOx uroliths recur is unknown.

To determine the frequency of urolith recurrence, the records of dogs with CaOx uroliths admitted to our hospital between 1983 and 1990 were reviewed retrospectively. Cases were included if postsurgical radiographs confirmed surgical removal of all uroliths. 45 cases fulfilled this criteria; however, only 33 dogs were evaluated beyond the immediate postsurgical period. Of these 33 cases, urolith recurrence was detected by radiography or urolith retrieval in 17 (52%). The recurrence rate increased with the length of times that dogs were evaluated: 3% occurred after 3 months, 9% after 6 months, 36% after 1 year, 42% after 2 years, 48% after 3 years, and 52% after 6 years. Most dogs without recurrence were available for evaluation for only a short period following surgery: 81% of dogs were evaluated greater than 3 months, 69% greater than 1 year, 31% greater than 2 years, and 12.5% greater than 3 years. The percentage of males and females were the same in both recurrent and nonrecurrent urolith formers; however, recurrent urolith formers were an average of 3 years younger than the dogs which did not reform uroliths.

Medical therapy of CaOx uroliths should be considered in most dogs to prevent recurrence. Prospective clinical trials are needed to more accurately determine the rate and risk factors for recurrence of calcium oxalate uroliths in dogs.

EFFECTS OF ORAL NaCl ADMINISTRATION ON URINARY OXALATE EXCRETION
J. Lulich, C. Osborne, L. Felice, T. Fletcher, R. Thumchai, S. Sanderson, University of Minnesota, St. Paul, MN

Oral administration of NaCl has been recommended for dogs with calcium oxalate uroliths to promote diuresis induced reduction of the concentration of calculogenic substances in urine. However, the effect of NaCl on urinary oxalate excretion in dogs is unknown. This study was designed to evaluate the effect of additional oral NaCl administration on urinary oxalate excretion measured by ion chromatography.

24-hr urinary oxalate excretion was determined in 5 clinically healthy Beagles during two, 6-week feeding periods: a low sodium period (Prescription Diet Canine u/d (u/d); Na=0.24%) and a high sodium period (u/d with additional NaCl; Na=1.2%). All dogs were fed a maintenance diet for 2 weeks prior to each feeding period to minimize carry-over treatment effects. 24-hr urine samples were collected at the end of weeks 0, 2, 4, and 6. A crossover design was used so that the order of each feeding period (low Na or high Na) was randomly assigned to each group of 3 dogs. Urinary oxalate excretion (µmol/kg/24hr) during consumption of u/d was not significantly different from urinary oxalate excretion during consumption of u/d supplemented with NaCl. Urinary oxalate excretion during the maintenance diet was almost 2 times greater than urinary oxalate excretion during consumption of u/d with NaCl (p < 0.001). Oral administration of NaCl does not alter urinary oxalate excretion in normal dogs consuming u/d. However, normal urinary oxalate excretion is diet dependent.

NON-INVASIVE DETERMINATION OF CANINE EFFECTIVE RENAL PLASMA FLOW
R.J. Itkin, D.R. Krawiec, A.R. Twardock and H.B. Gelberg, College of Vet. Med. Univ. of Illinois

Technetium 99m-mercaptoacetyltriglycine (99mTc-MAG3) is a renal radiopharmaceutical which has been used as an agent to assess effective renal plasma flow (ERPF) in human beings via quantitative renal scintigraphy (QRS).

Effective renal plasma flow was assessed in dogs by performing simultaneous clearances of para-aminohippuric acid (PAH) and scintigraphic uptakes of 99mTc-MAG3. Each dog underwent 2 separate assessments of renal function to establish reproducibility.

The dogs were then treated with a known nephrotoxic drug in an attempt to induce renal failure. ERPF was then reassessed using the same protocol. Utilizing linear regression analysis, equations were derived in order to determine the relationship between PAH clearance and renal percent dose uptake of 99mTc-MAG3.

Preliminary results show that the depth corrected percent dose uptake of 99mTc-MAG3 by the kidneys correlates well with ERPF as determined by the clearance of PAH (r=0.895). Based on these results, we anticipate QRS utilizing 99mTc-MAG3 will be an excellent means to estimate ERPF in healthy and diseased canine kidneys.

These studies were performed on conscious, non-pharmacologically restrained dogs. Consistent with other studies, we noted hepatobiliary and gall bladder uptake of 99mTc-MAG3. All of our subjects experienced emesis following administration of 99mTc-MAG3, which has not been previously reported.

PREDICTIVE VALUE OF URODYNAMIC MEASUREMENTS IN THE MANAGEMENT OF ECTOPIC URETERS IN THE DOG
IF Langan, MR Lappin, HB Seim. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

Urodynamic measurements were utilized to assess urinary bladder and urethral function and the probability of post-operative continence in 9 dogs with ectopic ureters. Prior to surgical intervention, baseline cystometrograms (CMG) and urethral pressure profiles (UPP) were obtained under xylazine sedation. UPP abnormalities consistent with urethral incompetence were documented in 7 dogs (77.8%) and CMG abnormalities suggesting reduced bladder capacity were present in 5 dogs (55.6%). Dogs with UPP abnormalities were treated with the alpha agonist phenylpropanolamine (PPA) and the UPP was reevaluated 14 to 30 days later. UPP measurements improved significantly in 3 dogs following PPA.

Following surgical repair of the ectopic ureter(s) in 8 dogs, 2 dogs were continent without medication (25%) and 2 dogs (25%) were continent with PPA administration. Variable degrees of incontinence persisted in the remaining 4 dogs (50%), 3 of which had been treated with PPA with minimal UPP response. These 3 dogs improved with increased PPA dosages. The fourth dog was determined to have a persistent patent ectopic ureter and awaits further surgery. Post-operative continence was associated with sedated maximal urethral pressures > 29 cm H2O and maximal urethral closure pressures > 20 cm H2O with or without PPA. Using these criteria, predicted outcomes would have been correct in 7/8 dogs undergoing surgical repair, with the one incorrect prediction resulting from surgical failure.

We conclude that reduced bladder capacity and urethral incompetence are commonly associated with ectopic ureters in dogs and that pre-operative urodynamic evaluation can be utilized to predict post-operative outcome.
45 MEASUREMENT OF GFR IN DOGS USING ENDOGENOUS CREATININE CLEARANCE. DR Finco, SA Brown, JA Barwa nti. College of Veterinary Medicine, The University of Georgia, Athens, GA.

Endogenous creatinine clearance is not a reliable measure of GFR in dogs because traditional methods of creatinine analysis (Jaffe reaction) are not specific for creatinine. A specific method (creatinine RIA) for creatinine analysis is now available. In this study, we compared Jaffe creatinine clearance (JCR) and PAP creatinine clearance (PCR) with inulin clearance (IN) to determine if PCR measured GFR.

Six normal dogs and 12 dogs with reduced renal mass had GFR measured (IN). Simultaneously, JCR and PCR were measured, and results were compared to IN.

The range of IN was 0.70 to 3.92 ml/min/kg. Paired T-test comparison of PCR and IN revealed no significant difference; the PCR/IN ratios were 1.04 ± 0.08. Paired T-test comparison of JCR and IN revealed that JCR was significantly less (P < 0.05); the JCR/IN ratios were 0.94 ± 0.08. Level of function did not seem to influence ratios of IN to either JCR or PCR.

We conclude that the creatinine PAP method of creatinine analysis allows use of endogenous creatinine clearance for reliable measurement of GFR in dogs.

46 A NEW FAMILIAL MEMBRANO-PROLIFERATIVE GLOMERULONEPHRITIS IN BERNESE MOUNTAIN DOGS. C. Reuschen R.L. Relford, G.E. Lees and R.A. Green. School of Veterinary Medicine, Texas A&M University, College Station, TX.

When treated in this way, all dogs developed mild to massive proteinuria with inactive urine sediment. Three of 5 dogs met our criteria for NS (U Pr > 5.0, serum albumin < 2.5 g/dl, and serum cholesterol > 250 gm/dl) and remained nephrotic for 28-109 days after CBA injection. In general, 20 mg CBA was given for 4 consecutive days then the dogs were rested for 3 days. This protocol was followed for 3 weeks increasing the dose by 25 mg weekly, after which time CBA injection were given daily until day 46. A maximum dose of 120 mg was given to dogs weighing < 20 kg and 200 mg to dogs weighing > 20 kg.

When treated in this way, all dogs developed mild to massive proteinuria with inactive urine sediment. Three of 5 dogs met our criteria for NS (U Pr > 5.0, serum albumin < 2.5 g/dl, and serum cholesterol > 250 gm/dl) and remained nephrotic for 28-109 days after CBA injections were stopped. (The other 2 dogs were less substantially proteinuric even though daily injections of CBA were continued until day 57. All of the dogs maintained urine concentrating ability, and their serum concentration of urea, creatinine, and phosphorus remained within normal limits throughout the study.

47 EXPERIMENTAL PRODUCTION OF GLOMERULONEPHRITIS AND THE NEPHROTIC SYNDROME (NS) IN DOGS. R.L. Relford, G.E. Lees and R.A. Green. School of Veterinary Medicine, Texas A&M University, College Station, TX.

Cationic bovine serum albumin (cBSA) was used to experimentally induce glomerulonephritis in dogs. Five, mixed breed, male dogs were hyper-immunized with a subcutaneous injection of cBSA emulsified in 1 ml of Complete Freund's Adjuvant on day 1. Based on previous pilot studies, the hyper-immunization dose was intended to be 5 mg cBSA; however, the actual dose given was an unknown but approximately ten-fold higher amount because of a technical error that was discovered only after the project was underway. The hyper-immunization dose used differs in this study.

Diphenhydramine (0.5 kg IV) was given 1 hour before cBSA injection. The hyper-immunization dose used for all dogs was the same. Dogs were rested for 2 weeks, and then daily IV injections of cBSA were begun. Diphenhydramine (0.5 /kg IV) was given 30 minutes before each CBA injection. In general, 20 mg CBA was given for 4 consecutive days then the dogs were rested for 3 days. This protocol was followed for 3 weeks increasing the dose by 25 mg weekly, after which time CBA injection were given daily until day 46. A maximum dose of 120 mg was given to dogs weighing < 20 kg and 200 mg to dogs weighing > 20 kg.

When treated in this way, all dogs developed mild to massive proteinuria with inactive urine sediment. Three of 5 dogs met our criteria for NS (U Pr > 5.0, serum albumin < 2.5 g/dl, and serum cholesterol > 250 gm/dl) and remained nephrotic for 28-109 days after CBA injections were stopped. The other 2 dogs were less substantially proteinuric even though daily injections of CBA were continued until day 57. All of the dogs maintained urine concentrating ability, and their serum concentration of urea, creatinine, and phosphorus remained within normal limits throughout the study.
49 Nephrotoxicity of Easter Lily (Lilium Longiflorum) When Ingested by the Cat. Jeffrey O. Hall, National Animal Poison Control Center (NAPCC), Urbana, Illinois.

Through the review of the National Animal Poison Control Center data for the years 1989 and 1990, a clinical syndrome of Easter lily associated renal failure in cats was first recognized. Ingestion of leaves and/or flowers resulted in the acute onset of gastrointestinal upset, depression and anorexia. Furthermore, these cats were found to have developed renal failure between 48 and 96 hours post exposure. In 1990, 100% of the NAPCC cases (5) of Easter lily ingestion by cats resulted in renal failure and death within 5 days post ingestion.

The syndrome of Easter lily associated renal damage was reproduced in an experimental cat, but attempts to produce toxicity in rats and rabbits were unsuccessful. The experimental cat developed vomiting within 1 hour and became progressively more depressed over the next 12 hours. At 12 hours post administration, the cat was polyuric and about 5% dehydrated. Urine obtained at 12 hours post exposure had numerous tubular epithelial casts, protein, and glucosuria, indicating severe renal tubular damage.

NAPCC case follow-ups during 1991, allowed development of clinical treatment guidelines. Four cases decontaminated prior to 6 hours post ingestion via emesis, activated charcoal, saline cathartic, and fluid diuresis, had no indication of renal failure. However, all four cases recognized more than 18 hours post exposure developed renal failure and died.

51 Feline Leukemia Virus Detection in Paraffin-Embedded, Formalin-Fixed Tissues by Polymerase Chain Reaction and Immunohistochemistry. M.L. Jackson, D.M. Haines, S.M. Meric, V. Misra. Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Saskatchewan.

The prevalence of both detectable Feline Leukemia Virus (FeLV) p27 antigen and proviral genomic DNA was assessed in tumor tissues from 56 cats with lymphosarcoma diagnosed by histopathology. Formalin-fixed, paraffin-embedded, protease-digested tissue sections were tested for immunohistochemical (IHC) detection of FeLV p27 antigen using polyclonal goat antisera and the avidin-biotin-peroxidase complex (ABC) technique. DNA was extracted and purified from corresponding tissue sections for amplification of a 165 base pair region of the FeLV long terminal repeat (LTR) using the polymerase chain reaction (PCR).

In total, PCR results were positive for 40 of the 56 cases; IHC results were positive for 30 of the 56 cases. IHC was positive in 1 case that was negative by PCR. PCR was positive in 11 cases that were negative by ICH. FeLV ELISA results were available for 22 of the 56 cats. PCR and IHC results were positive for 13 of the 14 ELISA positive cases. PCR results were negative for all 8 ELISA negative cats. PCR results were positive in 4 of the 8 ELISA negative cats. The results indicate that IHC and PCR are useful means of detecting FeLV antigen in formalin-fixed tissues, and IHC and ELISA results correspond favorably. FeLV DNA can be demonstrated by PCR in additional cases without detectable viral antigen. These PCR positive, antigen negative cases may represent infection with non-replicating or defective virus.

50 Verapamil and Quinine as Modifiers of Drug Resistance in Canine Lymphoma. M.K. Klein and W.S. Dalton. Arizona Cancer Center, University of Arizona, Tucson, AZ.

Drug resistance remains the primary cause of death in canine and human lymphoma patients. Resistance reversal agents, verapamil and quinine, were added to the treatment regimen of spontaneously occurring canine lymphoma patients. Impact on disease free interval, survival data, and morbidity were assessed.

Twenty-two canine lymphoma cases received doxorubicin and vincristine as a six-hour infusion. Those animals that did not demonstrate a complete response had verapamil and quinine added to their treatment regimen. Those animals that did demonstrate a complete response were randomized into two groups: one receiving verapamil and quinine in conjunction with the four subsequent treatments and one control group receiving chemotherapy alone. All dogs received verapamil and quinine at the time of relapse.

The addition of verapamil and quinine to the initial treatment regimen significantly increased morbidity and mortality without increasing the duration of remission. When added to the reinduction regimen, verapamil and quinine may increase the duration of the second remission. Two of eight dogs that did not achieve a complete response initially, were able to do so following the addition of verapamil and quinine.

52 An Epidemiological Evaluation of 1202 Dogs with Testicular Neoplasia. M.A. Vonderhaar, R.F. Teclaw. Purdue University Comparative Oncology Program.

The purpose of this investigation was to determine if the incidence of canine testicular neoplasia differed between the general or referral veterinary practice and whether breed relative risk estimate rankings have changed concurrently with the change in breed popularity. Dogs with testicular tumors were abstracted from the Purdue Comparative Oncology Program Tumor Registry (449 dogs, 52 breeds) and the Veterinary Medical Data Program (753 dogs, 63 breeds). Hospital location, tumor type, age, breed, and weight were compared using appropriate statistical methods and relative risk estimates calculated. Data was further compared to registry records obtained from the American Kennel Club to determine the relationship between breed relative risk estimate rankings and popularity.

Hospital location was not significant (p > 0.05). Dogs were not likely to develop one tumor type over any other tumor type. The overall incidence of testicular tumor was 0.91%. Significant epidemiological features included age (10-15yr), weight (20-30kg), and breed relative risk (p < 0.05). Relative risk estimate ranks have changed compared to those calculated 15 and 40 years ago and are associated with the changing patterns of breed popularity.
A novel model of hepatic metastasis has been developed in severe combined immunodeficiency (SCID) mice. The PEF/PLC/5 human hepatocellular carcinoma cell line contains an integrated hepatitis B surface antigen gene and secretes hepatitis B surface antigen (HBsAg) in proportion to cell growth. The cell line also lacks the asialoglycoprotein receptor found on normal hepatocytes. A multiple drug resistant clone of this cell line was developed by selection in doxorubicin. This clone retains the properties of the parent cell line and also overexpresses Gp 170, the plasma membrane protein which functions as an ATP driven drug efflux pump in multiple drug resistant cell lines. Cell suspensions, 1-5 X106, were injected intrasplenic into SCID mice and spleen tumor volume was monitored with nuclear magnetic imaging. The agent binds to normal mouse hepatocytes and significantly decreases signal intensity. The tumor cells travel via the portal circulation and engraft in the liver. In preliminary studies, 11/17 and 2/10 mice injected with the parental and drug resistant clone respectively developed tumors. Tumors were detected by monitoring mouse serum for the presence of HBsAg by conventional radioimmunoassay. HBsAg titers correlated with tumor volume as monitored with nuclear magnetic imaging. A novel contrast agent, an arabinogalactan stabilized ultrasmall superparamagnetic iron oxide, which targets the asialoglycoprotein receptor was used. This agent binds to normal mouse hepatocytes and significantly decreases signal intensity. The tumor cells lack the receptor and do not bind the contrast agent. The net result is enhanced tumor/liver contrast.

The selective use of chemotherapeutic agents may be used to modulate immunotherapy approaches. Doxorubicin is a potent antitumor agent and has been shown to have very significant effects on augmenting monocyte-mediated cytotoxicity and natural killer cell activity in humans and mice. Liposome-muramyl tripeptide (L-MTP) has been shown to activate monocytes/macrophages in vivo to become tumoricidal and has been used to prevent the development of metastasis in canine osteosarcoma. The purpose of our study was to determine the effect of doxorubicin on monocyte activity in vitro and in vivo and to use these data to enhance the treatment of advanced facial tumors in cats.
57 ANTIBODIES BOUND TO THE SURFACE OF PLATELETS FROM DOGS WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA ARE ANTI-PLATELET AUTOANTIBODIES. D.C. Lewis, K.M. Meyers, N. Menard, L.E. Perryman. College of Veterinary Medicine, Washington State University, Pullman, WA.

Canine idiopathic thrombocytopenic purpura (ITP) is frequently assumed to be an autoimmune disease. The purpose of this study was to determine whether antibodies bound to the surface of platelets (platelet-bound antibodies) from dogs with ITP are autoantibodies.

A diagnosis of ITP was based on presence of thrombocytopenia, normal to increased numbers of bone marrow megakaryocytes, exclusion of other causes of thrombocytopenia, and platelet count increase in response to corticosteroid therapy. Five dogs with ITP have been studied to date. A solid phase ELISA to detect platelet-bound antibodies was performed on platelets from dogs with ITP. Reference range (mean +/- 2 standard deviations) for platelet-bound antibodies, from 20 normal dogs, was 0.000-0.082. All five dogs with ITP had increased concentrations of platelet-bound antibodies (mean: 0.876; range: 0.432-1.776). Platelet-bound antibodies were eluted by acidification of a platelet suspension containing 10^8 total platelets. Eluates were tested (by ELISA) for the ability of eluted antibodies to bind to pooled homologous normal platelets. The reference range (mean +/- 2 standard deviations) for elute re-binding, from 10 normal dogs, was 0.000 to 0.053. Antibodies in platelet eluates from four of the five dogs with ITP demonstrated re-binding to homologous normal platelets (mean 0.286; range 0.115-0.450).

This indicates that antibodies bound to the surface of platelets from dogs with ITP are anti-platelet autoantibodies. This supports the hypothesis that canine ITP is an autoimmune disease.

58 EFFICACY OF AN ULTRA-PURIFIED, POLYMERIZED HEMOGLOBIN BASED OXYGEN CARRYING SOLUTION. V.T. Rentko, J.E. Harris, C. Beaminini, M.S. Gawryl, C.W. Rausch. Biopure Corporation, Boston, MA.

The efficacy of an ultra-pure, polymerized bovine hemoglobin based oxygen carrying solution was investigated in a canine normovolemic anemic model. The efficacy in transporting oxygen and carbon dioxide was analyzed. Twenty eight beagle dogs in dosing groups of 1/2 X, 1 X, and 2 X and a colloid control group were anesthetized and instrumented for hemodynamic monitoring and blood gas and oxygen content determinations. Initially, blood was withdrawn and replaced with lactated Ringer's solution to reduce the hemoglobin concentration to approximately 3.0 g/dl. Following baseline measurements of cardiac output, pulmonary capillary wedge pressure, arterial blood gas and oxygen content analyses, the hemoglobin solution was infused. Measurements were repeated immediately and 60 minutes following dosing. The dogs were anesthetized and reinstrumented for final measurements at 24 hours post dose.

Preliminary data demonstrate an increase in oxygen delivery over pre-dose values in a dose related manner. Arterial and venous oxygen contents increase over pre-dose measurements. Venous oxygen saturation decreases with the induction of anemia and increases in a dose dependent manner following treatment. Cardiac output increases during induction of anemia and approaches baseline at 24 hours post treatment. The efficacy of an ultra-purified, polymerized hemoglobin solution was demonstrated by an increase in oxygen delivery, arterial oxygen content and venous oxygen saturation compared to measurements following induction of anemia.

59 EFFECTS OF LOW-DOSE ASPIRIN AND THROMBOXANE SYNTHETASE INHIBITION ON PLATELET FUNCTION IN DOGS. G.E. Gray, B.J. Rose, L.A. Toolan, M. Trinh, and S.P. Colgan. College of Veterinary Medicine, Colorado State University, Fort Collins, CO.

Previously, we assessed the effects of treatment with 3-methyl-2 (3-pyridyl)-1-indenonic acid (CQS 12970), a specific thromboxane synthetase inhibitor, in dogs with glomerulonephritis. The purpose of the present study was to compare the effects of low-dose aspirin (3.5 mg/kg PO, q 12h) with CQS 12970 (10 mg/kg PO, q 8h) on platelet aggregation and ATP secretion in blood from healthy, adult female beagle dogs. Platelet aggregation was assessed in whole blood by electrical impedance. The addition of arachidonic acid to whole blood suggested a glycolytic block at the PK step. Occasional, was severely decreased (1.4-2.4 IU/gib) to less than 15% of controls (16-34 IU/gib). Other glycolytic enzymes were normal to increased compared to controls. The residual PK activity showed similar substrate affinity and mobility on cellulose acetate electrophoresis. There was no evidence of persistent H+-coupled PK expression in the presence of PK deficient dogs. The proband's queen was found to have half-normal erythrocyte PK activity, supporting an autonal recessive inheritance pattern. We conclude inherited erythrocyte PK deficiency in an Abyssinian cat caused a severe hemolytic anemia that appeared partially responsive to splenectomy. PK deficiency should be considered in the differential diagnosis of a young cats with hemolytic anemia.

60 INHERITED ERYTHROCYTE PYRUVATE KINASE (PK) DEFICIENCY CAUSING HEMOLYTIC ANEMIA IN AN ABBYSINIAN CAT. E.C. Duesberg, E. Beutler, and P. Wang. University of California, Davis, CA; University of Pennsylvania, Philadelphia, PA; Scripps Clinic and Research Foundation, La Jolla, CA.

Inherited erythrocyte PK deficiency has been described in humans and several breeds of dogs. We document here the PK deficiency based on clinicopathologic, biochemical, and family studies. A one-year-old male Abyssinian cat with mild exercise intolerance and splenomegaly had a severe and highly regenerative anemia that was Coombs negative. Although there was marked erythroid hyperplasia, there was no evidence of osteosclerosis. At 1/2 years of age, splenectomy was performed which increased the PCV from 10-37% (mean 23%) to 23-32% (26%) and decreased the reticulocyte count fro 10-35% (11%) to 3-7% (5%). For the last 5 months the cat has been transfusion independent. Analysis of metabolic intermediates in blood suggested a glycolytic block at the PK step. Erythrocyte PK activity of this cat, measured on three occasions, was severely decreased (1.4-2.4 IU/gib) to less than 15% of controls (16-34 IU/gib). Other glycolytic enzymes were normal to increased compared to controls. The residual PK activity showed similar substrate affinity and mobility on cellulose acetate electrophoresis. There was no evidence of persistent H+-coupled PK expression in the presence of PK deficient dogs. The proband's queen was found to have half-normal erythrocyte PK activity, supporting an autonal recessive inheritance pattern. We conclude inherited erythrocyte PK deficiency in an Abyssinian cat caused a severe hemolytic anemia that appeared partially responsive to splenectomy. PK deficiency should be considered in the differential diagnosis of a young cats with hemolytic anemia.
61 IMMUNE-MEDIATED HEMOLYTIC ANEMIA IN THE DOG: A RETROSPECTIVE STUDY OF 42 CASES. E. Klug, U. Giger, F.S. Schofer. School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Clinical parameters of 42 cases of canine immune-mediated hemolytic anemia (IMHA) were studied retrospectively. Criteria for inclusion were a positive Coombs' test or persistent autoagglutination, anemia, and clinical evidence of hemolysis. Dogs with identifiable underlying disease were excluded. Data evaluated in all dogs included signalment, vaccination history, clinical signs, Coombs' test results, month of diagnosis, PCV and corrected reticulocyte count on presentation, maximum serum bilirubin levels, numbers of blood transfusions received, presence of concurrent disease, and outcome of hospitalization for IMHA. All blood samples were evaluated for the presence of spherocytosis and microscopic autoagglutination. Dogs ranged in age from 1-13 years with a mean age of 6.4 years ± 3.4 years. The majority of dogs (74%) tested with IgG, IgM and C, antisera were positive for IgG antibodies without the presence of complement. A marked seasonal incidence (p < 0.0001) was observed, with 40% of all cases seen during the months of May and June. Sixteen dogs (38%) presented with moderate to severe reticulocytosis, 12 dogs (29%) presented with mild reticulocytosis, and 14 dogs (33%) presented without reticulocytosis. Observed mortality during hospitalization was 29%. Risk of death was significantly increased in dogs presenting with present levels of greater serum bilirubin (p = 0.004) and lower PCVs (p = 0.01), and in dogs with maximum serum bilirubin levels of greater than 10 mg/dl (p = 0.03). It was concluded that reticulocytosis should not be used to rule out a diagnosis of IMHA on presentation; the majority of dogs with Coombs' positive IMHA are IgG positive with or without complement; and that degree of reticulocytosis, PCV, and serum bilirubin levels are useful prognostic indicators for dogs with IMHA.

63 TREATMENT OF NASAL ASPERGILLOSIS WITH TOPICAL CLOTRIMAZOLE. A. Davidson, J. Komtebedde, D. Papagianis and R.F. Hector. School of Veterinary Medicine and School of Medicine, University of California, Davis, Ca 95616

Topical clotrimazole therapy was evaluated in 21 dogs with nasal aspergillosis. The diagnoses were based on history, clinical signs, rhinoscopic and radiographic findings, as well as histopathology, serology, and culture results. Thirteen dogs had previously undergone other systemic or topical antifungal therapy unsuccessfully. One dog was previously treated surgically unsuccessfully. Therapy consisted of bilateral infusion of 1 g clotrimazole, suspended in 100 ml polyethylene glycol, into the frontal sinuses and nasal passages. Clotrimazole was infused through infant feeding tubes placed into the frontal sinuses by the patient. We were unable to culture E. canis organisms in non-inoculated control cell cultures. We conclude that Ehrlichia canis antigen titers have remained ≥ 2,560 during the 21 months followup period.

In July, 1989, canine ehrlichiosis was diagnosed in an 8-year-old mixed breed dog on the basis of a compatible clinical history, anemia and thrombocytopenia, and a positive antibody titer (5,120) to Ehrlichia canis antigen. Although clinical improvement was noted after appropriate antirickettsial drug therapy, the dog has remained thrombocytopenic (platelet counts generally less than 10,000/ul) and E. canis antibody titers have remained ≥ 2,560 during the 21 month followup period.

In October, 1989, May and September, 1990 and February, 1991, clinical, hemotologic, and immunologic tests, and tissue culture inoculation studies were performed in an attempt to better characterize the disease syndrome. Additionally, in February, 1991, we transfused a healthy canine recipient with 25 ml of blood from the patient. We were unable to culture E. canis organisms in monocyte cultures or DH-82 cell cultures, polymerase chain reaction analysis of stored EDTA blood from the patient and recipient failed to detect E. canis DNA, and the recipient dog, despite becoming thrombocytopenic, has not seroconverted to E. canis antigen.

We have detected an increase in manganese-dependent reverse transcriptase activity in both recipient plasma and patient plasma and bone marrow inoculated DH-82 cell culture supernatants, compared to non-inoculated control cell cultures. We conclude that Ehrlichia canis is not contributing to the thrombocytopenia in these dogs, and that we have cultured a novel manganese-dependent, reverse transcriptase producing infectious agent.
DEMONSTRATION OF TOXOPLASMA GONDII-ANTIGEN CONTAINING IMMUNE COMPLEXES IN THE SERUM OF CATS. M.R. Lappin, S. Cayatte, C.C. Powell, A. Gigliotti, C. Cooper, and S.M. Roberts. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

The purpose of the study described herein was to develop ELISA for the detection of Toxoplasma gondii-antigen containing IgM immune complexes (IgM-IC) and IgG immune complexes (IgG-IC) in serum from cats with naturally occurring toxoplasmosis.

Serum samples were assayed for T. gondii-specific IgM, T. gondii-specific IgG, T. gondii-specific antigens (AG), T. gondii-specific IgM-IC, T. gondii-specific IgG-IC, and antibodies against FIV. Serum samples positive for T. gondii-specific IgM, IgG or both were available from naturally infected cats: with clinical evidence of intraocular inflammation (n = 64); with clinical signs of toxoplasmosis other than ocular (n = 48); naturally infected with FIV (n = 30); and that were healthy (n = 40). Serum samples were also available from some clinically ill cats positive for T. gondii-specific AG without (n = 18) concurrent presence of T. gondii-specific IgM and IgG.

Cats with ocular disease (X^2 = 4.7587; P < 0.05), FIV-seropositive cats (X^2 = 36.9063; P < 0.0005), and the combination of all clinically ill cats (X^2 = 8.6668; P < 0.005) were more likely to have T. gondii-specific IC in serum than healthy cats. Some cats had T. gondii-specific IC in serum but were negative in the serum for the respective antibody. Of the FIV-seropositive cats with T. gondii-specific IgG-IC in serum, 55.6% (15/27) were seronegative for T. gondii-specific IgG. Toxoplasma gondii-specific IgM-IC were detected only in clinically ill cats. Of the cats that were seropositive for T. gondii-specific AG without antibodies, 66.7% (12/18) were seropositive for T. gondii-specific IC.

It was concluded that T. gondii-specific IC form in the serum of cats, may play a role in clinical disease development, and effect the results of T. gondii-specific IgM, IgG, and AG serologic assays.

EVIDENCE FOR PERINATAL TRANSMISSION OF FELINE IMMUNODEFICIENCY VIRUS. Rance K. Sellon, Suzanne Kennedy-Stoskopf, Terri Wasmoen, Wayne Tompkins. North Carolina State University College of Veterinary Medicine and Ft. Dodge Laboratories, Ames, Iowa.

Perinatal transmission of feline immunodeficiency virus (FIV) has not been considered an important route of infection to date. Kittens born to queens with active NCSU - FIV infections were evaluated for FIV by polymerase chain reaction (PCR) of peripheral blood mononuclear cell DNA, flow cytometric analysis of peripheral blood lymphocyte subsets, and measurement of FIV antibodies by ELISA. A feline lymphocyte cell line (CD4E) were inoculated with milk from one queen and assessed for reverse transcriptase (RT) activity. Mammary gland (MG) and placental explants from infected queens were examined by PCR and in situ hybridization (ISH). CD4E cells were cocultivated with explanted MG, inoculated with MG and placental explant supernatants, then examined by PCR, RT activity and ISH.

Two of three kittens born to a queen infected 19 days prior to parturition were positive for FIV by PCR and ELISA antibody on day 72 postpartum. Both kittens subsequently developed inverted CD4/CD8 ratios. One of four kittens born to a queen infected 4 days prior to delivery was positive by PCR and ELISA on day 49 postpartum, and developed inverted CD4/CD8 ratios. CD4E cells inoculated with milk from the first queen developed FIV RT activity. MG explants were positive for FIV by PCR and cocultivation by PCR, ISH, and RT activity. CD4E cells inoculated with media from placental explants were positive for FIV by PCR, ISH and RT activity.

Though the route of transmission is undetermined, these findings suggest that perinatal transmission of FIV may occur and implicate milk and placenta as potential routes of perinatal transmission.

THE USE OF LIPOSOMAL AMPHOTHERICIN B IN MYCOTIC AND ALGAL DISEASES IN THE DOG. J.W. Olsen University of California, Davis.

The efficacy and therapeutic index of a liposomal formulation of Amphothericin B was evaluated in the treatment of clinical mycotic and algal disease in the dog.

Four dogs with clinical mycotic disease (three with coccidiomycosis, one with histoplasmosis) and one dog with protothecosis were treated with a total cumulative dose of Amphothericin B ranging from 10 to 15 mg/kg. This Amphothericin B was encapsulated into liposomes made up of a 9:1 ratio of phosphatidyl choline and phosphatidyl glycerol and created with a custom designed sonifier. The liposomal Amphothericin B was administered intravenously as a slow push three times weekly for three to five weeks. Each administration was preceded and followed by a four hour diuresis with isotonic saline. Treatment was continued until complete remission (based on physical exam, serology, blood counts and chemistries, or biopsy) or a total dose of 10 to 15 mg/kg Amphothericin B with azotemia present.

Complete remission was achieved in all five dogs. Follow-up for 6 to 22 months revealed no persistent azotemia and maintenance of clinical remission.

Liposomal formulation of Amphothericin B appears to allow administration of larger cumulative doses without apparent toxicity. This may improve the clinical response in difficult cases or poorly responsive diseases such as protothecosis.

HEPATOCELLULAR CYTOPROTECTION AGAINST THE HEPATOTOXIC EFFECTS OF THIACETARSAMIDE USING DEXTROSE AND N-ACETYL-L-Cysteine in the Dog. H.E. McKern, P.-T. Daoust, P. Hanna, A. Singh, M. Novotny, E.P. Harsham. Atlantic Veterinary College, Charlottetown, Prince Edward Island.

Pretreatment effects with N-acetyl-L-cysteine (NAC) and dextrose (D) upon hepatocellular toxicity of thiacetarsamide (T) in dogs was investigated. Normal dogs were randomly assigned to 3 groups. Percutaneous-transabdominal hepatic needle biopsies and blood samples for CBC and ALT were obtained from each dog prior to any treatments. Pretreatments were given 5 minutes before each injection of T. Group I was pretreated with .7 ml/kg of .9% NaCl IV (n=9). Group II was pretreated with 10 ml/kg of 10% D IV (n=6). Group III was pretreated with .3 ml/kg of 20% NAC IV (n=9). T was then given at 3.3 mg/kg IV BID for 2 days to all groups. Blood tests were repeated each day during and for 2 days after the treatments. Another hepatic biopsy sample was obtained from each dog 24 hours after the last treatment. All dogs survived the experiment. Hepatic biopsy samples were coded and scored by one person (MKH). Data was evaluated using oneway ANOVA and Newman-Keuls Tests. Rank correlation was used for biopsy scores versus ALT.

T induced variable hepatic pathology within groups. Mean differences of ALT and biopsy results between groups were consistent with a worsened effect of dextrose (p < .05). A significant cytoprotective effect of NAC was seen with biopsy scores (p < .01) and ALT values (p < .05). No correlation existed between biopsy scores and ALT levels for individuals. Dextrose increased the hepatic cytopathology of T. N-acetyl-L-cysteine was a significant hepatocellular cytoprotectant against the effects of T.
69 CYTOPROTECTION OF NCTC 1469 MOUSE HEPATOCYTE CELLS AGAINST THE TOXIC EFFECTS OF THIACTERASIDE USING N-ACETYL-L-CYSTEINE. M.E. Hill, R.J.F. Markham, M. Novotny, P.Y. Daoust. Atlantic Veterinary College, Charlottetown, P.E.I.

This project investigated N-acetylcysteine (NAC) for its effect on thiacteraside T-induced cytotoxicity in vitro using NCTC 1469 (murine transformed hepatoma) cells. Experiments were performed on confluent cell cultures still in log phase. Viabilities were evaluated by dye exclusion with 0.2% Trypan blue. Initial concentrations were determined using estimated extracellular fluid concentrations (EFC) as based upon canine IV dosages of 3.3 mg/kg of T and 140 mg/kg of NAC. The EFCs were used as the 1X media concentrations for T and NAC. A sigmoid lethality concentration curve (LC) was established for T using varying times of exposure with T present (5-1440 minutes), incubation following exposure (T removed) (4-48 hours), and varying concentrations of T (0.1, 0.3, 1, 3, 10 30X). An LC50 was found at the 1X-3X of T with 4 hours exposure and 24 hours incubation. NAC was evaluated for cellular effects at the same exposure and incubation time and concentrations. NAC had no effect on cell cultures at 3X or lower but was consistently toxic at 30X. Bonferroni T-tests and probit analysis were used in subsequent analysis of data. A series of 3 experiments were performed with simultaneous use of (0.1, 0.3, 1, 3, 10 30X) of NAC and T. Exposure to T was 4 hours. NAC was in the media during the exposure to T (4 hr) in the first, during the incubation (24hr) in the second, and during both (28 hr) in the third. Marked cytoprotection with NAC was seen as a shift of LC curves to the right at the [1 to 10X]. There was no difference from the control well (no T) at [3 or 10X] of NAC (p < .01). In this in vitro model NAC was a marked cytoprotectant against the effects of T.

70 COMPARISON OF INDOLYLANE GREEN, CAFFEINE AND ANTIPYRINE DISPOSITION KINETICS IN DOGS WITH EXPERIMENTALLY-INDUCED PROGRESSIVE LIVER DISEASE. Boothe DM, Calvin JA, Jenkins WL et al. Texas A & M University, College Station, TX 77843.

The purpose of this study was to compare the ability of 3 drugs eliminated by the liver to discriminate among different stages (severities) of dimethylnitosamine (DMNA)-induced hepatic disease. Two capacity-limited drugs, antipyrine (AP) and caffeine (CAFF), and one flow-limited drug, indocyanine green (ICG) were studied in 22 Beagles. DMNA was administered orally in 18 of the dogs for up to 56 weeks while 6 dogs served as non-diseased controls (G1). Three stages of liver disease were defined by histologic features: mild (G2; n=5), moderate (G3; n=6), and severe (G4; n=5). The disposition of each drug was studied following a single IV dose 3 weeks after DMNA was discontinued in each dog. ICG (0.5 mg/kg) was studied first, followed by AP (10 mg/kg) 24 hrs later and CAFF (10 mg/kg) 24 hrs later. Serum ICG was measured within 24 hrs using spectrophotometry and serum AP and CAFF were analyzed using high performance liquid chromatography. Data from each drug was subjected to a standard pharmacokinetic analysis from which was determined mean residence time (MRT) and clearance (CL) for each dog. Analysis of variance and Duncan's multiple range testing were used to identify significant differences among groups for the MRT and CL of each drug. To compare differences in the effects of each stage of disease on the elimination of each drug, AP-CAFF, ICG-CAFF and ICG-AP ratios and log ratios of MRT and CL were determined for each dog and compared among groups. For all 3 drugs, MRT and CL differed among groups (Pc = 0.004) with CL being slowest and MRT highest in G3 and G4 compared to G1 and G2. G3 CL was 24 %, 41% and 20% of G1 for AP, CAFF and ICG respectively. Ratios and logratios of CL and MRT did not significantly differ among groups for any drug. The results suggest that in this model of experimentally-induced hepatic disease, elimination of each drug changed in a similar manner as disease progressed and each drug was equally effective in discriminating moderate and severely diseased animals from mildly diseased and non-diseased dogs. This suggests that either ICG behaved as a capacity-limited drug or decreased elimination of capacity-limited drugs paralleled decreased elimination of flow-limited drugs as disease progressed.

71 IRON STATUS IN 12 DOGS WITH CONGENITAL PORTOSYSTEMIC SHUNTS. S.E. Bunch, HL Jordan, RK Selkon, JE Smith, SEB, HU, RKS, Kansas State University (JES).

Microcytosis is a common hematologic finding in dogs with congenital portosystemic shunts (PSS). Iron (Fe) deficiency or abnormal incorporation of Fe into the heme molecule associated with inflammatory disease is most often the cause of microcytosis with normo- or hypochromia in dogs. Despite the frequency of microcytosis in dogs with congenital PSS, there is no information regarding its pathogenesis.

Twelve dogs with confirmed congenital PSS were evaluated prospectively for Fe status before surgical correction. Two dogs were littermates; one was examined at the University of Florida. In addition to standard laboratory analysis, serum Fe, total Fe-binding capacity and ferritin, and erythrocyte (RC) protoporphyrin were measured in all dogs. Bone marrow analysis for stainable Fe and RBC morphology was possible in 8 of 12 dogs.

Ten breeds of dogs were represented, ranging in age from 4-22 mos (median 6 mo). There were 3 males and 9 females. Ten of 12 dogs had MCV ≤ 600, 11 of 12 had marginally low MCHC (32.7-33.7 g/dl), and 10 of 12 had increased RDW (11.2-19.2%). Though serum Fe (mean ± SEM) was low (64.58 ± 10.84 µg/dl, range 18-142), total Fe-binding capacity (215.33 ± 13.12 µg/dl, range 117-283), ferritin (569.17 ± 130.88 ng/ml, range 105-1825), and RBC protoporphyrin (22.25 ± 2.83 µg/dl, range 9-40) values were not suggestive of Fe deficiency. Bone marrow RBC morphology was normal in examined dogs, and stainable Fe ranged from none detectable (5 dogs) to normal (1 dog) to normal to increased (2 dogs).

The results of this study suggest that a mechanism other than Fe deficiency is responsible for disordered hemoglobin synthesis and microcytosis in dogs with congenital PSS.

72 CONGENITAL PORTOSYSTEMIC VASCULAR SHUNTS IN CATS. JK Levy, SE Bunch, College of Veterinary Medicine, North Carolina State University, Raleigh, NC.

A retrospective study using the Veterinary Medical Data Program was undertaken to characterize congenital portosystemic vascular shunts in cats. Congenital shunts were confirmed in 52 cats at 17 veterinary institutions from 1982-1991. There were slightly more males (56%) than females (44%). Mixed breed cats accounted for 73% of the cases, and 2 related breeds (Persians and Himalayans) comprised another 23% of the cases. Clinical signs attributed to hepatic encephalopathy were reported by the owners by 6 months of age in 80% of cats, although diagnosis of the disorder was often delayed. Heart murmurs were ausculted in 13% of cats, and 24% of the males were cryptorchid. The most common clinical signs were salivation (85%), stunted growth (83%), seizures (67%), ataxia (60%), vision deficits (54%), tremors or twitching (48%), and mydriasis (38%).

Microcytosis was present in 36% of cats tested. High ALT and ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively). Urine specific gravity was below 1.024 cases, ALP activity and low BUN and creatinine concentrations were the most common biochemical changes (in 39%, 38%, 45%, and 35% of cats tested respectively).
EVALUATION OF FASTING AND POSTPRANDIAL BILE ACIDS AS A DIAGNOSTIC AID IN DETECTING FELINE HEPATIC DISEASE.

C.L. Gartrell, CA Johnson, KR Refsal, RF Nachreiner, TP Mulaney. College of Veterinary Medicine, Michigan State University, East Lansing MI.

To answer the question of whether postprandial bile acids yield more useful diagnostic information than do fasting bile acids alone, we prospectively evaluated clinical findings, clinical laboratory data, fasting bile acids, postprandial bile acids, and hepatic cytology/histopathology in 50 sick cats. Group 1 had primary hepatic disease (n=18). Group 2 had non-hepatic disease as the primary illness (n=32). Sensitivities, specificities, positive predictive values, and negative predictive values were calculated. Mean fasting bile acids were significantly higher than postprandial bile acids (118.6 ± 29.0 μmol/L vs 24.6 ± 11.3 μmol/L). The sensitivities of fasting and postprandial bile acids were 94% and 100%, respectively; however, the specificities of fasting and postprandial bile acids were 41% and 59%, respectively. The positive predictive values of fasting and postprandial values were 47% and 50%, respectively. The negative predictive values of fasting and postprandial were 93% and 100%, respectively. These results indicate that when either fasting or postprandial bile acids are normal, hepatic disease is rarely present. Whereas, when either fasting bile acids or postprandial bile acids are abnormal, cats may have non-hepatic disease as a primary illness.

LIPID COMPOSITION OF LIVER AND ADIPOSE TISSUES FROM NORMAL CATS AND CATS WITH HEPATIC LIPIDOSIS. J.R. Hall, L.A. Barstad, B.E. Voller, W.E. Connor. Oregon State Univ, Corvallis, OR and Oregon Health Sciences Univ, Portland, OR.

The purpose of this study was to characterize the lipids in cats with idiopathic hepatic lipidosis. Concentrations of triglyceride, phospholipid phosphorus, and free and total cholesterol were determined in lipid extracts of liver homogenates from cats with hepatic lipidosis (n=5) and healthy cats (n=5). Total fatty acid analyses from liver and adipose tissues were also compared. Lipids were extracted by the method of Folch. The fatty acid compositions, and free and total cholesterol were determined by gas-liquid chromatography. Triglyceride mass was determined with an enzymatic reagent kit (Gilford Diagnostics). Phospholipid phosphorus was measured spectrophotometrically. Triglyceride accounted for 34% of liver by weight in lipidosis cats vs 1% in healthy cats (p<0.001). Phospholipid phosphorus and free and total cholesterol concentrations were similar in both groups. Liver fatty acid compositions of the two groups differed (p<0.05). Palmitate was increased (19.5% in normals vs 9.2% in normals), stearate decreased (8.5% vs 16.8%), oleate increased (41.2% vs 31.1%), and arachidate decreased (1.2% vs 6.0%). Except for linolenate, 0.2% in normals vs 0.7% in normals, p<0.05), the fatty acid compositions of adipose were similar between the 2 groups. In the abnormal cats, the fatty acid composition of liver and adipose were similar. These results reflect the fact that triglyceride in the abnormal livers is very high, and support the hypothesis that the origin of hepatic triglyceride in cats with hepatic lipidosis is the mobilization of fatty acids from adipose.

L-CARNITINE REDUCES HEPATIC FAT ACCUMULATION DURING RAPID WEIGHT REDUCTION IN CATS. P.J. Armstrong, E.M. Hardie, J.M. Cullen, B.W. Keene, M.S. Hand, C.A. Babineau. University of Minnesota, St. Paul, MN; North Carolina State University, Raleigh, NC; and Mark Morris Associates, Topeka, KS.

The objective of this study was to determine whether dietary L-carnitine supplementation of commercial cat foods would protect cats from hepatic lipid accumulation during food restriction. After evaluation at their baseline weights (Period 1), 18 adult domestic cats were divided into 2 equal groups and group housed for 7 months (Period 2). The diet fed to all cats during Period 1 (5 weeks) and to Control cats during Period 2 contained 144 nM total L-carnitine/gram of product as fed. Carnitine cats received an identical diet during Period 2 (4.7 kcal/g, 34% protein, 26% fat, 33.7% carbohydrate, 1.8% fiber on a dry matter basis), except that it contained 3669 nM L-carnitine/gram. The groups were pair-fed, based on ad lib intake of Control cats. Weight reduction was achieved during Period 3 by imposing a 72 hour fast followed by restricting energy intake for each cat to 25% of maintenance at its Period 1 weight. During Period 3, cats were fed a diet providing 3.2 kcal/g, 38% protein, 8.2% fat, 30.1% carbohydrate, and 18.5% fiber on a dry matter basis. Total L-carnitine content of the diet for Control cats was 172 nM/g vs 84.26 nM/g for Carnitine cats. An evaluator blinded to group and period scored the lipid content of liver biopsies obtained on all cats at the end of each period.

Mean weight gains during Period 2 (expressed as % above baseline weights) were: Control cats 42.2±26.6 (SD). Carnitine cats 50.4±17.7. During Period 3, the mean time required for all cats to reach baseline weights was 70 days, range 16-129. At Period 1, mean hepatic lipid scores were higher in Carnitine cats than in Control cats (p<0.05). Control cats, however, had significant gains in hepatic lipid scores between Periods 1 and 3, whereas Carnitine cats did not (p<0.05). These results suggest that abundant dietary carnitine may protect cats from hepatic lipid accumulation during experimental induction of hepatic lipidosis.
77 PORTAL GLUCOSE DELIVERY FAILS TO ALTER THE COUNTERREGULATORY RESPONSE TO HYPOGLYCEMIA. L.C. Holste, C.C. Connolly, D.W. Neal, A.D. Cherrington. VANDERBILT UNIVERSITY, NASHVILLE, TN.

A negative arterial-portal (A-P) glucose gradient resulting from portal glucose infusion has been shown to be a potent stimulus for hepatic glucose uptake during simulated feeding. In contrast, the hormonal responses to hypoglycemia stimulate the liver to produce glucose. To examine the interaction of these signals, paired studies were performed in 5 conscious, 18h-fasted dogs receiving either intraportal glucose (3.0 mg/kg*min, Po) or saline (Pe) during insulin-induced (5mU/kg*min; arterial conc. 307 ± 28 μU/ml) hypoglycemia. Glucose concentrations fell to 50 mg/dl during the first hour of insulin infusion and were then clamped at that level with a peripheral glucose infusion to 50 mg/dl during the first hour of insulin infusion and were saline (Pe) during insulin-induced (5mU/kg*min; arterial conc. 307 ± 28 μU/ml) hypoglycemia. Glucose concentrations fell to 50 mg/dl during the first hour of insulin infusion and were then clamped at that level with a peripheral glucose infusion (1.0 ± 0.7 mg/kg*min, Po; 4.0 ± 1 mg/kg*min, Pe) for 2h.

Hepatic glucose metabolism was assessed using tracer (2-3H-glucose) techniques. Tracer-determined hepatic glucose production (2.6±0.3 and 2.8±0.4 mg/kg*min), utilization (6.7±0.7 and 7.0±0.7 mg/kg*min), and clearance (13.3±1.7 and 13.8±1.5 ml/kg*min) during the last 2h of hypoglycemia were not different between Po and Pe, respectively. Glucoregemonic, lipolytic, and ketogenic parameters also did not differ between the two groups. In summary, despite the presence of portal glucose delivery, the metabolic responses to hypoglycemia were essentially unchanged. Thus the hypoglycemic signal pre-empts the signal generated by a negative A-P glucose gradient when both are present simultaneously.

78 DEVELOPMENT OF A MODEL OF FOOD ALLERGY IN THE DOG. W. G. Guilford and J. W. Badcock. Veterinary Faculty, Massey University, New Zealand

The objective of this study was to develop a canine model of food allergy. Twenty, 3 week-old pups, were sensitized to codfish by oral (10 mg sid for 2 days) & parenteral (300 ug IP & 200 ug SQ, 4 times, 7-14 days apart) administration of cod protein. During oral sensitization, the 20 pups were randomly assigned to one of four groups receiving a 2 day pulse of either cyclophosphamide (12.5 mg PO), castor oil (1.5 ml/kg bid PO), cyclophosphamide and castor oil, or no drugs. After sensitization, the pups were challenged orally with 50 g of codfish daily for 8-10 days. Observations included clinical signs, intradermal & prick skin tests, antigen-specific IgE (Biomedical Services), gastroscopic food sensitivity tests (GFSF), and mucosal histology (H&E, LUNO's).

The protocol was well tolerated. Consistent responses to 1/1 histamine were not seen until 50 days of age. All sensitized pups developed positive I/D skin tests within 10 days of the fourth antigen injection. I/D testing was more sensitive than prick testing. Serum levels of antigen-specific IgE increased markedly in all sensitized dogs, peak levels occurring 1 week after the 2nd injection. Oral cod challenge caused transient vomiting and pruritus in 20% & 85% of sensitized pups, respectively. Three of four vomiting pups had a positive GFSF to cod. Mild-moderate diarrhoea developed in the majority of sensitized pups. Preliminary histology revealed no change in the stomach but mild increase in degranulated eosinophils in the duodenum & colon.

In conclusion, the protocol successfully induced food allergy. Few significant between group differences were seen.

79 EFFECTIVENESS OF TEMPERATURE SENSITIVE-FELINE INFECTIOUS PERITONITIS VIRUS VACCINE AGAINST A FELINE ENTERIC CORONAVIRUS. L.D. Hopkins, W.G. Henk, J Storz, and M.T. Kearney, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA.

The effectiveness of commercially available temperature sensitive-feline infectious peritonitis vaccine for preventing feline enteric coronavirus (FECV)-induced disease in specific pathogen-free kittens was examined. One group of seronegative kittens was vaccinated on days 0 and 21 days; a second group of seronegative kittens served as nonvaccinated controls. All kittens were challenged at 14 days post vaccination with 5x10^6 PFU of WSU-1683 strain of FECV and sacrificed 5 days post challenge. All vaccinated kittens developed low anti-coronavirus antibody titers following intranasal vaccination. Vaccinated kittens exhibited milder enteric disease following FECV challenge than did nonvaccinated kittens, but there was no significant difference between these groups based on clinical scores. There was a significant reduction in the amount of FECV isolated from the duodenum, jejunum, and mesenteric lymph nodes of vaccinated kittens. Morphometric analysis of duodenum and jejunum indicated that villus height was less affected in vaccinated kittens than in nonvaccinated kittens. There was significant difference in villus height for the jejunum but not for the duodenum in the vaccinated group. Results of this study indicate that temperature sensitive-feline infectious coronavirus induced humoral responses in all vaccinated kittens but partially protect against FECV-induced enteric disease.

80 THE EFFECT OF SUB-TOTAL NEPHRECTOMY ON CIRCULATING TRYPSIN-LIKE IMMUNOREACTIVITY, AMYLASE, LIPASE AND GASTRIN IN THE DOG. K.W. Simpson, M. Starkey, S. Dibartola, D. Chew, M. McLauglin and D.A. Williams. College of Veterinary Medicine, Ohio State University and Kansas State University.

The kidney appears to have a role in the elimination of the enzymes amylase and lipase, trypsin-like immunoreactivity (TLI) and the peptide hormone gastrin. The present study sought to determine whether mild renal dysfunction could cause increases in the circulating levels of amylase, lipase and TLI which would affect their usefulness as diagnostic indicators of pancreatitis, or increases in gastrin which could be of pathologic significance in the development of gastric ulceration.

Nine Beagle dogs underwent sub-total nephrectomy. Serum activities of amylase and lipase, and concentrations of TLI, BUN and creatinine were determined prior to, and 30 weeks after nephrectomy. Pre- and post-prandial plasma gastrin concentrations were measured in control dogs (19 Beagles), and study dogs 30 weeks after nephrectomy. Endogenous 24hr Creatinine clearance (ml/min/kg ; mean±SE) 30 weeks after nephrectomy (0.87 ± 0.1) was significantly (P<0.01) lower than control values (2.5 ± 0.3 ; n=13; JAAHA 16, 537-546;1980), but serum concentrations of BUN and creatinine were unchanged. Induced renal dysfunction was associated with significant increases (PRE : POST : 0.01 in TLI (7.1 ± 0.6 × 1.5 ± 1.8 μg/l) and amylase (673 ± 30,1347 ± 42 IUL), but lipase (524 ± 188 ; 342 ± 76 IU/L) and gastrin (Control 0 ml/min/0.2 ± 0.9, 120 min/18 ± 1.4 ; 0.0 min/12 ± 1.7, 120 min/14.5 ± 1.1 pmol/l) were unaffected.

The present study illustrates that serum levels of TLI and amylase can be affected by non-azotemic renal disease and suggests up to 2 fold increases may occur in dogs with pre-azotemic renal disease.
81 EVALUATION OF RADIOASSAY METHODS FOR ANALYSIS OF CANINE SERUM COBALAMIN AND FOLATE.

David A. Williams, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

Competitive binding radioassay kits for human serum cobalamin and folate utilize either boiling or alkaline denaturation to degrade endogenous vitamin binders. Some also utilize binding proteins immobilized on a solid phase to avoid a charcoal separation step. In this study results obtained using charcoal boil (CB) and solid phase no-boil (SPNB) kits marketed by one company (Diagnostic Products Corporation) to assay cobalamin and folate in canine serum (n=20) were compared. Results obtained using the CB method were also compared with those obtained using Lactobacillus casei (folate) and Euglena (cobalamin) bioassays (n=11).

For folate assays results of each method correlated well (r>0.96, p<0.0001). For cobalamin assays there was good agreement between bioassay and the CB method (r=0.98, p<0.0001), but agreement between CB and SPB methods was less good (r=0.81, p<0.0001), and that between CB and SPNB methods was poor (r=0.35, p=0.13). Cobalamin assay results were slightly greater using CB radioassay than bioassay (slope=1.25), and results obtained by SPB assay results were greater than those obtained by CB assay (slope=1.1).

It is concluded that the CB method is most suitable for assay of canine serum cobalamin and folate. Care should be exercised when selecting a laboratory for radioassay of cobalamin and folate in canine serum. In particular, laboratories employing “no boil” methods may report unreliable results for canine serum samples, perhaps because of failure of these methods to denature all endogenous canine cobalamin binding proteins.

82 THE USE OF MISOPROSTOL FOR PREVENTION OF GASTRODUODENAL HEMORRHAGE AND ULCERATION ASSOCIATED WITH ASPIRIN THERAPY. R.J. Murtaugh, M.E. Matz, M.A. Labato, R.J. Boudrieau. Tufts University School of Veterinary Medicine, North Grafton, MA.

The purpose of this study was to compare the effects induced by oral administration of therapeutic dosages of aspirin to that of aspirin in combination with misoprostol on arthritic dogs.

A prospective, randomized, double blind, placebo controlled study was conducted over 14 days on 20 arthritic dogs administered aspirin (25 mg/kg TID) and placebo or aspirin and misoprostol (100 μg/dog [2.5 μg/kg] TID). The misoprostol (N=10) and placebo (N=10) groups were primarily compared by sequential gastroduodenoscopic evaluation (days 0, 14), changes in packed cell volume (days 0, 7, 14), and the prevalence of gastrointestinal disturbance (daily).

Endoscopic evaluation in the misoprostol group at the end of the study period revealed significantly less gastroduodenal hemorrhage, erosion, and ulceration when compared to the placebo group (p<0.001). Packed cell volumes from Day 0 to Day 14 for dogs within the placebo group decreased significantly (p<0.029), with no significant differences detected within the misoprostol group or between groups. Significantly less vomiting was noted in the misoprostol group compared with the placebo group (p = 0.03). No significant difference in the prevalence of diarrhea was found between the study groups.

We conclude that misoprostol administration promotes protective mechanisms that inhibit the gastrointestinal hemorrhage, erosion, and ulceration accompanying administration of aspirin.

83 COMPARISON OF DIAGNOSTIC TESTS IN DOGS EXPERIMENTALLY INFECTED WITH GIARDIA. M S Leib, A M Zajac, N Hahn, S King, M Matz. COLLEGE OF VETERINARY MEDICINE, VIRGINIA TECH, BLACKSBURG, VA.

Giardia infection was established in eleven 6 month old puppies (nine received 1000 Giardia cysts orally and 2 sentinel puppies were spontaneously infected). Following infection zinc sulfate fecal flotation tests were initially done daily. After cysts were recovered they were done 3 times per week. Duodenal aspiration was done weekly for 8 weeks and then every 4 weeks for a total of 32 weeks. A fecal ELISA (Prospect T™, Alexonine) for Giardia was performed on dogs, and only the fecal immediately prior and 1 following 12 weeks of infection. No diarrhea occurred.

Positive instances of infection were detected by either a positive fecal (2 prior and 1 following aspiration) or positive duodenal aspiration 81 times: duodenal aspiration 71 (87.7%), at least 1 of 3 fecals 78 (96.3%), at least 1 of the 2 fecals prior to aspiration 73 (90.1%), and only the fecal immediately prior to aspiration 62 (76.5%). Three fecals detected a significantly greater number of positive cases that duodenal aspiration (chi square 4.1, p=0.042).

Ninety-six fecal samples had concurrent ELISA and zinc sulfate flotation. Equivocal results were obtained in 3 samples, agreement was seen in 35 negative and 43 positive samples (83.9%). Fourteen (15.1%) positive ELISAS occurred with negative fecals and 1 negative (1.1%) elisa occurred with a positive fecal. The authors conclude that 3 zinc sulfate fecals were superior to duodenal aspiration in detecting infection.

Limited experience with a fecal ELISA yielded similar results when compared to fecal examination.

84 EVALUATION OF A FECAL ELISA AND PERORAL STRING TESTS FOR THE DIAGNOSIS OF CANINE GIARDIASIS. S.C. Barr, D.D. Bowman, H.N. Erb. College of Veterinary Medicine, Cornell University, Ithaca, NY.

Dogs infected with the protozoan Giardia canis can show a wide spectrum of disease from subclinical to severe diarrhea resulting from maldigestion and malabsorption of nutrients. Because signs are not pathognomonic, definitive diagnosis relies on laboratory means. Examination of stool samples for Giardia cysts using a zinc-sulfate concentration technique (ZSCT) is still considered the most practical and efficient means of diagnosis. However, the diagnostic success rate of single ZSCT tests in dogs is low, partly because fecal cysts are excreted intermittently. The purpose of this study was to evaluate the sensitivity, relative specificity, and practicality of 2 commercially available tests, the fecal antigen-capture enzyme-linked immunosensor ProSpecT™ /Giardia™ (ELISA), and the Enteroc-T™ (string test), a peroral nylon string test, and compare these tests with a ZSCT for the detection of canine giardiasis.

Thirty-three of 77 dogs, and 52 of 164 fecal samples (from these dogs) were found to be infected on the ZSCT. The ELISA gave false negative results in 10% and 14% of ZSCT-positive dogs and fecal samples, respectively, and relative false-positive results in 13% and 10% of ZSCT-positive dogs and fecal samples, respectively. Fourteen of the 18 string-test dogs were positive by the ZSCT. Of the 4 dogs that were ZSCT-negative, 2 were positive by the ELISA. Of the 21 string tests performed on the 18 dogs, only 3 strings reached the duodenum, and none were positive for Giardia. Because the string broke in 1 dog (therefore producing a risk of a string foreign body) further string tests were not done. It was concluded that the ELISA had low sensitivity for Giardia diagnosis in asymptomatic dogs and has lower relative specificity than the ZSCT. Furthermore, in our hands the string test is an insensitive, dangerous, and impractical method for giardiasis diagnosis.
DEVELOPMENT OF PANCREATIC ACINAR ATROPHY (PAA) IN A GERMAN SHEPHERD DOG

E. Westermarck, R.M. Batt, M. Wiberg and C. Vaillant. College of Veterinary Medicine, Helsinki, Finland, Department of Small Animal Medicine and Surgery, Royal Veterinary College, London, and Department of Veterinary Preclinical Science, University of Liverpool, UK.

Sequential studies were performed on a female German shepherd dog bred from parents with exocrine pancreatic insufficiency (EPI) in order to determine whether PAA represents a congenital or acquired pancreatic abnormality in this breed.

The dog remained clinically healthy and determination of serum trypsin-like immunoreactivity (TLI), BT-PABA and fecal soyabean concentration but also results of the BT-PABA and SST tests were consistent with EPI, but the SST test was normal. Within one month, the dog had developed clinical signs of EPI, and not only serum TLI concentration but also results of the BT-PABA and SST tests were compatible with a severe loss of exocrine pancreatic tissue. This loss was confirmed by gross and histopathological examination of the pancreas at 25 months which showed typical features of PAA, the exocrine pancreas being reduced to small isolated groups of acinar cells.

These findings have documented for the first time that PAA can be the result of a progressive and rapid loss of exocrine tissue from an apparently normal pancreas.

ENDOSCOPIC PLACEMENT OF A PERCUTANEOUS GASTRODUODENOSTOMY FEEDING TUBE IN THE DOG

MA McCrackin, RM Bright, RC DeNovo, RL Toal. University of Tennessee, Knoxville, TN.

This project was designed to develop a technique for endoscopic placement of a percutaneous enteric feeding tube in the dog. Thirty-one healthy adult dogs (8-30 kgs) were used. A 20 or 24 French percutaneous endoscopic gastrostomy (PEG) tube was placed in each dog using general anesthesia. A 12 French weighted (5 dogs) or 10 French nonweighted (8 dogs) enteric feeding tube was then passed through the PEG tube into the stomach and guided endoscopically into the proximal duodenum. Tube location was verified fluoroscopically on days 1, 2, 3, 7 and 14. This was confirmed by gross and histopathological examination of the pancreas at 25 months which showed typical features of PAA, the exocrine pancreas being reduced to small isolated groups of acinar cells.

The tubes were removed and replaced at 2-22 days; 10 of 14 attempts in dogs 6-22 months of age, gross and histopathological examination of the pancreas at 1-14 days. Compliant profiles and indirect calorimetry data were collected on each cat.

There were no significant differences in indirect calorimetry measurements, or fecal and urine nitrogen levels between diets. Significantly decreased plasma amino acid levels (p < 0.003) were noted in cats receiving Jevity + Promod and Feline ClinCare compared to cats fed Feline C/D. One cat developed signs of hepatic encephalopathy after 4 days of Feline ClinCare; these signs resolved after resuming ad lib feeding of Feline C/D. These findings suggest that Hill's Feline C/D may be a more optimal diet currently available for feeding debilitated cats.

130 ACVIM ABSTRACTS
90 DHEA IN THE TREATMENT OF CANINE OBESITY. K.G. MacKenzie, I.D. Kurzman, and D.L. Panciera. School of Veterinary Medicine, University of Wisconsin, Madison, WI.

Canine obesity is an extremely common problem; it is estimated that between 25% and 50% of pet dogs are overweight. The exact role of hormonal abnormalities in the development of obesity is not clearly understood. In rodents and man, the adrenal steroid dehydroepiandrosterone (DHEA) has been associated with loss of body weight and reduction in total body fat content. In a previous study, we showed that oral administration of DHEA, without a change in caloric intake, resulted in weight loss in spontaneously obese dogs. The mechanism of action of the antiobesity effect of DHEA is unclear. The recommended treatment for obese dogs is caloric restriction, however, this method is often unsuccessful. We hypothesize that treatment of obese dogs with DHEA in combination with a low calorie, high fiber diet will result in greater weight loss when compared to dogs on the same diet without DHEA.

We are conducting a randomised, double-blind study in obese euthyroid dogs at our Veterinary Medical Teaching Hospital. All dogs are placed on a uniform diet which is low in calories and high in fiber (Hill's r/d prescription diet) at the daily caloric intake recommended by the manufacturer. Dogs are randomized to receive either placebo or DHEA at 60 mg/kg/day. A total of 42 dogs have been entered into this study. Of these, 39 are evaluable and 3 have been removed from the study for various reasons. Thus far, the code has been broken for eleven dogs treated with DHEA and six dogs treated with placebo. The mean total body weight loss for the DHEA group was 3.59 ± 0.75 kg versus 2.38 ± 0.66 kg for the placebo group; p=0.02. The percent excess weight loss per mouth for the DHEA group was 15 ± 2.8 versus 8.2 ± 2.1 for the placebo group; p<0.05. The code was broken when 28/39 dogs died of a non-related cause. The remaining 11 dogs in this study and final results will be presented. The results thus far indicate that DHEA when combined with a low calorie, high fiber diet enhances the excess body weight when compared to just diet modification alone.

91 HYPERCHOLESTEROLEMIA IN BRIARDS IN THE UNITED KINGDOM. P. Watson, K.W. Simpson, R. M. Odedra, P.G.C. Bedford. Royal Veterinary College, University of London, U.K.

Elevated fasting plasma cholesterol concentrations were identified in 78 of 78 clinically healthy Briards presented during 1991 as part of a specific examination scheme for retinal pigment epithelial dystrophy (RPED). The object of this study was to define the nature of the hypercholesterolemia.

Samples were obtained from 15 clinically healthy Briards for urinalysis, hematology and clinical biochemistry (including triglyceride and T4 concentrations). TSH and ACTH stimulation tests were performed on 3 of these animals. The results of these tests were normal, apart from significant (p<0.01) elevations of plasma cholesterol (mmol/L, mean±SD) in the Briards (8.0±0.5), compared to 12 control dogs (4.1±0.3). Lipoprotein electrophoresis performed on fresh plasma samples demonstrated a marked increase in the density of the alpha2 band (HDL1) in all 15 Briards compared to the controls. This increase in density was reduced to normal by dextran sulphate-Mg2+ precipitation of Apo B and Apo E containing lipoproteins in the plasma.

The present study has documented a hyperlipidemia in Briards which is characterized by a reduction of normal triglyceride concentrations. The absence of obvious metabolic derangements associated with secondary hypercholesterolemia, suggests that Briards in the UK may have a primary abnormality in cholesterol metabolism. The increased density of the precipitable lipoprotein which migrates in the alpha2 band suggests that the hypercholesterolemia is due to an abnormal accumulation of HDL, most likely HDLc. The possibility that an abnormality in lipid metabolism might play a role in the development of RPED in Briards is currently being investigated.

92 BLOOD CHEMISTRY CHANGES IN DOGS COMPETING IN A LONG DISTANCE SLED RACE. K.W. Hinchcliff, J. Olson, C. Crusberg, R. Long, W. Royal, W. Weber, and J. Buehler, Dept. Veterinary Clinical Sciences, The Ohio State University, 1935 Coffey Rd., Columbus, OH 43210.

Prolonged submaximal exertion is associated with marked changes in the serum constituents of certain species. The purpose of this study was to define the serum biochemical changes occurring in dogs competing in a long distance sled dog race. A total of 55 blood samples were collected from 28 dogs competing in the 1991 Yukon Quest International Sled Dog race. Blood was collected after a 36 hour mandatory rest at the midpoint of the race, and again at 2 subsequent checkpoints. Hematocrit, the concentration of serum constituents and cortisol, and serum enzyme activities were measured using conventional laboratory techniques. Data were analyzed using Student's t-test for paired data. The average speed of dogs between checkpoints was 4.5 mph. There were no significant (p > 0.025) increases in hematocrit, serum total protein, potassium, or creatinine concentration. The average speed of dogs between checkpoints was 4.5 mph. There were no significant (p > 0.025) increases in hematocrit, serum total protein, potassium, or creatinine concentration. The average speed of dogs between checkpoints was 4.5 mph. There were no significant (p > 0.025) increases in hematocrit, serum total protein, potassium, or creatinine concentration. The average speed of dogs between checkpoints was 4.5 mph. There were no significant (p > 0.025) increases in hematocrit, serum total protein, potassium, or creatinine concentration. The average speed of dogs between checkpoints was 4.5 mph.
PHYSIOLOGICAL ALTERATIONS OCCURRING DURING A LONG DISTANCE SLEDDOG RACE. J. Burr, G. Reinhardt, and R. Swenson. The Iams Company, Lewisburg, OH.

To evaluate the physiological changes during a long-distance sled dog race, hematological and biochemical profiles were performed on a team of Alaskan sled dogs racing in the ‘91 Iditarod. The team of 20 was tested 7 days prior to the race and 17 were resampled during the 13-day race after being dropped or at the completion of the race. Chemistry profiles, CBC, serum lactate, pyruvate, folate, glucagon, insulin, and KBC folate were analyzed using routine testing procedures. The data were analyzed using the paired t-test with a significance level of 0.05. Prerace values were significantly higher than postrace values for albumin/globulin, albumin, monocytes, band neutrophils, P, Ca, Hct, Hgb, K, BCP, TP, WBC, and triglycerides. Prerace values were significantly lower than postrace values for SAP, AST, BUN, CPK, MCH, BUN/creatinine, BUN/creatinine, KBE folate, and uric acid. There were no significant differences between pre- and postrace samples for ALT, cholesterol, GGT, MCHC, creatinine, serum folate, MCV, globulin, glucagon, serum lactate and pyruvate, glucose, insulin, lymphocytes, LDH, and total bilirubin. Since minimal work has been done under these conditions, the changes may be a reflection of the physiological demands on the dogs; therefore, this data may serve as baseline information. Energy expenditure and hydration are concerns of race participants. The blood data revealed that the animals maintained normal hydration while racing. Finally, although dogs were not dropped due to musculoskeletal difficulties, the magnitude of change in the CPK levels is clinically interesting. Whether the damaged muscle cell walls directly or indirectly resulted in the dogs being removed from the team is a matter of speculation. Further work is warranted.

95 Determination of extent of milk malabsorption in diarrheic calves. G. Nauppert, and J.M. Naylor. WCVM, University of Saskatchewan, Canada.

The objectives of our project were to determine the frequency and severity of milk malabsorption in diarrheic calves using breath hydrogen analysis. Twelve healthy and 38 scouring calves were used. Fecal samples were collected to identify the pathogens present in scouring calves. All scouring calves received intravenous fluids to correct their metabolic acidosis and dehydration after determination of their blood gas deficit. They were fed lactose and xylose (2.5% body weight 46 g/L) at 48 and 36 h after admission respectively. Breath samples and blood samples were collected at 1 h intervals from 0 to 7 h.

All diarrheic calves had: A) an elevated peak breath hydrogen after feeding with lactose (24.9 ppm ±1.5 versus controls 12.2 ppm ±1.2) and xylose (30.0 ppm ±9.6 versus controls 13.2 ppm ±2.5); B) a lower than normal peak blood glucose (4.6 mmol/L ±0.4 versus controls 6.4 mmol/L ±0.5) and blood xylose (3.0 mmol/L ±0.4 versus controls 5.7 mmol/L ±0.5). The pathogen commonly involved were rotavirus and coronavirus. It was concluded that malabsorption rather than a specific lactose maldigestion is a significant problem in diarrheic calves. The number of pathogens was not related to the severity of malabsorption. Villous atrophy caused by viral infection resulted in decreased absorption of lactose and xylose. Although the absorption of carbohydrates was decreased in all diarrheic calves, it was not related to the severity of their acid-base deficit.

94 CIMETIDINE, AMINOPHYLLINE INTERACTION IN FOALS. W.M. Duckett, B.A. Breuhaus and D. Aucoin. College of Veterinary Medicine, North Carolina State University, Raleigh, NC.

Cimetidine, an H2 blocker, is used to treat and prevent gastric ulcers in foals and horses. Cimetidine has an inhibitory effect on the hepatic microsomal P450 enzyme systems, thus an inhibitory effect on the metabolism of other drugs. Aminophylline is one drug where this interaction is recognized in humans. Aminophylline is used in human and equine medicine for its bronchodilatory and other beneficial effects on the respiratory tract in chronic airway and infectious respiratory disease. Theophylline (the active ingredient of aminophylline) has a narrow therapeutic index. In horses, the reported therapeutic blood levels are 6-16 µg/ml. Adverse signs are associated with levels ≥ 15 µg/ml.

To investigate whether concomitant administration could potentially result in toxic blood levels of theophylline in horses, a pilot group of 4 weanlings of 6-7 months of age and mean weight of 178 kg. were given cimetidine at 8.8 mg/kg TID and aminophylline at 7.5 mg/kg BID orally for five days. On day one and day five, blood samples were drawn at 0, 15, 30, 60, 120, 240, 360, 480, and 720 minutes post aminophylline administration. Serum samples were analyzed for theophylline levels by Abbott TDX fluorescent polarization. On day one, the mean level peaked at 5.26 µg/ml (with a range of 2.72-7.16 mg/kg) at 4 hours post drug administration. On day five the peak mean was 16.42 µg/ml (with a range of 11.97-19.48) at 4 hours post drug administration. Theophylline clearance decreased from a mean of 2.67 ml/kg/min on day one to 0.76 ml/kg/min on day five. Modification of therapeutic regimens and close monitoring is recommended when using these drugs concurrently.

96 INFLUENCE OF INTRAVENOUS SODIUM PROPIONATE ON ABOMASAL EMPTYING RATE IN DAIRY CATTLE. G.J. Koenig, P.D. Constable, and B. L. Hull. College of Veterinary Medicine, The Ohio State University, Columbus, OH.

To determine if a relationship exists between volatile fatty acid concentration, insulin re- lease, alkalemia, and abomasal motility, the change in abomasal emptying rate (AER) following intravenous administration of sodium propionate (SP) or hypertonic saline (HS) (2.5, 6, 10, 15, 20, and 25 mM/kg) in lactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula. Baseline and post-treatment AER, blood gas values, serum glucose (SG), and plasma insulin (PI) concentrations were compared in lactating and nonlactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula. Baseline and post-treatment AER, blood gas values, serum glucose (SG), and plasma insulin (PI) concentrations were compared in lactating and nonlactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula. Baseline and post-treatment AER, blood gas values, serum glucose (SG), and plasma insulin (PI) concentrations were compared in lactating and nonlactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula. Baseline and post-treatment AER, blood gas values, serum glucose (SG), and plasma insulin (PI) concentrations were compared in lactating and nonlactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula. Baseline and post-treatment AER, blood gas values, serum glucose (SG), and plasma insulin (PI) concentrations were compared in lactating and nonlactating cattle treated with equal sodium loads of HS or SP. SP induced a metabolic alkalosis and decreased AER in lactating and nonlactating cows. AER was determined by periodic measurement of digesta flow through a permanent duodenal fistula.
APPLICATION OF GASTRIC pH-METRY IN HORSES: MEASUREMENT OF 24 HOUR GASTRIC pH IN HORSES FED, FASTED, AND TREATED WITH RANTIDINE
Michael J. Murray and Gerald F. Schusser. Marion duPont Scott Equine Medical Center, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Leesburg, VA 22075

Previous studies on the effects of H2 antagonists on gastric acidity in horses have all examined gastric fluid in horses that had been fasted for several hours. The effect of this class of anti-ulcer drugs has not been examined in fed horses. This study was done to develop a technique for assessing 24 hour gastric pH in horses and to compare the effects of withholding feed, feeding, and feeding plus ranitidine on 24 hour gastric pH profiles.

A commercial indwelling combination silver-silver chloride pH electrode was placed into the lumen of a 16 fr nasogastric feeding tube with a weighted tip and was positioned within the stomachs of 5 adult horses by endoscopy. The electrode was connected to a recorder worn by the horses and gastric pH recordings were made every 6 minutes. Following a 24 hour recording, data was transferred into a commercial spreadsheet program on a PC computer.

Each horse was studied under the following conditions: 1) permitted free access to Timothy grass hay for 24 hours; 2) withheld from all feed, but not water, and kept off of bedding material for 24 hours; 3) permitted free access to Timothy grass hay and treated with ranitidine, 6.6 mg/kg, every 0.8 hour for 48 hours. The mean of 24 hour pH recordings when hay was available was greater than when feed was withheld (3.4 ± 0.9 vs 1.9 ± 0.5). The means of both 24 hour pH recordings during ranitidine treatment were greater than for the 24 hour period of hay availability but no ranitidine treatment (4.4 ± 0.6 and 4.8 ± 0.8 vs 3.4 ± 0.9). Statistical analysis was not completed at the time of abstract preparation.

EVALUATION OF TWO POTENTIAL TREATMENTS OF EQUINE ENDOTOXEMIA. M. M. Durando and R. J. MacKay, College of Veterinary Medicine, University of Florida, Gainesville, FL.

We evaluated two endotoxin-binding agents, an anti-endotoxin antiserum (Endosema®) and the antibiotic polymyxin B, in a model of equine endotoxemia. Six 3-5 month-old foals were given each of the following treatments at 2-week intervals according to a randomized block design: endotoxin (LPS) alone (0.25 µg/kg, IV), LPS 30 minutes after polymyxin B (6000 U/kg, IV), or LPS 30 minutes after antiserum (1.5 ml/kg, IV). Clinical signs were monitored, and blood was collected at intervals until 6 hours after LPS infusion for measurement of tumor necrosis factor (TNF) and interleukin-6 (IL-6) activities, and complete blood counts.

Endotoxin alone caused rises in temperature and heart and respiratory rates. In addition, there was profound neutropenia and marked transient, increase in circulating TNF and IL-6. Polymyxin B-treated foals had significantly lower peak plasma TNF (106.6 U/ml) and IL-6 (297.9 U/ml) activities than LPS only foals (624.9 and 1055.4 U/ml, respectively), less severe clinical signs, and significantly less neutropenia. In contrast, antiserum-treated foals had significantly higher circulating TNF and IL-6 activities (2168.3 and 5671.4 U/ml, respectively), markedly lower neutrophil counts, and more severe clinical signs, compared to control (LPS alone) foals. These results suggest that polymyxin B has potential as a treatment for equine endotoxemia. Anti-endotoxin antiserum had no positive effect in this model, and, under certain conditions, may exacerbate the actions of endotoxin.

INTERLEUKIN-6 IN SUBLETHAL INTRAVENOUS ENDOTOXIN CHALLENGED NEONATAL FOALS. L.A. Robinson, G.K. Allen, E.M. Green, and H.E. Garner. College of Veterinary Medicine, Univ. of Missouri, Columbia, MO.

The effects of sublethal intravenous (IV) endotoxin challenge on serum levels of interleukin-6 (IL-6) was investigated in 22 neonatal foals. Foals were randomly divided into 4 groups: 1. Colostrom-fed/endotoxin challenged (CF-LPS=10), 2. Colostrum-deprived/endotoxin challenged (CD-LPS=6), 3. CF control/saline-treated (CF-SAL=4), and 4. CD control/saline-treated (CD-SAL=2). Serum samples were collected prior to challenge and every 15 min for 4 hrs post bolus IV-LPS (0.5 µg Escherichia coli 055:B5 LPS/kgBW) or saline injection. TPR, nursing frequency, defecation/feal consistency, and CRT/mucous membrane color were monitored prior to injection and hourly thereafter. A depression index (DI = 1 - bright, alert, responsive -> 4 - comatose) was used to rate mental awareness. An in vitro proliferative bioassay with murine B-cell hybridoma (B9) cells was used to measure IL-6 in heat-inactivated serum. The CF-LPS group had higher levels of IL-6 than the CD-LPS group. IL-6 levels persisted through 4 hrs in both LPS-treated groups. IL-6 was not detectable in serum from the SAL-treated groups. Clinically, both SAL groups remained within normal limits for all parameters, with a DI of 1. The LPS treated groups developed pyrexia, tachycardia, hyperpyrexia, diarrhea, decreased nursing, injected mucous membranes with prolonged CRT, and DI scores of 2-4, consistent with endotoxemia. CF-LPS foals appeared to be more severely affected by endotoxin challenge (some becoming comatose) than CD-LPS foal (none of which became comatose). All foals recovered and were clinically normal within 12-24 hrs post challenge. Results of this study support the involvement of IL-6 in neonatal equine endotoxemia. Colostrum feeding appears to enhance the detrimental effect of endotoxin challenge on neonatal foals.

MYELOID HYPOPLASIA IN RELATED STANDARDBREDS. Catherine Kohn, Guillermo Couto, Christine Swardson, Patricia Provost, Douglas Antczak, and Robert Gilbert. School of Veterinary Medicine, The Ohio State University, Columbus, OH.

Moderate to profound neutropenia associated with myeloid hypoplasia (M:H <0.3) was documented in 7 young Standardbred horses stabled by the same stallion. Six of 7 horses were intermittently thrombocytopenic. Evaluation of serial neutrophil counts in 2 horses suggested that a cyclic variation in neutrophil numbers was present. Cyclic variations in platelet and/or lymphocyte counts were also present in 3 horses. The site of the affected horses was clinically healthy. A hemogram from this stallion revealed a neutrophil count of 2.6 X 109/L (reference range 2.3-8.5 X 109/L) and 109,000 platelets/L. Preliminary bone marrow culture studies suggested that myeloid progenitor cells were present in the affected horses tested and that these cells were able to respond to exogenous growth factors. Lymphocyte and neutrophil function studies in 2 horses indicated no abnormalities. These tests were limited by the difficulty in harvesting sufficient numbers of cells from cell-poor blood. Six of 7 affected horses died from complications of infectious diseases and/or thrombocytopenia. Necropsies in 3 cases did not reveal a cause for the myeloid hypoplasia. A heritable cyclic neutropenia is suspected.
101 **BLAD (BOVINE LEUKOCYTE ADHESION DEFICIENCY): CLINICAL IMMUNOLOGY AND SYMPTOMS. M.E. Kehrl, Jr.; M.R. Ackermann, D.E. Shuster; and R.O. Gilbert. USDA-Agricultural Research Service-National Animal Disease Center, Ames, IA; Cornell University, Ithaca, NY.**

Bovine leukocyte adhesion deficiency (BLAD) has recently been recognized as an autosomal recessive genetic disease in Holstein cattle. BLAD results in severe immunologic dysfunction and various infectious diseases causing premature death of affected animals. The genetic disorder results from a point mutation in the gene encoding the beta subunit of the beta integrins. This Asp->Gly mutation occurs in a phylogenetically conserved region of the CD18 protein (amino acid position 128). The beta-integrins are a family of adherence proteins which mediate cell-cell and cell-substrate interactions in the host. The immunologic aberrations include failure of neutrophils to adhere to vascular endothelial cells and migrate into infected tissues. Opsonization of bacteria by complement proteins also fails to optimally facilitate phagocytosis by the iC3b receptor on neutrophils and macrophages. Approximately 14.8% of nearly 1700 registered Holstein bulls tested to date have been found to be carriers of the D128G allele for CD18. Cattle or BLAD result in severe immunologic dysfunction and various infectious diseases with BLAD suffer from stunted growth, recurrent fevers, chronic nodes, severe peridontal gingivitis (with eventual tooth loss), and mucosal infections such as gingivitis, diarrhea and bronchopneumonia. Gross lesions include: tooth loss, oral ulcers, ulcerative enteritis lymphadenitis, pneumonia and dermatitis. Typical histologic lesions in BLAD calves are mucosal ulcerations that lack significant infiltrates of neutrophils, bone marrow granulocytic hyperplasia and vascular leukocytosis. Diagnostic tests include: flow cytometry of whole blood using antibodies against the beta subunit, polymerase chain reaction (PCR) test using formalin-fixed, paraffin-embedded tissues, and immunogold labeling of isolated neutrophils using the scanning or transmission electron microscope.

102 **BOVINE LEUKOCYTE ADHESION DEFICIENCY (BLAD): AN AUTOSOMAL RECESSIVE DISEASE OF HOLSTEINS CAUSED BY IMPAIRED EXPRESSION OF THE $\beta_2$ INTEGRINS (MAC-1, LFA-1 AND P 150,95). R.M. Ackermann, M.E. Kehrl, Jr., D.E. Shuster, and R.O. Gilbert. National Animal Disease Center, Ames, IA; and Cornell University, Ithaca, NY.**

Bovine Leukocyte Adhesion Deficiency (BLAD) is an autosomal recessive disease of Holsteins caused by impaired expression of the $\beta_2$ integrins (Mac-1, LFA-1 and p 150,95). It is a newly recognized disease of Holsteins and has been identified in animals from the United States, Germany, and Japan. Affected calves are stunted in growth, and despite antibiotic therapy develop a marked neutropenia (>100,000 cells/µl) and mucosal infections such as gingivitis, diarrhea and bronchopneumonia. Gross lesions include: tooth loss, oral ulcers, ulcerative enteritis lymphadenitis, pneumonia and dermatitis. Typical histologic lesions in BLAD calves are mucosal ulcerations that lack significant infiltrates of neutrophils, bone marrow granulocytic hyperplasia and vascular leukocytosis. Diagnostic tests include: flow cytometry of whole blood using antibodies against the beta subunit, polymerase chain reaction (PCR) test using formalin-fixed, paraffin-embedded tissues, and immunogold labeling of isolated neutrophils using the scanning or transmission electron microscope.

103 **ELECTROLYTE, LACTATE AND HEMOGLOBIN SATURATION CHANGES WITH EXERCISE INTENSITY. C.K. Fenger, K.W. Hinchcliff, K.H. McKeever, C.W. Kohn. Department of Veterinary Clinical Sciences, The Ohio State University College of Veterinary Medicine, Columbus, Ohio.**

This study was performed to evaluate changes in plasma [Na], [K], [Cl], [lactate] and [hemoglobin] during exercise to determine their influence on acid-base balance and therefore on the saturation of hemoglobin. Seven mares were exercised for 90s at each step of an incremental exercise test. Blood for measurement of blood gases, hemoglobin saturation, packed cell volume, plasma [protein], [hemoglobin], [lactate], [Na], [K] and [Cl] was collected at the end of each step. Oxygen consumption was measured continuously using a flow-through calorimeter. The oxyhemoglobin dissociation curve was determined for blood collected from horses at rest, 50% VO2max, and 100% VO2max. Blood constituent concentrations were compared to relative work (%VO2max) by simple linear regression. Significant increases in plasma [Na], [K], [lactate], [protein], PCV and [hemoglobin] were found with increasing %VO2max. The hemoglobin P50 was increased from 22.9±6.0 mmHg to 31.8±5.0 mmHg (p<0.05) at 100% VO2max independent of the change in CO2. This effect was attributed to the fixed acid Bohr effect, exerted by the metabolic component of the decrease in pH. Because the increase in the strong anion, lactate, was offset by the increase in [Na] and [K], the decrease in pH was probably mediated in part by the increase in protein and unmeasured anions.

104 **BLOOD VISCOSITY IN HORSES AFTER INTENSE EXERCISE. C. Sommersdahl, F. Andrews, and D. Geiser. College of Veterinary Medicine, University of Tennessee, Knoxville, TN.**

The effects of intense exercise on blood viscosity were investigated in event horses. Total plasma protein (TP), packed cell volume (PCV), whole blood viscosity (WBV), and plasma viscosity (PV) were measured in 21 horses before and after the cross country jumping event at a horse trial. Blood samples were drawn from the jugular vein of the horses at rest, the evening prior to, and immediately after completion of the cross country course. WBV and PV were measured at 6 rpm (shear rate=21/sec) using a rotational cone-and-plate viscometer. This low shear rate was chosen because it most simulates blood flow through small vessels and capillaries. PCV and TP were measured using standard methods. Differences between resting and post exercise values were compared using a matched pairs t-test and statistical significance was considered when p<0.05.

Mean(SD) values at rest were PCV 358(3), TP 6.2 g/dl(0.7), WBV 5.91 centipoise [cp](2.78), and PV 2.61 cp(3.11). Mean(SD) values after exercise were PCV 558(7), TP 6.7 g/dl(0.7), WBV 10.71 cp(2.99), and PV 2.84 cp(1.51). PCV, TP, and WBV increased significantly (p<0.05) after exercise in the horses in this study. PV increased after exercise, but was not statistically significant (p=0.0517). Increased PCV and TP during intense exercise contributes to increased WBV and PV leading to altered tissue perfusion. This alteration in blood flow may predispose these horses to exertional diseases.

*Brookfield Engineering Lab., Inc., Stoughton, MA.*
105 Effects of Pentoxifylline on Blood Flow Properties in the Horse. 

R.J. Geor, D.J. Weiss, S.M. Burris, and C.M. Smith. College of Veterinary Medicine, University of Minnesota, St. Paul, MN.

The purpose of this preliminary investigation was to determine the effects of pentoxifylline (PTX) on blood flow properties in the horse. Hemorheologic parameters were examined weekly in 4 horses given PTX (8.5 mg/kg bwt, q 12h, PO) for 28 days. In addition, hematologic responses to epinephrine (1 mg IV) were determined on days 0, 14 and 28 of PTX treatment. Hematologic and rheologic tests included complete blood count, red blood cell (RBC) morphology, erythrocyte sedimentation rate (ESR), whole blood viscosity (WBV), and RBC and neutrophil filterability through polycarbonate filters with an average pore size of 3 μm.

PTX treatment was associated with a significant (P<0.01) decrease in packed cell volume (PCV) and increase in ESR. These changes were evident by day 7 of treatment and persisted until the end of the study. However, decreases in hematocrit and RBC count were not observed. PTX treatment was not associated with changes in resting WBV. However, despite significant increases in PCV and RBC count after epinephrine administration on days 14 and 28 of treatment, increases in WBV were minimal. PTX treatment resulted in a significant (P<0.01) decrease in the initial filtration increment (P/P.) of the RBC filtration curve. Neutrophil filtration curves did not change. It was concluded that PTX has beneficial effects on RBC filterability and post-epinephrine changes in WBV, which may contribute to improvements of microcirculatory blood flow.

106 Additive and Synergistic Pharmacological Inhibition of Coagulation Factor XIIIa Transglutaminase Activity: Potential Therapeutic and Adhesion Alternative. C.P. Coyne, Joseph E. Smith, Kansas State University, Manhattan, Kansas 66506.

A variety of pharmaceutical compounds were evaluated for their ability to inhibit XIIIa transglutaminase activity in equine plasma. Selection of experimental pharmaceuticals was based upon the biochemical mechanism of action exerted by factor XIIIa and chemical composition and molecular configuration of amino acid residues involved in cross-linking during fibrin monomer polymerization. In this context, laboratory investigations were conducted to determine the ability of 9 compounds (0.0 to 40.0 mM) to inhibit coagulation factor XIIIa-like activity. Pharmaceuticals serving as competitive substrate inhibitors were classified as (a) carbamylamine acceptor or (b) amine donor compounds which respectively inhibit phase 1 and phase 2 of factor XIIIa-mediated process of fibrin polymerization. Selective inhibition of factor XIIIa biochemical activity was recognized by the formation of (a) transparent plasma solution of high spectrophotometric transmittance at 605 nm, (b) solubilization of transparent gels in concentrated urea, and (c) consumption of native fibrinogen fractions analogous to serum controls. Pharmaceuticals possessing carbamylamine functional groups which inhibited phase 1 of the fibrin polymerization process mediated by coagulation factor XIIIa include eftuxoxime, Girard's Reagent, and prolinamide. Alternatively, pharmaceuticals with terminal amine groups which functioned to inhibit phase 2 of the fibrin polymerization included D-arginine and lysine. Synergistic inhibition of coagulation factor XIIIa (e.g. phase 1 and 2 of the polymerization process) was achieved with combinations of D-arginine: eftuxoxime, D-arginine: Girard's Reagent, and lysine: prolinamide.

107 Pharmacological Neutralization of Lipopolysaccharide-Induced Macrophage TNF-alpha Synthesis. C.P. Coyne, B.W. Fawick, Kansas State University, Manhattan, Kansas 66506.

Polymyxin B was evaluated to determine its ability to neutralize the cytotoxic properties of lipopolysaccharide fractions from E. coli (J5), E. coli (B4:0111), Salmonella typhimurium, Salmonella minnesota, Klebsiella pneumoniae, and Pseudomonas aeruginosa gram negative bacteria. Experimental protocol involved incubating gradient concentrations of polymyxin B (0.0 to 1000 IU/ml) with fixed amounts of highly purified lipopolysaccharide (endotoxin) fractions. These formulations were incubated in growth media with strain TIB-71 murine macrophage populations propagated in tissue culture for 4 hours at 37 C in a 10% carbon dioxide environment. A 4 ul portion of this solution was then transferred to actinomycin D sensitized murine WEHI clone 164 fibrosarcoma cells grown in tissue culture which are exclusively sensitive to the cytotoxic properties of tumor necrosis factor-alpha (TNF-alpha). Following incubation at 37 C in a 10% carbon dioxide atmosphere for 18 hours, survival of monolayer fibrosarcoma populations was determined by MTT vitality staining methodology. These studies were supplemented by the assay of lactate acid produced by macrophage populations propagated in tissue culture after an 18 hour incubation period at 37 C in a 10% carbon dioxide atmosphere. Polymyxin B displayed an obvious ability to neutralize lipopolysaccharide-induced TNF synthesis by murine macrophage populations in a dose related fashion pertaining to four of the lipopolysaccharide fractions. A similar inverse relationship was noted between polymyxin B concentrations and macrophage lactic acid production. Significance of these investigations are that they illustrate the ability of polymyxin B to effectively neutralize the cytotoxic of certain lipopolysaccharide fractions synthesized by gram negative species of bacteria.

108 In Vitro Lysis of Equine Herpesvirus-1 Infected Target Cells by Equine Peripheral Blood Mononuclear Cells. L. M. Edens, M. V. Crisman, J. P. Coyle, A. C. M. Murray, T. E. Toth, S. A. Ahmed, Virginia-Maryland Regional College of Veterinary Medicine, Leesburg, Blacksburg, Virginia.

The objectives of this study were to 1) determine if peripheral blood mononuclear cells (PBMC) from adult horses could lyse equine herpesvirus-1 (EHV-1) infected equine dermis cells (EDC) in vitro, 2) evaluate the ability of interleukin-2 (IL-2) to enhance the lytic activity of PBMC against EHV-1 infected EDC and 3) compare the cytotoxic activity between PBMC from 5 pregnant and 5 non-pregnant mares against EHV-1 infected EDC.

A standard 4 hour chromium-51 (51Cr) release assay was performed by incubating either EHV-1 infected or non-infected EDC with PBMC. PBMC were added to the assay system immediately following isolation or after a 72 hour incubation with IL-2. The percent of cytolytic activity was determined by the amount of 51Cr in the supernatant.

Results indicated that unstimulated equine PBMC did not consistently demonstrate cytolytic activity against EHV-1 infected EDC (2.44 ± 2.51%). Following 72 hours of stimulation with IL-2, PBMC exhibited significant (p<0.001) cytolytic activity against EHV-1 infected EDC (11.427 ± 10.529%) when compared to uninfected EDC (5.206 ± 5.394%). Although the cytolytic activity against EHV-1 infected cells was greater in the pregnant mares (8.5 ± 9.8%) than the non-pregnant mares (6.7 ± 5.8%) the difference was not significant (p>0.15). We concluded that equine PBMC develop significant in vitro cytolytic activity against EHV-1 infected EDC following stimulation with IL-2 for 72 hours. There was no significant difference in the in vitro cytotoxic activity of PBMC between pregnant mares and non-pregnant mares against EHV-1 infected EDC.
109 DIARRHEA ASSOCIATED WITH ROTAVIRUS CHALLENGE IN FOALS: CLINICAL, VIROLOGIC AND SEROLOGIC EVALUATION. Joseph J Bertone, Linda J Saif, Stephen M. Reed, Susan Shibley, Fernando Fernandez. Department of Veterinary Clinical Sciences, The Ohio State University, College of Veterinary Medicine and Food Animal Health Research Program, The Ohio Agricultural Research and Development Center.

Our hypothesis was that foals challenged with a known quantity of live rotavirus will develop diarrhea. Five mixed breed, newborn foals were used for this study. Foals were isolated from their dams at birth and not allowed to nurse. These foals were kept in isolated stalls. Foals were challenged orally at 24 hr of age (> 400 mg/dl). On day 3 of life, 2 foals received 25 ml of sterile saline and 3 foals were challenged orally with 25 ml of live rotavirus (U425, 10^3 TCID50/ml grown on monkey kidney MA 104 cell line in MEM supplemented with 2.5 µg mycophenolic acid/ml, passaged 7 times). One foal was given antiserum orally with a known concentration of antibody. Fecal cultures and clinicopathologic evaluations were performed daily. All challenged foals shed rotavirus and 1 showed increased titers to rotavirus in serum. Bacterial pathogens associated with diarrhea were not identified in fecal samples. Control foals developed diarrhea in the period when foal heat diarrhea may have been expected (7 and 13 days). This diarrhea was mild and resolved as expected (2 days). Experimental foals developed diarrhea at an average of 3 days after challenge. This diarrhea was watery and estimated to be moderate to severe in volume. Watery diarrhea persisted for an average of 10 days. The diarrhea became less severe and persisted at least a mean of 45 days after challenge. The foals were able to maintain themselves on oral fluids. Necropsy and histopathologic evaluation revealed no significant lesions. This study indicates that diarrhea can be induced by administering live cell passaged rotavirus orally to foals and that the virus plays an important role in foal diarrhea.

110 WILD-TYPE EQUINE INFECTION ANEMIA VIRUS REPLICATES PREDOMINANTLY IN MATURE TISSUE MACROPHAGES, NOT IN PERIPHERAL BLOOD MONONUCLEAR CELLS. D.L. Clabough, L. Coggins, F. Fuller. College of Veterinary Medicine, North Carolina State University, Raleigh, NC.

In order to determine the in vivo cellular sites of viral replication during acute infection with wild-type Wyoming strain of equine infectious anemia virus (EIAV), two horses were experimentally infected with EIAV and tissue samples obtained at the peak of the first febrile episode. In situ hybridization and immunohistochemistry were used to localize cells supporting viral replication and identify the specific cell type, respectively. Serum reverse transcriptase activity was measured to correlate the magnitude of viremia with the febrile response. In situ hybridization identified the liver, spleen, lymph nodes, kidney, lung, and adrenal gland as the primary host tissue sites for viral transcription during acute infection. Combined immunohistochemistry, using a monoclonal antibody recognizing a cytoplasmic antigen of equine mononuclear phagocytes, and in situ hybridization for viral RNA, identified most infected cells as mature tissue macrophages. In contrast, in situ hybridization of adherent peripheral blood mononuclear cells collected from horses on various days during the first two weeks post-infection with Wyoming strain of EIAV, failed to detect any viral RNA in these cells. Serum reverse transcriptase activity in these two ponies corresponded with the degree of replication detected in tissue macrophages on the day of euthanasia. These results suggest that unlike other lentivirus infections in which tissue macrophages accumulate cytoplasmic viral RNA to a high level but fail to produce infectious virions, mature tissue macrophages are the primary source of the high titer viremia present during acute infection with EIAV. If other cell types are concurrently infected, their number is small and they do not appear to contribute markedly to virion production during this stage of infection.

111 PRELIMINARY INVESTIGATIONS OF THE FETAL INFECTIVITY OF EHRICLIA RISTICII IN BROODMARES. M.T. Long, T.E. Goetz, I. Kakoma, et.al. Univ. of Illinois at Urbana-Champaign, Urbana, IL.

The fetal infectivity of E. risticii was investigated in 8 broodmares negative for antibodies against E. risticii between 100 and 150 days of gestation. Six mares were infected and 3 mares served as noninfected controls. Each aborted fetus was necropsied and tissue samples from the liver, bone marrow, spleen, and mesenteric lymph nodes were inoculated into canine monocyte cell cultures. Each infected mare developed clinical signs of equine monocytic ehrlichiosis (EME), was confirmed to be ehrlichemic by serologic blood culture, and developed a high IFA titer against E. risticii. Four infected mares aborted between 77-110 days post-infection; E. risticii was isolated from 3 of these abortions. All of the abortions had similar histologic findings including enterocolitis, perportal hepatitis, and lymphoid hyperplasia of the mesenteric lymph nodes and spleen. None of the control mares developed clinical signs of EME, became ehrlichemic, seroconverted or aborted. Two of the infected mares delivered normal, healthy, term foals which had a positive presuckle antibody titer against E. risticii and one which was seronegative. This confirms that E. risticii can cross the equine placenta causing infection in the fetus which may then cause abortion.

112 INTERACTION OF BLUETONGUE VIRUS WITH BOVINE BLOOD MONONUCLEAR CELLS. S.M. Barratt-Boyes, J.L. Stott, P.V. Rossitto and N.J. MacLachlan. School of Veterinary Medicine, University of California, Davis, CA.

The in vitro bluetongue virus (BTV) infection of bovine peripheral blood mononuclear cells (PBMC) was investigated. Cultures of adherent, unstimulated non-adherent and interleukin-2 and mitogen-stimulated non-adherent PBMC were inoculated with BTV-10. Cells were harvested at various intervals up to 48 h after inoculation. A panel of bovine leukocyte-specific monoclonal antibodies (MAb), specific for CD2, CD4, CD8, monocytes and granulocytes, B cells, CD1 and CD35 cells and interleukin-2 receptor, were directly conjugated to fluorescein isothiocyanate, and a MAb specific for BTV major protein VP7 was directly conjugated to phycoerythrin. Cells were labelled with conjugated MAb in single and double-label immunofluorescence studies to determine the specific identity of BTV-infected cells. Viability of cells was determined by propidium iodide exclusion, and all analyses were performed using flow cytometry. The data revealed a clear difference between subpopulations of bovine PBMC in susceptibility to infection with BTV in vitro. Monocytes were readily infected with BTV, as were stimulated CD4+ cells. Infection was cytopathic to monocytes and stimulated lymphocytes, and the proportion of infected cells decreased after 24 h in all cultures. It was concluded that monocytes and CD4+ lymphocytes are probably important in the pathogenesis of BTV infection of cattle.
Four Quarter horse foals were presented for episodes of upper airway stridor when excited or stressed. There were 3 fillies (foals 1-3) and 1 colt (foal 4) and they ranged in age from 6 days to 2 months. Foals 1, 3, and 4 showed fasciculations and tensesness of their limb muscles during episodes of upper airway stridor. Foal 2 was recurrent upon presentation and had been so for approximately 24 hours. Endoscopy of foals 1 and 3 revealed that there was laryngeal and pharyngeal collapse or spasm occurring during these episodes of upper airway stridor. Electromyography of limb muscles in all foals and the dams of foals 1, 3, and 4 revealed spontaneous activity including fibrillation potentials and bizarre high frequency discharges. Foals 1 and 4 were documented to be hyperkalemic during episodes of upper airway stridor. Therapy of affected foals included limiting exposure to stressors, treatment with acetazolamide, and intravenous fluids (foal 2). An emergency tracheostomy and unilateral arytenoidectomy was performed on foal 1.
CONTRAST-ENHANCED COMPUTED TOMOGRAPHY IN SIX HORSES WITH CERVICAL STENOTIC MYELOPATHY. B. Reis Moore, T.C. Holbrook**, J. D. Stefanacci*, S.M. Reed, L.P. Tate*, M. Menard* The Ohio State University, Columbus, OH. *North Carolina State University, Raleigh, NC. **University of Georgia, Athens, Georgia. The use of contrast-enhanced computed tomography (CECT) to identify spinal cord compression associated with cervical stenotic myelopathy (CSM) was investigated. Myelograms (ante-mortem), CECT (post-mortem) and necrospy examinations were performed on six CSM affected horses and three unaffected horses. Histopathology of the spinal cord identified 10 compressive lesions in the 6 affected horses. Myelography and CECT demonstrated the 10 spinal cord compressive lesions, however, myelography falsely identified 2 sites and CECT falsely identified one site as spinal cord compressive lesions, which were not supported by histopathology. Additional information was obtained by CECT regarding the source and severity of spinal cord compression. Computed tomography identified stenosis of the vertebral canal with circumferential loss of contrast agent and documented lateral compressive lesions of the spinal cord due to malformed articular facets. Peripheric nerve compression was identified by CECT as impingement of the intervertebral foramen by malformed articular facets. Minimum sagittal diameter (MSD) values obtained from CECT images strongly correlated to necropsy MSD values, validating CECT as an accurate method for MSD measurement. The MSD values in the CSM affected horses were significantly narrowed (p < 0.05) from C3-C6, regardless of the site of spinal cord compression, when compared to the unaffected controls. This finding supports previous reports that suggest vertebral canal stenosis is an important feature in the pathogenesis of cervical stenotic myelopathy.

COMPARISON OF FIVE COMMERCIAL INSULIN RIA KITS FOR USE IN CATS - T.A. Lutz and J.S. Rand, School of Veterinary Science, University of Queensland, Brisbane, Australia

In the present study, we compared five commercially available human RIA kits for measurement of immunoreactive insulin (IRI) for their suitability for reliable use in cats.

The validation procedure of RIA kits was performed by investigating specificity (dilutional parallelism), sensitivity (10%-displacement value of tracer binding) and precision (by calculating mean coefficients of variation (CV)). Accuracy could not be determined because of the lack of a teline standard. Four samples of pooled cat plasma were used. The following insulin kits were compared: A) ESL Insulin Kit (ICN), B) Coat-A-Count (DPC), C) Immophase (Corning), D) Insulin RIA Kit (Amersham) and E) Phadeeph (Pharmacia).

Dilutional parallelism was best in kits A, B and E with a variation from the expected values of max. 50%. The kits performed well for low dilutions but yielded larger deviations from expected values for higher dilutions. Specificity in kits C and D was poor. Sensitivity was very high in kits B(3.4µIU/1kU/ml) and E(2.5), acceptable in kits A(6) and C(5), but unacceptable in kit D(13). Intraand interassay precision was best in kit E(2CV=8.8% resp.3.8%), kit A(8.4;9.4) and B(9.5;8.0). Kits C and D had CVs over 1% which was considered unacceptable.

In conclusion, only three of the insulin kits can be recommended for cats (kit A from ESL, kit B from DPC, kit E from Pharmacia). Unfortunately, the kits yielded absolute values for IRI differing by more than 100%, so that it seems to be necessary to establish separate reference values for every insulin RIA kit.

REGULATION OF ACTH AND MSH SECRETION FROM DOG ANTERIOR AND INTERMEDIATE LOBE PITUITARY CELLS IN LONG TERM CULTURE. C. Zerbe*, T. Clark, J. Sartin and R. Kemppainen. College of Veterinary Medicine, Auburn University, AL and 'University of Pennsylvania, Philadelphia, PA.

The effects of long term incubation with ovine corticotropin-releasing hormone (CRH) or dexamethasone (DEX) containing media, on ACTH and alpha-melanocyto stimulating hormone (MSH) secretion were determined for cultured rat and dog anterior (AL) and intermediate lobe (IL) cells. The amount of ACTH secreted per mg/dl respectively at less than 2 days of age. These values did not change over time. This study reports the normal CSF parameters for foals of various ages.

NORMAL CEREBROSPINAL FLUID VALUES IN THE FOAL: BIRTH TO 42 DAYS OF AGE - M. D. Furr, and H. Bender. Marion duPont Scott Equine Medical Center, Virginia-Maryland Regional College of Veterinary Medicine, Leesburg, Va.

The purpose of this project was to evaluate the normal CSF parameters in healthy foals from birth thru 42 days of age to provide age-specific normal ranges. Fourteen clinically normal, spontaneously delivered cross-bred foals had CSF collected and analyzed for sodium, potassium, magnesium, total protein, WBC, and RBC. Samples were collected at least 48 hours in 3 foals, 11-14 days of age in 4 foals, 21-22 days of age in 3 foals, and 31-42 years of age in 4 foals. Each foal was sampled only once, to avoid the unknown effects of CSF collection on subsequent analysis. Results show that foals less than 2 days of age have a CSF protein value of 109.3 ± 9.7 mg/dl (mean ± 1 SD). 109.3 ± 22.7 was found in foals 10-14 days old, 60.4 ± 22.4 in foals 21-22 days old, and 58.5 ± 17.0 in foals 31-42 days old. CSF sodium, potassium and magnesium were 148.0 ± 7.2 (mmol/L), 2.02 ± 0.7 (mmol/L), and 2.43 ± 0.16 mg/dl respectively at less than 2 days of age. These values did not change over time. This study reports the normal CSF parameters for foals of various ages.

NORMAL CEREBROSPINAL FLUID VALUES IN THE FOAL: BIRTH TO 42 DAYS OF AGE - M. D. Furr, and H. Bender. Marion duPont Scott Equine Medical Center, Virginia-Maryland Regional College of Veterinary Medicine, Leesburg, Va.

The purpose of this project was to evaluate the normal CSF parameters in healthy foals from birth thru 42 days of age to provide age-specific normal ranges. Fourteen clinically normal, spontaneously delivered cross-bred foals had CSF collected and analyzed for sodium, potassium, magnesium, total protein, WBC, and RBC. Samples were collected at least 48 hours in 3 foals, 11-14 days of age in 4 foals, 21-22 days of age in 3 foals, and 31-42 years of age in 4 foals. Each foal was sampled only once, to avoid the unknown effects of CSF collection on subsequent analysis. Results show that foals less than 2 days of age have a CSF protein value of 109.3 ± 9.7 mg/dl (mean ± 1 SD). 109.3 ± 22.7 was found in foals 10-14 days old, 60.4 ± 22.4 in foals 21-22 days old, and 58.5 ± 17.0 in foals 31-42 days old. CSF sodium, potassium and magnesium were 148.0 ± 7.2 (mmol/L), 2.02 ± 0.7 (mmol/L), and 2.43 ± 0.16 mg/dl respectively at less than 2 days of age. These values did not change over time. This study reports the normal CSF parameters for foals of various ages.
EVALUATION OF C-PEPTIDE RADIOIMMUNOASSAY KITS FOR USE WITH FELINE AND CANINE SERUM AND URINE.

W.E. Monroe, W. Chickering, L. Eng. Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, Virginia

Radioimmunoassay kits for analyzing human C-peptide were screened for validity for use with canine serum and urine. Blood and urine were collected prior to and 1/4 and 2/3 hours respectively after giving 6 mg/kg of dextrose IV to each of 3 cats. Samples were similarly drawn from 3 dogs before and after giving 600 mg/kg of dextrose IV. Serum was collected, pooled and frozen at -70 C. Urine was pooled and divided into two aliquots, one neutralized, and frozen at -70 C. Samples were assayed according to each kit manufacturer's directions. Kits tested using feline fluids included Diagnostic Products Corporation's Double Antibody kit, Diagnostic Systems Laboratories Inc. C-Peptide, Antiserum K6. All of the above except Diagnostic Products Corporation's kit were also used with canine fluids. Antibodies in the kits were not specific for canine or feline C-peptide as demonstrated by a failure to detect a normal biological response (increase in serum and urine C-peptide concentration after administration of dextrose). Dilutional parallelism was also not evident. None of the kits tested, therefore, appeared to be valid for use with canine or feline sera or urine.

EFFECTS OF ENALAPRIL ON HEALTHY CATS

B. Sandberg, R. Flamin, T. Buffington, and J. Blaisdell; College of Veterinary Medicine, The Ohio State University, Columbus, OH.

The precise incidence of systemic arterial hypertension (SAH) in cats is unknown, but it occurs in well over 50% of cats azotemic from primary renal disease. Enalapril (E), an angiotensin converting enzyme (ACE) inhibitor, is useful for treating SAH in man and therefore may be useful for the cat. This study was conducted to provide information about oral dose and frequency of administration for E in cats. Sixteen healthy cats were given orally either once or daily for 10 days, 0.25 or 0.5 mg/kg body weight (BW). BW, feed and water intake, urine (U) volume (V) and electrolyte output, and plasma concentrations of ACE were measured. A 95% reduction in ACE occurred between 2 and 4 hours after either dose, and it remained depressed to less than 50% of control for 2 to 3 days. Neither feed consumption nor UV changed; however, U excretion of Na+ and Cl- increased slightly, and plasma concentrations of electrolytes remained unchanged. Conclusions for E in cats are: (1) it does not decrease appetite or BW, (2) it promotes U loss of both Na and Cl, and does not increase UV, (3) surprisingly, it did not reduce, but paradoxically either promoted or did not change K+ excretion.

EVALUATION OF C-PEPTIDE RADIOIMMUNOASSAY KITS FOR USE WITH FELINE AND CANINE SERUM AND URINE.

ACVIM ABSTRACTS

139
EVALUATION OF LINCOMYCIN IN HEALTHY DOGS USING A NON-INFECTED AND INFECTED TISSUE CAGE MODEL. J. McDavitt, R.D. Walker, R. Yancey, J.M. Kruger. College of Veterinary Medicine, Michigan State University, E. Lansing, MI, The Upjohn Co., Kalamazoo, MI.

Lincomycin has been used for treating Staphylococcus intermedius induced pyoderma in dogs. Lincomycin was administered orally at 22 mg/kg, q12 hours for a total of 7 doses. Serum and fluid from subcutaneous tissue cages (TC) were collected sequentially beginning immediately post inoculation with the 7th dose in 3 healthy dogs. Lincomycin concentrations were determined by bioassay. After a wash-out period the TC in these dogs were infected with a S. intermedius (6.7 x 10^6 cfu/TC)-gelatin bead suspension. Six hrs after infection, the above mentioned dosing and sampling protocol was repeated. In addition, concentrations of viable S. intermedius were determined in all TC fluids. Differences in lincomycin concentrations from infected vs noninfected studies were compared statistically. Peak serum concentrations (C_max) were greater in dogs with infected TC than in dogs with noninfected TC although the time to C_max was the same for both groups. Peak TC fluid concentrations from infected TC were also greater. The concentration of S. intermedius in TC fluid immediately post infection was 3.6 x 10^6 cfu/ml. S. intermedius concentration peaked at 2.4 x 10^9 cfu/ml 12 hrs after therapy was initiated and averaged 2.0 x 10^8 cfu/ml for the rest of the study. These results suggest that an infection significantly alters lincomycin disposition in dogs.

CLINICAL UTILITY OF VENOUS BLOOD GAS ANALYSIS IN DOGS. SH Kilborn, HA Pook, BN Bonnett. Ontario Veterinary College, University of Guelph, Guelph ON.

Although clinical examination is a powerful tool for generating diagnoses and therapeutic plans, its use has not been quantified in veterinary medicine. This study evaluated the use of clinical examination in generating acid-base status and its effect on fluid therapy decisions in 200 canine referral cases. Two clinicians (a faculty member and resident in internal medicine) predicted the acid-base status (base excess) in each of these cases and made recommendations for fluid therapy after sequential calculation of the following: 1) history and physical examination; 2) serum total carbon dioxide (TCO2), anion gap, and biochemical profile; 3) venous blood gas (VBG). This study evaluated the agreement between the predicted base excess (based on clinical evaluation) and the base excess (BE) measured by VBG analysis. The agreement between the two clinicians, and changes in fluid therapy recommendations at each level. Agreement was assessed using the Kappa statistic (the appropriate measurement of agreement beyond chance).

Based on the BE from VBG analysis, 69% of dogs were normal, 28% were acidicotic, and 3% were alkalotic. Agreement between the predicted BE and the BE from the VBG analysis resulted in Kappa values of 0.44 and 0.38 for each clinician. The magnitude of error was greatest in the 6 cases that were alkalotic. Agreement between the two clinicians following the clinical examination resulted in a Kappa value of 0.49. Modification of initial therapeutic plans in each clinician occurred in 28% of cases following evaluation of TCO2, anion gap, and biochemical profile but in only 2% of cases following VBG analysis. In conclusion: 1) the agreement between actual and predicted BE was low for both clinicians; 2) agreement between the two clinicians was not dependent on previous levels of clinical experience was moderate; 3) VBG results rarely altered case management decisions that were based on previous clinical and laboratory data.

ANTIBODY RESPONSE TO BOVINE RESPIRATORY SYNCYTIAL VIRUS PROTEINS IN COLOSTRUM-FED AND COLOSTRUM-DEPRIVED CALVES. E.B. Belknap, J.K. Collins, V.K. Ayers. College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

Bovine respiratory syncytial virus (BRSV) is an important cause of respiratory disease in calves. Colostral-feeding as a source of passive immunity modifies the severity of BRSV infections. The purpose of this project was to determine if antibodies which react with certain BRSV proteins play a role in this protection. Serum antibody responses were measured initially by radioimmuno precipitation (RIP) assay and SDS-polyacrylamide gel electrophoresis, and later by Western blots. Antibody responses were determined initially by radioimmunonprecipitation (RIP) assay and SDS-polyacrylamide gel electrophoresis, and later by Western blots. Antibody responses are detected by 35S methionine labeling of antigen in the RIP assays, and the observed protein bands on polyacrylamide gel electrophoresis, and later by Western blots. Antibody responses are detected by 

THE EFFECT OF DIETARY FIBRE ON OR0 CAECAL TRANSIT TIME IN DOGS. K. Papasouliotis, D.V., T.J. Gruffydd-Jones BVet Med, PhD, University of Bristol Veterinary School, Avon, UK. S. Righy, J.W. Johnson BSc, PhD, Waltham Centre for Pet Nutrition, Leicestershire, UK.

Dietary fibre decreases post prandial hyperglycaemia in man and dogs and has proved beneficial in the management of diabetes mellitus. Decreasing or0 caecal transit time (OCTT) could be a contributory factor in achieving this effect. This study investigated breath hydrogen profiles as a measurement of OCTT in six male Beagles (aged 18 months) following the addition of soluble fibre (20g guar) and insoluble fibre (20g wheat bran) to a standard complete canned food (STD).

Readings were taken every 15 minutes and treated by capusum analysis to assess the rate of increase of hydrogen production. OCTT was taken as a rise of 5 ppm of hydrogen sustained for three consecutive readings. Results are summarised below:

| Diet       | OCTT | OCTT Range |
|------------|------|------------|
| STD        | 135 mins | 120-150 mins |
| STD + guar | 150 mins | 90-240 mins |
| STD + wheat bran | 128 mins | 105-195 mins |

No significant differences were detected in OCTT between the three diets (P>0.05, ANOVA) although the levels of fibre supplementation were considerably higher than levels which have previously been shown to reduce postprandial hyperglycaemia.
neonatal calves were freely assigned to receive E. coli LPS at 0 (saline), 0.2, 2.0, 20 μg/kg, be similarly compromised. The differences among groups biochemical responses in calves vary depending on dosage method, or interaction effects for respiratory rate, fecal bolus or infusion over 50 minutes. Clinical variables were subjectively scored. Heart rate, respiratory rate, temperature, mean arterial pressure (MAP), hematocrit (HCT), plasma protein (PP), leukocyte (WBC) count, and plasma glucose and lactate levels were also measured. Within one hour of LPS exposure, all calves appeared to be similarly compromised. The differences among groups became more evident with time. Among LPS treated calves, sickness was induced a few isolated significantly different responses in calves but did not effect the general response to endotoxin.

The changes in the urinary gamma glutamyl transferase/urinary creatinine ratio of fresh urine samples were documented in healthy horses and in hospitalized horses treated with gentamicin for pneumo-nia/pleuroneumonia. The \( \text{uGGT/SCr} \) ratio was measured on days 1, 3 and 10 in five adult healthy horses, in five adult healthy horses treated with gentamicin at recommended dosage and in nine adult horses treated with gentamicin at recommended dosages for pleuroneumona. The plasma creatinine as well as the gentamicin trough levels were measured on the same days.

The sick horses had a significantly higher \( \text{uGGT/SCr} \) ratio (12.0-497.9 i.u./gCr) than the two groups of normal horses (10.5-93.3 i.u./gCr); without any significant changes in the plasma creatinine or elevation in the gentamicin trough level. The changes over time were not significant. The \( \text{uGOT/SCr} \) ratio was higher in the normal horses (17.1-51.4 i.u./gCr) than in previous reports. This data suggests elevations of the \( \text{uGOT/SCr} \) ratio can occur without clinically significant renal impairment requiring changes or withdrawal of the gentamicin administration.

In the horse, the amniotic sac floats free in the allantoic cavity attached only by the umbilical stalk. The allantoic cavity stores waste products of the fetal kidneys which are passed through the urachus. Amniotic fluid allows for growth and movement of the fetus and accumulates epithelia cells and nasopharyngeal secretions. The purpose of this study was to compare biochemical values for amniotic fluid against allantoic fluid.

Amniocentesis was performed on 10 normal mares in late gestation (323.8±10.2 days) and fluid was collected from both allantoic and amniotic cavities. The samples were immediately analyzed using methods routinely used for equine serum biochemistries. Variables were compared by one-way ANOVA. Compared to amniotic fluid values, allantoic fluid valves were significantly higher for specific gravity, SDH, T.bilirubin, GGT, Cr, P, total protein, and globulin and were significantly lower for Na, Cl and alkaline phosphatase. These results provide useful data for future investigations of equine amniotic fluid and might potentially be useful in assessing health of the fetus.

The hemorheologic effects of furosemide were investigated in 4 horses. Hematologic and rheologic tests included complete blood count, red blood cell (RBC) morphology, erythrocyte sedimentation rate (ESR), whole blood viscosity (WBV), and RBC filterability through polycarbonate filters with an average pore size of 3 μm. To simulate exercise-associated splenic contraction, 1 mg of epinephrine was administered IV. Blood samples were drawn for hemorheologic tests before and 3 min after epinephrine administration. The next day, hemorheologic changes were determined before and 3 h after administration of furosemide (1 mg/kg bwt IM), and after epinephrine administration at the 3 h sampling.

Administration of epinephrine resulted in significant (P < 0.05) increases in packed cell volume (PCV), RBC count and WBV, and a decrease in ESR. Furosemide treatment was associated with significant (P < 0.05) increases in mean cell hemoglobin concentration and WBV, but morphology and filterability of RBC did not change. Post-epinephrine values for PCV and WBV after furosemide treatment were higher compared to values observed after administration of epinephrine alone, but the changes were not statistically significant. It was concluded that administration of epinephrine closely simulates the equine hemorheologic response to exercise. Further, furosemide may exacerbate exercise-associated hyperviscosity in the horse.
ATRESIA COLI IN FOALS: 7 CASES (1964-1990).
G. Naëder, S. Laverty, R. Drolet and J. Naylor.
Western College of Veterinary Medicine,
University of Saskatchewan, and Faculté de médecine vétérinaire, Université de Montréal,
Canada.

Intestinal atresia is uncommon in foals. The distal large colon and proximal small colon are the most common missing segments. The etiology of atresia coli is unknown but hereditary factors are believed to be involved in the horse. The occurrence of equine atresia coli was 0.44% in the Veterinary Medical Data Base. In addition, an occurrence of equine intestinal atresia of 1.3% was obtained at the Large Animal Hospital, University of Montreal. Five cases records from Veterinary Medical Data Base and two from the University of Montreal were reviewed. Breed distribution of cases was: Appaloosa (2 foals), Morgan (1), Standardbred (1), Thoroughbred (1), Paint Horse (1) and Quarter Horse (1). Five foals had type III or blind-end atresias and two foals had type II or cord atresias. The pelvic flexure was absent in two cases. Clinical signs were progressive abdominal distension, colic, lack of fecal production and lack of response to enema administration. Two cases presented a blind ending rectum on digital palpation. Surgical correction was attempted in three foals and was unsuccessful in all cases. A grave prognosis should be given when this condition is diagnosed in foals.

PHARMACOKINETICS OF CEFOTAXIME IN NEONATAL PONY FOALS. S.Y. Gardner,
R.W. Sweeney, T.J. Divers. School of Veterinary Medicine, New Bolton Center, University of Pennsylvania, Kennett Square, Pennsylvania.

The pharmacokinetics of cefotaxime after a single intravenous dose in neonatal foals was investigated. Cefotaxime was administered at a dose of 40 mg/kg body weight to 5 healthy 7-day-old pony foals. Serum samples were collected prior to injection and at 5, 10, 20, 30, 45, 60, and 90 minutes and at 2, 3, 4, 6, and 8 hours following administration. Cefotaxime concentrations in serum were determined by HPLC. Cefotaxime disposition was best described by a two-compartment model with rapid distribution ($t_{1/2\alpha} = 0.07$ h) and elimination ($t_{1/2\beta} = 0.6$ h). The mean apparent volume of distribution and systemic clearance were 0.29 L/kg and 0.31 L/kg/h, respectively.