Poster #1, Clinical Case Report/Series

RENAILOSTEODYSTROPHY ASSOCIATED WITH JUVENILE NEPHROPATHY IN A 6-MONTH-OLD LABRADOR RETRIEVER
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Renal secondary hyperparathyroidism is a common sequela of chronic renal failure in the dog, but is not commonly observed in juvenile patients. A 6 month old female Labrador retriever with juvenile nephropathy and associated renal osteodystrophy is presented. Older dogs with this condition typically have highly pliable facial bones due to increased parathormone-induced osteoclastic activity subsequent to progressive hyperphosphatemia and decreased serum ionized calcium. The pathogenesis in this dog is similar with reduced glomerular filtration rate causing pronounced hyperphosphatemia [23 mg/dL (2.5-5)], decreased ionized calcium [0.58 mmol/L (1.25-1.45)], and increased parathormone levels [62.0 pmol/L (0.5-5.8)]. Other abnormalities included marked renal azotemia [BUN 171 mg/dL (8-24), creatinine 5.5 mg/dL (0.5-1.4)], isosthenuria (urine specific gravity 1.009), hypocalcemia [6.1 mg/dL (8.8-11.2)], and anemia [HCT 14.4% (34-60)]. Many cases of juvenile nephropathy also show concurrent signs due to decreased formation of calcitriol, which may include predisposition towards fibrous osteodystrophy and rickets. The osseous lesions in this case were limited to the facial bones which were markedly firm and swollen due to hyperostosis and fibrous osteodystrophy. 25-hydroxyvitamin D was within normal limits [106 nmol/L (60-125)]. The lesions are typical of a familial nephropathy, which is suspected in this case. Such disorders have not been described in the Labrador retriever and an individual renal developmental disorder cannot be excluded. The dog was fed a commercial dog food and no familial history of renal disease was reported. Nutritional secondary hyperparathyroidism is more common in juvenile dogs but presents with progressive lameness and long bone abnormalities. Vitamin D-dependent rickets, type I and type II, was also considered as a differential diagnosis but was also excluded.

Poster #2, Clinical Case Report/Series

A RETROSPECTIVE STUDY OF EQUINE ACTINOBACILLOSIS, 1999-2011
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Actinobacillus spp. can cause disease in both foals and adult horses. The goal of this retrospective study was to conduct a pathological review of archived equine cases from which Actinobacillus spp. was isolated during 1999-2011. Necropsy cases and clinical cases from which specimens were submitted for culture were included. Clinical history, signs, bacterial species isolated, and associated lesions were documented from necropsy, histopathology, cytology, and bacteriology records. Archived histopathology slides were reexamined, and lesions were classified. From 116 equine cases, 129 Actinobacillus spp. were isolated primarily from foals (0-6 months) and adults (> 2 years). Isolates included Actinobacillus equuli subsp. equuli (34.1%), Actinobacillus spp. (species not identified) (31.0%), and hemolytic Actinobacillus spp. (21.7%); Actinobacillus ureae, Actinobacillus lignieresii, and Actinobacillus pleuropneumoniae were isolated less frequently. Of the 32 necropsy cases, 30 cases, including 7 adult horses, had septicemia-associated lesions. Histologically, important lesions included: embolic pneumonia and nephritis, splenic lymphoid necrosis, hepatocellular necrosis, adrenalitis, and encephalitis. From 84 clinical cases, Actinobacillus spp. was isolated most commonly from the respiratory tract of foals and adults (15 and 18 isolates, respectively). In conclusion, Actinobacillus spp. are important pathogens of both foals and adult horses, and septicemic Actinobacillosis can occur in adult horses. Both hemolytic A. equuli subsp. haemolyticus and A. suis are associated with equine disease, and both bacteria produce a hemolytic RTX toxin. The role of RTX toxins in the pathogenesis of equine Actinobacillosis remains unclear, because greater numbers of Actinobacillus equuli subsp. equuli were isolated than were hemolytic Actinobacillus spp.
Poster #3, Experimental Disease

A COMPARISON OF TWO HEMATOLOGY ANALYZERS USING BLOOD FROM LABORATORY RATS
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It is imperative that new instruments acquired for the completion of the clinical pathology studies (e.g., hematology analyzers) be examined for precision and performance. The purpose of this study was to compare two hematology instruments using blood from laboratory rats. Blood collected in EDTA was analyzed for a complete blood count using two different hematology analyzers – the Hemavet 1700 and the Advia 2120i. The results indicated that for most analytes, both instruments exhibited excellent precision (CV ≤ 5%). In general, a strong relationship was observed between instruments for the hematocrit, hemoglobin, red blood cell count, mean corpuscular volume, and white blood cell count values (r ≥ 0.87). Correlations were not as strong for mean cell hemoglobin, mean cell hemoglobin concentration, and platelet count. The Advia analyzer demonstrated some positive and negative biases compared to the Hemavet analyzer, but, in general, did not exceed 10%. Due to apparent inaccuracies, the WBC differential for the Hemavet analyzer was not evaluated. A strong agreement was demonstrated. The Advia analyzer does not measure reticulocyte counts. Thus, the Advia analyzer reticulocyte counts were compared to a manual reticulocyte count and showed a strong relationship (r = 0.94). In conclusion, both instruments demonstrated reliable hematology results useful for research studies. However, since bias did exist, the instruments are not interchangeable. Thus, a single instrument would need to be used throughout a particular study for hemato logic evaluations.

Poster #4, Experimental Disease

NODULAR ASTROCYTOSIS IN SIMIAN IMMUNODEFICIENCY INFECTED Rhesus macaques (MACACA MULATTA)
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Simian immunodeficiency virus (SIV) is used extensively as a model for human immunodeficiency virus (HIV) pathogenesis and is associated with a myriad of neuropathologic changes including encephalitis and peripheral neuropathy. Herein we report the histologic and immunohistochemical findings of a unique presentation of nodular astrocytosis in SIV infected rhesus macaques (Macaca mulatta). Five SIV-infected rhesus macaques were selected from 1,206 SIV-infected rhesus macaques necropsied from 1997-2008 (0.4%). 5/5 animals had concurrent opportunistic infections consistent with simian AIDS and 0/5 had concurrent SIV encephalitis. 2/5 had neurologic dysfunction noted during clinical examination and 3/5 had incidental findings during histologic examination. Histologic examination revealed multifocal nodular masses in predominately the gray and white matter of the thalamus and brainstem that were characterized by interlacing plump to elongate astrocytes that had abundant cytoplasm and large, reactive nuclei. There was moderate atypia and the nodules were often interlaced around small capillaries. Immunohistochemistry for Simian Virus 40, rhesus cytomegalovirus, and rhesus lymphocryptovirus failed to detect any antigen. The cause of this unique presentation of nodular astrocytosis in SIV infected rhesus macaques is unknown; however the intense immunoreactivity of p53 in the lesions compared to adjacent tissue suggests that a local derangement in astrocyte hypertrophy and function may play a role.
**Poster #5, Experimental Disease**

**IN VIVO ANALYSIS OF MENINGEAL STROMAL CELLS IN THE LIVING BRAIN DURING VIRAL MENINGITIS**

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Neurotropic viruses and their associated diseases represent a major global health concern. Only by fully understanding the immune response during these infections can we hope to develop therapeutic interventions. Meningitis is an immune-mediated disease induced by many pathogens including viruses commonly observed in humans. To better understand the pathogenesis of this disease, we study a model of infecting mice with lymphocytic choriomeningitis virus (LCMV). LCMV (a noncytopathic virus) induces a fatal disease entirely dependent on the immune system. We have recently shown that LCMV heavily infects fibroblast-like cells called meningeal stromal cells (MSCs) during meningitis development. Based on their anatomical position and similarity to lymphoid stromal cells, we postulate MSCs might serve as master regulators of immune cells that infiltrate the brain during infection. Consistent with this hypothesis, we observed virus-specific cytotoxic lymphocytes in close proximity to MSCs following LCMV infection. Using microarrays, we also observed that MSCs express genes for chemoattractants, antigen processing machinery, and immunoregulatory molecules in infected mice. By flow cytometry, we validated that two potent T-cell regulators, galectin 3 and 9, are highly upregulated on MSCs during acute viral meningitis. Thus, we theorize that MSCs play an important role in regulating immune cells arriving in the CNS during states of inflammation. To elucidate how MSCs function in the living brain, we developed a novel approach involving injection of fluorescently-tagged, MSC-specific antibodies into the living brain. We then visualized MSCs before and during infection by intravital two-photon laser scanning microscopy. This new approach allows us to study interactions between MSCs and immune cells in real time, which should reveal novel insights into how MSCs modulate immunity during CNS viral infection.

**Poster #6, Experimental Disease**

**TRANSFERRIN RECEPTOR EXPRESSION IN SERUM EXOSOMES AS A MARKER OF EQUINE REGENERATIVE ANEMIA**

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Evaluation of erythrocyte regeneration in horses is challenging, as they do not release reticulocytes into the peripheral blood. We investigated transferrin receptor (TfR) expression in exosomes as a non-invasive method of characterizing the regenerative response in anemic horses. TfR is highly expressed in equine bone marrow, primarily on erythroid precursors, where it plays a role in iron uptake. We hypothesized that TfR expression would increase during a regenerative response. Exosomes are 30-100 nanometer vesicles containing proteins and RNA, which are actively secreted from the plasma membrane of cells. Reticulocytes dispose of proteins, including TfR, through exosome secretion. Therefore, serum exosomes reflect processes occurring in the bone marrow. During a regenerative response, we expect bone marrow reticulocytes to secrete increased levels of TfR-containing exosomes. Six horses were phlebotomized to induce anemia. Serum exosomes were harvested by ultracentrifugation on Days 0, 4, 7, 10, 14 and 21. TfR levels on the exosomes were measured by Western blot and relative densitometry. Regenerative anemia was confirmed by decreased hematocrits and decreased bone marrow myeloid:erythroid ratios. In all horses, TfR expression increased significantly over Days 7-10. TfR levels peaked on Day 10 and were a mean 3-fold higher than Day 0 levels. To identify exosomes as the source of TfR, we confirmed the size of the harvested particles by transmission electron microscopy (TEM), flow cytometry, and density gradient centrifugation. Appropriately sized particles stained with TfR on flow cytometry, and were evident on TEM. Sucrose density gradient fractions expected to contain exosomes also contained TfR. These data suggest that serum exosome TfR expression may provide a marker for regeneration in anemic horses.
Sea otters are a species sensitive to marine environmental health, and evaluation of stranded animals is crucial to studies of their populations. Here, a rare case of aortic aneurysm in a young adult (~5 years old), male northern sea otter (Enhydra lutris kenyoni) is presented. Mortality was due to exsanguination following dissection of an aneurysm in the thoracic descending aorta. Histopathology showed an aortic wall severely disrupted by an inflammatory reaction with abundant rod-shaped bacteria; Aeromonas hydrophila was isolated from several organs. Sections of grossly normal aorta also showed histologic evidence of disruption in the tunica media. Endocardiosis was present in the mitral and aortic valves as well as bilateral degeneration of scapulohumeral and coxofemoral joints. There was no evidence of vascular parasitism, as has been described in wild coyotes and domestic horses. Unlike humans, aortic aneurysms are rare in wild mammals and this is the first published report of aortic aneurysm in a sea otter. A genetic component may exist, such as in bovine Marfan syndrome, and the degree of early-onset degenerative joint disease resembles aneurysm-osteoarthritis syndrome recently described in humans. Also, as A. hydrophila is environmentally common and typically an opportunistic pathogen, congenital, nutritional and/or environmental factors may have contributed to aneurysm formation. Examination of other archived cases is being pursued to further explore this rare phenomenon and determine the significance to otter populations.
CHARACTERIZATION OF A CYNOGLOSSUS MACAQUE MODEL OF POSTMENOPAUSAL CEREBROVASCULAR ATHEROSCLEROSIS  
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The extent and complication of carotid bifurcation atherosclerosis (CBA) is a major determinant for the risk of developing stroke. Progress in understanding the pathogenesis of atherosclerosis at this arterial site has been hampered by the lack of a suitable animal model. The purpose of this study was to define a nonhuman primate model of CBA by defining the plaque characteristics and risk factors associated with plaque progression among surgically postmenopausal cynomolgus monkeys (Macaca fascicularis) fed an atherogenic diet. Additionally, we sought to determine if estrogen replacement with conjugated equine estrogens (CEE) might reduce the extent and severity of CBA and whether the model shared with human primates the ability to remodel the carotid bifurcation to maintain adequate lumens during plaque progression. Left and right carotid bifurcations were not significantly different in terms of plaque size or severity. However, the right CBA carotid severity was modulated by factors (Hepatic Lipidosis Score and baseline plasma IL-18) that did not have an effect on the left. Total plasma cholesterol and low density+very low density lipoprotein cholesterol (LDLC+VLDLC) was positively associated with both CBA and coronary artery plaque size (P<0.007, R<0.55). However, the degree of decrease in high density lipoprotein cholesterol (HDLC) was not associated with decreased CBA extent or severity as is the case with coronary artery atherosclerosis. Estrogen replacement decreased the extent of left and right CBA but only decreased the severity of right CBA plaques. When treated with CEE, the extent and severity of CBA plaques did not decrease nearly as much as in the coronary arteries. In the cynomolgus model, remodeling of the carotid bifurcation occurs as it does in the coronary arteries, and is comparable to that of human primates.

SEGMENTAL SYRINGOMYELIA IN A HOLSTEIN-FRIESIAN CALF  
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A 1-year-old, intact male Holstein-Friesian calf presented to the University of Glasgow in good body condition with an abnormal hypermetric "hopping" gate and bilateral hyperextension of his hindquarters since birth. Analgesia did not visibly improve lameness. Serum biochemistry, hematology, and parasitology were unremarkable. Serum was antibody negative for louping ill virus and bovine herpesvirus 1, but positive for bovine viral diarrhea virus (BVDV). Due to the poor prognosis, the animal was humanely euthanized. On gross examination, the spinal cord at the level of the thoracolumbar intumescence (T8 to L4) was markedly enlarged by an intramedullary, soft linear swelling. On cut section, the central canal and grey matter were segmentally replaced by a large, well-demarcated cystic cavity. Histologically, the spinal cord was markedly dilated by a large, central syrinx that merged with and replaced the central canal. The syrinx was intermittently lined with remnants of ependyma of the central canal. The grey matter was markedly compressed and distorted on either side of the cavity; the white matter tracts were multifocally pale and loosened by clear spaces of myelin degeneration and edema, but did not communicate directly with the central syrinx. A post-mortem ear notch sample was antigen negative for BVDV. The segmental nature of the syringomyelia in this case is highly unusual. Given the lack of notable vertebral column abnormalities, morbidity in this calf likely resulted from a segmental syringomyelia as a result of dysraphism or, less likely, a dynamic spinal cord compression at the thoracolumbar intumescence.
CHARACTERIZATION OF IAPP IN A POLAR BEAR SUFFERING FROM A PANCREATIC ISLET CELL TUMOR

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Pancreatic insulin-secreting tumors, also known as insulinomas, are fairly common in the ferret but uncommon in other domestic animals such as dog, cattle and guinea pig. Although a β-cell insulin-secreting tumor was previously observed in a 15-year-old male raccoon, they are rarely reported in captive or wild animals. Pancreatic islet cell tumors may contain functional β cells releasing inappropriately high amounts of insulin. Diagnosis of insulinoma is suspected on the basis of clinical signs and concurrent hypoglycemia and hyperinsulinemia. However, the definitive diagnosis requires histopathologic examination of the tumor. Interestingly, amyloid fibril deposits (IAPP) have been established as a common pathological feature in insulinomas. Herein, we report a 25-year-old male polar bear suffering from a pancreatic islet cell tumor. The aim of this report is to present a case of this rare tumor in a captive polar bear. The implication of potential risk factors such as high carbohydrate diet or the presence of amyloid fibril deposits was assessed. Necropsy examination revealed pulmonary congestion, pericardial serous fluid and digitiform fibrous projection within atria. Several nodules observed in the liver, spleen, pancreas, intestine, and thyroid glands were submitted for histopathologic analysis. Interestingly, the multiple neoplastic nodules were unrelated and included a pancreatic islet cell tumor. Immunohistochemistry of the pancreas confirmed the presence of insulin and islet amyloid polypeptide (IAPP) within the pancreatic islet cells. The islet amyloid polypeptide (IAPP) gene was extracted from the paraffin-embedded liver tissue and sequenced. IAPP cDNA from the polar bear exhibits some differences as compared to the sequence published for several other species. Moreover, different factors responsible for neoplasms in bears such as diet, infectious agents and industrial chemical exposure are reviewed. This case report raised several issues that further studies may address by evaluating the prevalence of cancers in captive or wild animals.

CANINE ANAL SAC GLAND CARCINOMAS: COMPARISON OF CLINICAL AND HISTOPATHOLOGIC FEATURES OF TUMORS WITH AND WITHOUT METASTASIS

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Anal sac gland carcinomas (ASGCs) are a common neoplasm in dogs. Though complete surgical excision can be curative, a subset of ASGCs metastasize to regional lymph nodes and other viscera. We aim to identify clinical and histopathologic features of ASGCs that may predict metastasis. Medical records from 32 canine patients diagnosed with ASGC at the University of Pennsylvania School of Veterinary Medicine from 2006 to 2012 were reviewed for signalment data, primary neoplasm size, presence of hypercalcemia, and metastatic spread. Surgical biopsies from these patients were evaluated for histopathologic parameters: pattern of neoplastic cells (solid, tubular, rosette), mitotic index, nuclear pleomorphism, vascular invasion, and necrosis. Each parameter was then compared between dogs with ASGC metastasis (8/32) and dogs without (24/32). In this study, non-metastatic ASGCs varied widely in amount of tubular differentiation (<10% to >75%) and showed moderate to marked rosette formation. Metastatic ASGCs had 10-75% tubular differentiation with minimal rosette formation. Both groups showed similar nuclear pleomorphism (29/32 mild to moderate), necrosis (22/32 had <50%), mitotic index, and predominance of a solid neoplastic cell arrangement (26/32). Castrated males and mixed breed dogs were most commonly represented (22/32 and 15/32, respectively), and average age at diagnosis was similar between groups (mean 9.8yr). Hypercalcemia was reported in dogs from both groups, with higher incidence in dogs with metastatic ASGCs (5/8 vs 8/24). Given the subtle differences between metastatic and non-metastatic ASGCs in this population, the study will be expanded to a larger number of cases to determine which parameters, if any, are significantly associated with metastasis.
Poster #13, Experimental Disease

DOMOIC ACID TOXICOSIS IN CALIFORNIA SEA LIONS: A POTENTIAL NEW MODEL FOR HUMAN TEMPORAL LOBE EPILEPSY

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Rodents are commonly used to study temporal lobe epilepsy, the most common type of epilepsy in humans. However, in epileptic patients, hippocampal damage and shrinkage is more consistent and severe than that of the amygdala; whereas, in rodents the opposite is true. During some harmful algal blooms along the California coast, sea lions (Zalophus californianus) are exposed to domoic acid, which can cause status epilepticus and temporal lobe epilepsy. To begin testing whether sea lions might be a good model of human temporal lobe epilepsy, volumes of the hippocampus and amygdala were measured. Two control and three epileptic sea lions with poor clinical prognoses were intracardially perfused with fixative immediately after euthanasia. Brains were hemisected and divided into 2-cm-thick coronal blocks. The center block, which contained the temporal hippocampus and caudal amygdala (subregions that are damaged in patients with temporal lobe epilepsy), was sectioned (40 µm), and a 1-in-20 series was Nissl stained. Volumes were estimated by drawing contours around regions using Neurolucida. Compared to controls, epileptic sea lions had an average 30% reduction in amygdala and 50% reduction in hippocampal volume. This pattern differs from the kainate-treated rat model, which shows average reductions of 20% in amygdala and only 10% in hippocampus. In addition, damage was unilateral in sea lions but bilateral in rats. Compared to kainate-treated rats, the neuropathology of sea lions more closely resembles that of human patients. Sea lions therefore may be a useful animal model for learning more about the neuropathology of human temporal lobe epilepsy.

Poster #14, Experimental Disease

MICROVESICLES: POTENTIAL MEDIATORS OF INTERCELLULAR COMMUNICATION BETWEEN STEM CELLS

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Microvesicles (MVVs), also called oncosomes or shedding vesicles, are small membrane-enclosed packets of proteins and nucleic acids that are capable of budding from host cells and transferring their contents to neighboring cells, causing the behavior of the recipient cells to change, sometimes in dramatic ways. For example, MVVs originating from highly aggressive human cancer cells have the ability to confer upon normal cells the transformed properties of cancer cells. These findings, combined with the fact that MVVs are stable in the circulation of cancer patients, suggests that MVVs potentially play crucial roles in cancer progression by promoting primary tumor expansion, as well as metastasis. However, they also raise the question whether normal, non-transformed cell types are capable of generating MVVs. Here we show that MVVs are produced by mouse embryonic stem (ES) cells (E14Tg2a.4). Like cancer MVVs, MVVs from pluripotent ES cells contain a specific subset of host-cell proteins. When ES cell MVVs are collected and added to cultures of differentiating cells, they have the ability to delay cell differentiation. Proteomic analysis performed on the ES cell MVVs showed they contained at least 1500 different proteins, which included the pluripotent marker Oct-3/4 as well as a unique form of Ras (embryonic Ras) that is only expressed in pluripotent cells. Future experiments will be aimed at determining whether this unusual form of intercellular communication is important for maintaining stem cell pluripotency.
Poster #15, Clinical Case Report/Series

CANINE HEARTWORM DISEASE WITH CAVAL SYNDROME: A RETROSPECTIVE STUDY IN DOGS FROM GRENADA, WEST INDIES
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Canine heartworm disease caused by Dirofilaria immitis is an important disease of dogs. The aim of this retrospective study was to estimate the prevalence of canine heartworm disease and report on cases of caval syndrome in dogs from Grenada, West Indies. From 2001 to 2011, necropsies were carried out on dogs at the pathology diagnostic laboratory, School of Veterinary Medicine, St. George’s University. Out of 1,271 dogs necropsied, 193 were found infested with D. immitis, giving a prevalence of 15.2% (95% confidence interval, 13.3% to 17.2%). Among the 193 D. immitis positive cases, 30 dogs (15.5%) had caval syndrome. The majority of canine heartworm cases were just incidental, presented for necropsy due to other conditions. However, caval syndrome cases presented with concurrent clinical signs such as anorexia, vomiting, lethargy, weight loss, coughing, exercise intolerance, dyspnea, icterus and hematuria. Gross lesions associated with dirofilariasis with caval syndrome ranged from: right cardiac ventricle dilation with numerous heartworms, caudal vena cava dilatation with many heartworms, roughening of the pulmonic trunk, chronic passive hepatic congestion, ascites, pulmonary thromboembolism, icterus, hemoglobinuria and pale mucous membranes. Aberrant migration was also noted in 1 dog with caval syndrome. We report canine heartworm disease with caval syndrome for the first time in Grenada.

Poster #16, Clinical Case Report/Series

USING VIRTUAL MICROSCOPY IN THE CLINICAL PATHOLOGY ROTATION.
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Several advances in the use of virtual microscopy (VM) as a teaching modality in the veterinary curriculum have come about in the last decade. Whereas VM has mostly been used in larger classes such as histology, our goal was to characterize the functionality of this technology as a tool to prime small groups of fourth year students for the clinical pathology elective rotation. Lymphadenopathy was chosen for the first tutorial using VM. Lymph node aspirates (courtesy of Antech Diagnostics and Oklahoma State University teaching files) were scanned at a maximum of 83X magnification using an Aperio ScanScope CS with oil immersion. Utilizing the annotation features of the associated ImageScope software, lessons for each major differential of lymphadenopathy were created and made available online through Moodle, the course management system used at OSU. The functionality of this independent learning modality was assessed through its ability to create quality images and effectively communicate concepts. Despite the inherent variability of cytology samples, the ScanScope consistently generated quality resolution scans at high magnification illustrating cellular characteristics. While the ImageScope annotation feature has proven useful, there are limitations to the amount of information that can be presented. As such, interfacing with Moodle allowed for easy access to additional information and resources. Students were asked to review the lessons between rounds; initial feedback has been positive. In conclusion, virtual microscopy lessons created using Aperio technology are efficient supplemental resources for independent study of cytology. Further exploration of their capabilities and applications is warranted.
A MOUSE MODEL OF DUAL HELMINTH AND MYCOBACTERIUM BOVIS COINFECTION

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Coinfection with intestinal helminths and Mycobacterium bovis, the causative agent of bovine tuberculosis (bovine TB), is common in wildlife species. Helminth infection generally causes a T-helper type 2 (Th2) immune response, while control of bovine TB infection requires a T-helper type 1 (Th1) immune response. Because these responses are cross-regulated, there is potential for them to interact and influence disease susceptibility and severity. In a previous study on African buffalo (Syncerus caffer), anthelminthic treatment was associated with an increase in circulating levels of interferon-γ (IFN-γ), a Th1 cytokine, suggesting that helminth infection may inhibit the host's ability to combat TB. To examine the immune mechanisms driving this interaction, we utilized a mouse model including the intestinal helminths Heligmosomoides bakeri (H. bakeri) and Nippostrongylus brasiliensis (N. brasiliensis). We hypothesized that a host infected with intestinal helminths will have a dominating Th2 response that will inhibit the Th1 response to M. bovis, reducing the host’s ability to fight bovine TB. Mice were infected with either H. bakeri or N. brasiliensis, or coinfected with both helminths, followed eight days later by intratracheal infection with M. bovis. After 14 days of M. bovis infection, mice were euthanized, and lung and intestinal tissues were sampled for histopathology, inflammation, and alternation of immune cells. Tissues were scored for inflammation, severity of damage, and eosinophils, leucocytes elicited by a Th2 response. Enzyme-linked immunosorbent assay (ELISA) results did not support our hypothesis; instead, IL-4 and IFN-γ levels were both suppressed in TB-infected tissues. Co-infected and N. brasiliensis infected tissues had higher lung and intestinal eosinophil and inflammation scores. In conclusion, while the presence of helminths ultimately does affect host immunity, M. bovis infection appeared to have a dominant, suppressive effect.
HEMATOLOGIC FINDINGS ASSOCIATED WITH A YERSINIA ENTEROCOLITICA EPIZOOTIC IN A CAPTIVE COLONY OF AFRICAN GREEN MONKEYS (CHLOROCEBUS AETHIOPS SABAEUS)

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Yersinia enterocolitica is a zoonotic, gram-negative member of the family Enterobacteriaceae. It causes mesenteric lymphadenitis, terminal ileitis, acute gastroenteritis, and septicemia. This report discusses the hematologic findings associated with an outbreak of acutely fatal enteric disease in a captive colony of African green monkeys on St. Kitts. Pre- and post-antimicrobial treatment blood samples were obtained from 10 monkeys presented with hemorrhagic diarrhea and dehydration. Pre-treatment CBC results indicated a leukocytosis composed of a mature neutrophilia, monocytosis, and basophilia, with variable numbers of large granular lymphocytes (LGLs). Non-LGL lymphocytes were within the reference interval. Neutrophils were pale staining, had markedly decreased nuclear segmentation and pale chromatin; left shift was rare. LGLs had abundant pale blue cytoplasm, azurophilic granules that varied in number and size, and an occasional amoeboid nucleus. Non-LGL lymphocytes had increased amounts of cytoplasm, variably shaped nuclei, and open chromatin. Platelet clumping was marked in pre-treatment samples, absent from post-treatment samples, but thrombocytopenia was not noted in either sample set. All abnormal values returned to reference intervals two weeks post treatment. An additional monkey was sampled which died after treatment began. This individual had a leukopenia composed of a neutropenia and lymphopenia, and had marked toxic changes in neutrophils. Its biochemical profile indicated decreased albumin, azotemia, and elevated ALP and GGT. Biochemical profiles did not reveal consistent patterns in other monkeys. This is the first report on the hematologic findings of an epizootic event associated with Y. enterocolitica on St. Kitts.

DISTRIBUTION OF INTESTINAL GAMMA-DELTA T CELL SUBSETS IN UNINFECTED AND MYCOBACTERIUM AVIUM SUBSP. PARATUBERCULOSIS (MAP)-INFECTED CALVES

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Gamma-delta T cells (GDT) constitute a significant portion of bovine lymphocytes, but their functions remain incompletely characterized. These cells are thought to bridge innate and adaptive arms of host immunity, and have been shown to respond to mycobacterial antigens. They are traditionally divided into two major subsets based on the expression of the membrane protein WC1 (workshop cluster 1). The WC1+ subtype comprises approximately 90% of the circulating pool of GDT cells and are the most widely studied. The WC1- cells are found in higher proportions along mucosal sites and thus may have a role in surveillance and innate immunity. In this study, we used immunofluorescent microscopy to compare the phenotype of immune cells within the intestinal mucosa of uninfected calves to calves with experimental enteric Mycobacterium avium subsp. paratuberculosis (MAP)-infected calves. Our data show that in all calves, WC1- GDT cells are primarily intraepithelial, while WC1+ GDT cells are predominantly located in the lamina propria. Map-infected calves had a significantly higher proportion of intestinal CD3+ cells and GDT cells, which was primarily due to an increase in intraepithelial WC1- GDT cells. The GDT cell activation marker (ACT2) was expressed on lamina proprial but not intra-epithelial GDT cells. We used laser capture microdissection to isolate intestinal GDT cell subsets and quantitative reverse transcriptase PCR, to identify cytokine (IFN-gamma) RNA expression in uninfected and Map-infected calves. This study shows preferential anatomic localization for GDT cells, and suggests that intraepithelial intestinal WC1- GDT cells play a role in responding to mycobacterial infection.
RESPIRATORY SYNCYTIAL VIRUS (RSV) TITERS FOLLOWING NEBULIZATION
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Respiratory syncytial virus (RSV) is a common respiratory pathogen that can be severe in newborns, the elderly, and immune compromised patients. RSV is one of the main viral causes of lower respiratory disease leading to hospitalization, yet vaccination for RSV is currently unavailable. In vivo studies of RSV can be difficult due to variation in viral infection and disease severity in some animal models. One factor that may contribute to the variation is a decrease in viral titer from preparation and storage to administration of the virus. Nebulization is one inoculation method of RSV that provides even distribution of virus to the distal lung lobes. However, the exact quantity of the virus killed by the nebulization process is not defined. To test this, a series of in vitro experiments were conducted with RSV strain Memphis 37 stored at varying sucrose concentrations (0%, 3%, 5%, 8%, 10%, 15%, and 20%) as a possible cryo- and nebulization protectant. Prior to titering the virus on HEp2 cells, the virus was subjected to one freeze thaw cycle and a nebulization cycle. Forty-eight hours after viral plating, infectious foci were detected and counted through immunofluorescent imaging. Titers were determined after freezing and nebulization then compared to the stock titers (before freezing) as well as to one another to determine the loss of infectivity. Nebulization of virus in 0% sucrose had a 0.580 log reduction while the 20% sucrose concentration exhibited only a 0.297 log reduction. The data suggests there is a loss of infectivity due to nebulization; however, sucrose acts as a RSV protectant.

CHARACTERIZATION OF PLASMA MICROVESICLE POPULATIONS DURING ACUTE RETROVIRAL INFECTION
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Circulating cell-derived vesicles are small membrane-bound packets that bud from the plasma or endosomal membranes of a variety of cell types. Recent studies have shown the important role of these nano-vesicles in numerous biological and pathological processes. As such, they represent an emerging class of potential biomarkers. Using an established SIV/macaque model of HIV, we characterized changes in microvesicle profiles during successive stages of infection (acute, asymptomatic, and late), and examined the potential of cell-derived vesicles as biomarkers of acute retroviral disease. Using banked plasma samples from eight pig-tailed macaques (Macaca nemestrina), we investigated changes in microvesicle populations at multiple timepoints before and during SIV infection. This was done using Nanoparticle Tracking Analysis (NTA), which combines laser scattering with light microscopy to evaluate particle populations within a fluid medium. Populations were binned into three categories corresponding to exosomes (<100 nm), microvesicles (100-300 nm), and larger particles (>300 nm). An approximate three-fold decrease in vesicles < 100nm was seen during acute infection (day 7-10). Smaller decreases were seen in vesicles >100nm, and in all vesicle populations following acute infection (day 21, 70). Larger numbers of samples are needed to determine whether there is an association between microvesicle profiles and eventual severity of disease. The acute phase of retroviral infection is characterized by sharply declining numbers of circulating vesicles, followed by return to baseline levels during asymptomatic disease, and slight decreases during progression to AIDS. Previous work from our lab has shown that microRNA profiles exhibit decreased diversity during acute retroviral infection. As extracellular vesicles are known to be one of several carriers of microRNA in plasma, their decline may be one possible explanation for this observed decrease.
**Poster #23, Clinical Case Report/Series**

**UNILATERAL TRIGEMINAL NEURITIS AND BRAINSTEM ENCEPHALITIS ASSOCIATED WITH VEGETAL MATERIAL (PROBABLE GRASS AWN) IN A DOG**

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A 5-year-old, female, spayed Labrador Retriever was presented with a history of mildly depressed mental status of 10 days duration that had acutely progressed to non ambulatory tetraparesis and head tilt to the right side. Neurological examination revealed findings were consistent with a focal lesion affecting the sensory part of the right trigeminal nerve or his nuclei in the pons and rostral medulla oblongata on the right side. Full work up was declined by the owners for economic concerns and due to the severity of the condition. Humane euthanasia followed by a full necropsy was performed. A rounded, smooth mass 6 mm in diameter was present in the sensory root of the right trigeminal nerve near its canal. The mass was relatively firm with a friable central portion on cut section. A concave deformation was observed on the corresponding portion of the pons and, to a lesser degree, the right cerebellar hemisphere. A malacic and hemorrhagic linear lesion 4mm in diameter extended from the pons to the caudal medulla in the right dorsolateral portion of the brainstem. Microscopic examination of the mass revealed a severe suppurative neuritis (microabscess) extensively effacing the nerve fascicles. Chronic nonsuppurative trigeminal ganglioneuritis was also present. The brainstem lesions corresponded to abscesses surrounded by hemorrhages (abscess tract) involving among other structures the right vestibular nucleus. The abscesses were centered on large structures identified as plant material by polarized light and PAS. Gram-positive coccoid bacteria were numerous within the plant material and rare in the purulent exudate. Considering the gross and microscopic findings, trigeminal neuritis and encephalitis probably due to grass awn migration was the diagnosis.

**Poster #24, Clinical Case Report/Series**

**PANCREATIC ENDOCRINE TUMORS IN TWELVE BABOONS (PAPIO SPP.)**

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Twenty-one pancreatic endocrine tumors from twelve female baboons (Papio spp.) from the Southwest National Primate Research Center were evaluated. The average age of affected animals was 22 years. Only one tumor was noted at necropsy, measuring approximately 3cm in diameter, while all other tumors were less than or equal to 5mm in diameter. Four animals had more than one tumor. All tumors were considered incidental findings. Histologically, all tumors were rounded, well demarcated, exhibited neuroendocrine packeting, minimal cellular pleomorphism, and had a very low mitotic rate (less than 1 per 40X field). Less consistent histologic features included encapsulation (7/21), cytoplasmic granularity (6/21), rosettes (1/21), and prominent vascularity (1/21). Immunohistochemical staining for synaptophysin was positive in all tumors evaluated (17/17). Insulin was diffusely and strongly positive in 4/21 tumors and multifocally positive in 12/21. One tumor was diffusely and strongly positive for somatostatin, while 8/20 were multifocally positive. Multifocal staining for glucagon and pancreatic polypeptide was evident in a minority of tumors (6/20 and 2/17, respectively). Gastrin and vasoactive intestinal peptide were negative in all tumors evaluated. Nine tumors expressed more than one hormone marker. This is the first detailed pathologic study of pancreatic endocrine tumors in the baboon. The findings suggest that these tumors are generally benign and have similar morphologic and immunohistochemical features as those described in people, including the ability to express multiple hormones.
CHARACTERIZATION OF OVARIAN AGING IN VERVET MONKEYS (CHLOROCEBUS AETHIOPS SABAUEUS)
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Many chronic diseases have been associated with menopause and the postmenopausal period, including cardiovascular disease and cognitive dysfunction. As the number of postmenopausal women increases worldwide, there is an increased need for translational research using animal models of reproductive senescence. Vervet monkeys (Chlorocebus aethiops sabaues) are excellent models for aging studies due to their reproductive and cardio-metabolic similarities to women. However, reproductive senescence in vervet monkeys has not been well characterized. The purpose of this study is to characterize ovarian aging in vervets and to determine if a relationship exists between age and primordial follicle number. Archived ovaries from vervet monkeys aged 0-27 years (n=12) were serially sectioned (5 um), stained with hematoxylin and eosin, and digitally photographed. In every 100th section, the number of primordial, primary, and secondary follicles was determined using imaging software. Duplicate measurements were made and mean follicle numbers calculated for each ovary. Follicle numbers were square root transformed and a correlation between mean follicle numbers and age was determined using multivariate regression analysis. Significant correlations were observed between primordial and primary (r = 0.85, p = 0.002) and primary and secondary (r = 0.72, p = 0.01) follicles. Primordial follicles declined significantly with age (r = -0.62, p = 0.03) and primary follicles tended to decline with age but the relationship did not reach significance (r = -0.44, p = 0.15). Ovaries of older monkeys (23-27 years) had decreased primordial follicles (132 ± 188). In conclusion, this study indicates vervet monkeys experience ovarian senescence similar to other Old World nonhuman primates and women.

EVALUATION OF A TERBINAFINE IMPREGNATED SUBCUTANEOUS IMPLANT IN GEOMYCES DESTRUCTANS INFECTED BATS
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White-nose syndrome (WNS), caused by the fungus, Geomyces destructans (Gd), has killed an estimated 6 million insectivorous bats since its 2006 emergence in North America. The fungus primarily infiltrates the muzzle and wings. Previous environmental and bat anti-fungal treatment trials have been unsuccessful; therefore, we examined a novel, terbinafine-impregnated subcutaneous implant to treat Gd infection. While histologic confirmation is the gold standard, gross visualization of fungal growth under ultra-violet (UV) light is also possible in live bats. Forty little brown bats (Myotis lucifugus) were captured in December 2011 from two Tennessee hibernacula; no bats had gross evidence of Gd infection. Each bat received a subcutaneous implant containing 1 of 4 terbinafine concentrations (0, 2, 4, 8 mg), and was then inoculated with 20 µL (125,000 conidia) of Gd. Bats were placed into an artificial hibernaculum and UV and white light photos of wings were taken at monthly intervals; histology samples (wing, muzzle, liver, kidney, gonads) were prepared at the end of the trial. Wing and muzzle lesions were analyzed, using CellSens Digital Imaging and Image Pro Plus 7.0 analysis software. On histology, there were no signs of toxicity associated with terbinafine treatment; kidney samples in all treatment groups, except 2mg contained Klossiella parasites. The number of lesions per mm2 of tissue was lowest in the 8mg treatment group in muzzle tissue and in most wing samples. Gross photos showed moderate wing scarring of unknown cause and minimal to no fluorescence. With this research, we hope to develop a lasting, single-administration treatment to minimize handling stress and prevent further mortality in bats from WNS.
**Poster #27, Clinical Case Report/Series**

NOCARDIOSIS AND MYCOBACTERIOSIS IN WEAKFISH (Cynoscion regalis) HOUSED IN A CLOSED RECIRCULATION AQUACULTURE SYSTEM

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A population of wild-captured weakfish (Cynoscion regalis) in an 11,000 L saltwater recirculation system experienced chronic mortalities over four months. Four affected fish presented to Cornell University for necropsy. Grossly, three fish examined showed external areas of erosion on the skin and underlying muscle with numerous 1-3 mm diameter white foci on the kidneys. Histologic examination revealed poorly formed granulomas with numerous filamentous gram-positive acid-fast bacteria. Morphologic characteristics as well as molecular evidence from DNA isolated from formalin fixed, paraffin-embedded tissue showed that the bacteria were most closely related to previously described Nocardia spp. As there is no known effective treatment for Nocardiosis in fish, the recirculation system was depopulated and disinfected and a new population of fish acquired. One year later, 1-2 fish per day began circling and losing equilibrium. Two affected fish were euthanized and necropsied at the aquaculture facility, where white caseous material was found to fill the abdominal cavity. At this point, seven fish presented to Cornell University for necropsy. Multifocal, granulomatous lesions were observed in multiple organs. Histologically, the granulomas contained numerous rod-shaped, gram-positive, acid-fast bacteria. Molecular analysis showed that these bacteria were most closely related to Mycobacterium spp. To our knowledge, this is the first report of nocardiosis and mycobacteriosis in weakfish and highlights the potential for high-density, recirculation aquaculture systems to potentiate epidemics of fish diseases when raising fish with an unknown health history.

**Poster #28, Experimental Disease**

REDUCED OSTEOARTHRITIS SEVERITY IN AGED MIF KNOCKOUT MICE

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Osteoarthritis (OA) is an important age-related disease, but the mechanisms for its development are not fully understood. Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine produced by chondrocytes. The absence of MIF has recently been associated with increased lifespan in mice and with a significant reduction in OA severity in adult mice. The purpose of the present study was to determine if MIF-KO mice develop OA in advanced age or continue to remain relatively disease free during aging. Stifle joints from 2-year-old wild type (WT, n=15) and MIF-KO (n=16) mice were fixed in formalin, decalcified in 10% EDTA, and embedded in paraffin for sectioning and staining of a representative mid-coronal section with hematoxylin and eosin (H&E). The medial tibial plateau and medial meniscus were semiquantitatively evaluated for articular cartilage (AC) structural damage using a previously established murine grading scheme, and measurements were made of thickness and area of AC and subchondral bone (SCB) using an Osteomeasure Histomorphometry system. The number of viable chondrocytes, area occupied by dead chondrocytes in the AC, and weight-bearing meniscal area were also measured. The SCB thickness (p<0.05) and area (p<0.01) were significantly decreased in MIF-KO mice, while AC thickness (p<0.001) and area (p<0.001) were significantly increased. In addition, AC structure scores were significantly lower (p<0.01) in MIF-KO mice. Thus, aged MIF-KO mice had significantly reduced osteoarthritis severity compared with WT controls, further supporting previous evidence that MIF may be a key factor in the development and progression of age-related OA.
Poster #29, Clinical Case Report/Series

THE PARASITIC ROUNDWORM BAYLISASCARIS PROCYONIS: RACCOONS BRING A NEW ZOONOTIC THREAT TO ALBERTA, CANADA
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The North American raccoon, Procyon lotor, has become established in the province of Alberta over the past 30 years. This range expansion creates the potential for novel pathogens. The parasitic nematode Baylisascaris procyonis is a zoonotic pathogen of concern in raccoons. Although human infection with B. procyonis is rare, neural larval migrans, the aberrant migration of larvae to the brain, occurs most commonly in children and is frequently fatal. B. procyonis is ubiquitous in populations of raccoons throughout their range. In 1992, a surveillance study of over 30 raccoons from Southern Alberta failed to find B. procyonis. Consequently, the discovery of adult B. procyonis in the gastro-intestinal tract of two raccoons from Strathmore in 2010 initiated a second surveillance program. With the aid of Fish and Wildlife, raccoon carcasses were passively collected and full post-mortem exams were performed (n = 14). Adult nematodes were discovered in the intestine of a juvenile raccoon from Calgary. This sample, along with the two from Strathmore, are the first isolations of B. procyonis in Alberta. Given the low prevalence of raccoons in the province, a request was sent out to the public for information on raccoon sightings and known raccoon latrines (communal defecation areas). Fecal samples were analyzed using fecal centrifugation and flotation to look for ascarid eggs (n = 14). The request for public assistance in sample collection created a unique opportunity for public education; this was delivered through interviews and newspaper articles. Due to the novelty of raccoons in Alberta, and the proven occurrence of B. procyonis, public education is essential in the prevention, early detection and effective treatment of B. procyonis infection.

Poster #30, Clinical Case Report/Series

CHLAMYDIOSIS IN A RED TAILED HAWK (BUTEO JAMAICENSIS): A CASE REPORT
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An emaciated male red tail hawk (Buteo jamaicensis) was presented for veterinary care when found recumbent in a pasture and died despite resuscitative care. Necropsy revealed air sacculitis, diffuse coelomitis, and fibrinous pericarditis. Microscopically there was fibrinous epicarditis with intralesional chlamydia-like bacteria, fibrinous and heterophilic coelomitis, multifocal heterophilic and lymphoplasmacytic necrotizing hepatitis, fibrinonecrotizing and granulomatous air sacculitis with intralesional chlamydial-like bacteria, and heterophilic splenitis with multifocal necrosis. Multifocal intracytoplasmic Sarcocystis-like protozoans were observed within skeletal muscle. Raptors can be intermediate or direct hosts for cyst-forming coccidians. Frenkelia microti has been reported in red-tailed hawks, both experimentally and naturally acquired. A nematode was present in the proventricular lumen. Common ascarid genera in birds of prey include Ascaridia, Porrocaecum, and Contracaecum. Lesions in the heart, spleen, air sacs, and liver are consistent with avian chlamydiosis. PCR of liver and air sac was positive for Chlamydia spp. Immunohistochemistry was positive for Chlamydia spp. Chlamyphila psittaci is an obligate intracellular agent associated with avian and mammalian infections; this pathogen poses a zoonotic risk for veterinarians, pet owners, and abattoir workers. C. psittaci infections have been recognized in approximately 465 avian species across 30 different orders, most commonly in psittacines and pigeons. Numerous case reports have documented C. psittaci infection in wild and captive red tailed hawks.
Poster #31, Clinical Case Report/Series

CITROBACTER KOSERI SEPTICEMIA IN A CALF
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A 4-day-old, male Holstein calf was submitted alive for euthanasia and necropsy. The calf had dull mentation, nystagmus and blindness. Gross lesions included severe diffuse suppurative meningitis characterized by cloudy thickening of the meninges, bilateral hypopyon, and fibrinosuppurative polyarthritis in the hocks. Histologically, there was marked neutrophil and macrophage infiltration into the meninges and neuropile, intermingled with bacterial colonies. Bacilli were noted free in the exudate and within inflammatory cells. There was severe perivascular cuffing and occasionally necrotizing vasculitis throughout the cerebrum. Within the eyes, there was fibrinosuppurative endophthalmitis composed of fibrin mats and neutrophils in the anterior and posterior segments. Meningitis was noted around the optic nerves. Findings also included supplicative splenitis with lymphoid depletion and multiple renal medullary microabscesses. Failure of passive transfer was confirmed by serum IgG level below 22 mg/dL. Bacterial culture of ocular humor, brain, spleen, and intestine all yielded Citrobacter koseri identified by MALDI. Citrobacter koseri, a member of Enterobacteriaceae, is considered normal flora in humans and animals, and has been rarely isolated from fecal samples in diarrheic calves. In human neonates, Citrobacter koseri causes meningitis, vasculitis, and cerebritis. Infection is associated with significant morbidity and mortality and is more prone in very young or immunocompromised individuals. In this case, failure of passive transfer predisposed the calf to opportunistic infection. This appears to be the first characterization of septicemia in a calf caused by Citrobacter koseri, with lesions comparable to those described in human neonates.

Poster #32, Experimental Disease

EXAMINATION OF BIOMARKERS OF NEURODEGENERATION IN FELINE GM2 GANGLIOSIDOSIS
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GM2 gangliosidosis (GM2) is a lipid storage disease in which deficiency of a hydrolytic enzyme, hexosaminidase, leads to accumulation of GM2 ganglioside in lysosomes, resulting in neurodegeneration and subsequent inflammatory responses. GM2 affected cats provide a model to study the effectiveness of gene therapy to deliver the insufficient enzyme and impede disease progression. Biomarkers of disease progression are desired to characterize disease advancement and measure success of therapy. Pro-inflammatory cytokine, TNF-alpha, and chemokine, MIP-1alpha, are produced in chronic inflammatory states associated with neurodegeneration. Therefore, TNF-alpha, MHCII, and MIP-1alpha were analyzed as potential biomarkers. Cats affected with GM2 were treated by intracranial injections of an AAV-vector encoding feline hexosaminidase. Samples were collected from 3 cats 16 weeks post-treatment for short-term analysis, while 7 additional cats were followed to humane end point (9.8-21.5 mos.). Gene expression of TNF-alpha measured by qRT-PCR was 0.7-4 fold over normal in GM2 affected cats compared to normal and AAV-treated cats; however, there was substantial variation among treated cats. The variation correlated with neurodegeneration measured by MRI and presence of TNF-alpha in neurons detected by immunohistochemistry (IHC). Gene expression of MHCII was 1.8-9 fold over normal in GM2 affected cats. IHC for MHCII appeared to correlate with gene expression. MIP-1alpha gene expression was 2.4-4.6 fold over normal in GM2 affected cats and was statistically significant, (p< 0.01), compared with normal and GM2 AAV-treated cats. While TNF-alpha and MCHII had substantial variability, MIP-1alpha has potential as a clinical biomarker and must be further evaluated.
**Poster #33, Experimental Disease**

**VISUALIZATION OF UROPLAKIN EXPRESSION IN A MOUSE MODEL OF URINARY SCHISTOSOMIASIS**

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Urinary schistosomiasis is a parasitic disease with global impact, which causes chronic urinary tract infections as well as increased risk of bladder cancer and HIV infection. It is the most prevalent form of schistosomiasis in humans world-wide, and is closely related to veterinary diseases caused by other species of schistosomes. Infection with the causative parasite, Schistosoma haematobium, results in damage to the bladder urothelium as evidenced by the hematuria which is a hallmark feature of the disease. The presence of hematuria indicates damage to the bladder urothelium, which normally consists of an impermeable and flexible barrier. The primary component of this barrier is a meshwork made of tetramers of uroplakin proteins which form an interlocking structure on the luminal surface of the bladder. Previous work by our lab has shown that S. haematobium infection is associated with downregulation of uroplakin expression in the entire bladder. To investigate the expression of uroplakins specifically in the urothelial lining of the bladder, transgenic RFP-uroplakin 1b mice were experimentally infected via bladder wall injection with S. haematobium eggs. At 7, 14, and 21 days after experimental infection, mice were sacrificed and immunohistochemistry for multiple urothelial markers was performed on the bladders. Digital processing of the images allowed fluorescence signals from only the urothelium to be analyzed. The relative fluorescence intensities of each marker were quantified and compared. Although no significant difference in relative fluorescence intensity was found between infected and control vehicle-injected bladders, this may be due to a lack of sensitivity of the immunohistochemical techniques utilized. Pursuit of further methods to refine this technique for investigating uroplakin expression in the bladder urothelium is ongoing.

**Poster #34, Experimental Disease**

**MOLECULAR ALTERATIONS IN CHEMICALLY INDUCED UTERINE CARCINOMAS IN WISTAR HAN RATS MIMIC HIGH-GRADE TYPE I ENDOMETRIAL CARCINOMAS IN HUMANS**

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Endometrial cancer is a leading cause of cancer mortality in women in the United States. Human endometrial carcinomas generally fall into two subtypes (Type I and Type II) based on histology and molecular phenotype. In a recent National Toxicology Program 2-year carcinogenicity study, exposure of Wistar Han rats to a chemical compound was associated with uterine carcinoma development. This chemical has widespread human exposure, and unknown long-term health effects. This study's objective was to characterize these chemically induced uterine carcinomas based on criteria relevant for the human disease, including morphologic and molecular features including mutation spectra (Kras, Ctnnb1, Tp53), gene expression (qPCR), and protein expression (immunohistochemistry/IHC) associated with human endometrial carcinomas. In the chemically treated rats there was a dose-related increase in uterine carcinomas, 68% (15/22) of which were poorly differentiated. In tumor samples used for mutation analysis, 59% (13/22) had Tp53 mutations, 16% (3/19) had Ctnnb1 mutations, and 0% (0/17) had Kras mutations. In addition, most of the chemically induced carcinomas examined were ER-alpha positive by IHC. By qPCR, Ccnd1, Her2, and Cdh1 were all overexpressed. A majority of chemically induced uterine carcinomas in this study had overlapping features of Type I and Type II tumors (ER-alpha expression, aggressive phenotype, high Tp53 mutation rate), most similar to high-grade Type I endometrial carcinomas in humans.
**Poster #35, Experimental Disease**

ROLE OF SDF-1A AND CXCR-4 IN MESENCHYMAL STEM CELL RECRUITEMENT TO A LOCALIZED BONE DEFECT  
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Bone defects are a major health concern in the United States for both humans and veterinary species. In the healing and repair of bone defects, mesenchymal stem cells (MSCs) are recruited from distant sites and travel systemically to differentiate into osteoblasts, which lay down new bone. Previous studies have shown that the receptor chemokine receptor 4 (CXCR-4) on the MSC surface induces the recruitment of MSCs towards sites of inflammation. In our study, it was hypothesized that overexpressing CXCR-4 will increase the recruitment of MSCs to a bone defect releasing of stromal derived factor 1 alpha (SDF-1α), a pro-inflammatory cytokine and CXCR-4 ligand. It is further hypothesized that once these MSCs reach the defect site, they will differentiate into osteoblasts and form new bone. Twenty-one nude mice underwent surgery to create a 3mm bone defect in the mid-shaft of the right femur. MSCs were transfected to express CXCR-4, luciferin, and green fluorescent protein (GFP) and were injected through the intra-cardiac route. A fat tissue graft was introduced into the defect, which was transfected to express SDF-1α. The animals were monitored for 42 days. Bioluminescent imaging (BLI) was performed on days 1, 3, 5, 7, 9, 11, 13, 21, 28, 35, 42 and radiographs were taken on days 1, 14, 28, 42. After six weeks, the femurs were harvested and a micro computerized tomography (micro CT) scan was performed. The femurs were stained with hematoxylin and eosin (H&E) stain and anti-GFP stain. It was shown with BLI and the anti-GFP stain, that through the CXCR-4, SDF-1α axis, MSCs traveled to the bone defect. However, there was no significant indication of bone growth by radiograph, CT or H&E stain.

**Poster #36, Experimental Disease**

GENE THERAPY FOR TAY-SACHS DISEASE IN JACOB SHEEP  
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Tay-Sachs Disease (TSD) is a fatal lysosomal storage disease in humans caused by build-up of GM2 ganglioside in lysosomes of the CNS. Ordinarily, GM2 ganglioside is catalyzed by hexosaminidase A (HexA), a heterodimer composed of alpha and beta subunits, encoded by HEXA and HEXB genes. In TSD, HEXA is mutated causing malformation of the alpha subunit, resulting in a nonfunctional enzyme. Excess GM2 ganglioside storage leads to progressive neurodegeneration and death, usually by five years of age. Adeno-associated virus (AAV) vectors encoding wild type HEXA have been successful in transducing cells and producing functional HexA alpha subunit both in vitro and in vivo. Though lack of authentic animal models has hindered therapy development for TSD, the recent discovery of TSD in Jacob sheep has provided invaluable opportunities to perform translational research in animals whose brain size and complexity are similar to that of human infants. In this study one affected Jacob sheep was treated with AAV vector encoding HEXA, and another was treated with AAV vectors encoding both HEXA and HEXB. Injections were performed intracranially into the thalamus and lateral ventricle. Untreated TSD sheep lived for an average of 7 months, while HEXA and HEXA+HEXB treated sheep lived to 14.8 and 14.0 months, respectively. In untreated brains, HexA activity was 7.0% of normal controls. In HEXA and HEXA+HEXB treated sheep brains, HexA activity was detected throughout the cerebrum and cerebellum reaching up to 2.1 fold normal and 155.8 fold normal, respectively. These results demonstrate the effectiveness of AAV gene therapy in transducing cells and producing functional enzyme throughout the brain. The supranormal enzymatic activity levels seen in HEXA+HEXB treated sheep brain suggest that optimal production of HexA is achieved by co-expression of both subunits simultaneously. These results will be used in the design and implementation of human clinical trials for TSD.
Poster #38, Experimental Disease

DOES MOSSY FIBER SPROUTING CAUSE EPILEPSY?
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Temporal-lobe epilepsy is a serious condition in human patients, yet the mechanism of disease is poorly understood. One common neuropathological finding in temporal-lobe epilepsy patients is mossy fiber sprouting (MFS), the aberrant projection of granule cell axons into the granule cell layer and molecular layer. MFS is proposed to cause temporal lobe epilepsy by forming an abnormal positive-feedback circuit among excitatory neurons. A previous study has shown that rapamycin at 3 mg/kg suppresses mossy fiber sprouting but not seizure frequency in pilocarpine-induced epilepsy mice (Buckmaster and Lew, 2011). However, rapamycin at 3 mg/kg does not block mossy fiber sprouting completely. In this study, 10 mg/kg rapamycin was administered to more completely block mossy fiber sprouting and evaluate the effect on seizure frequency. Beginning 1 day after pilocarpine-induced status epilepticus, mice were treated with rapamycin at 10 mg/kg daily for 2 months. At the end of treatment, mossy fiber sprouting in mice treated with rapamycin (4.9 ± 0.4%) was similar to that of naïve-control mice (3.3 ± 0.5%) and significantly less than vehicle-treated epileptic mice (22.0 ± 0.5%), demonstrating that high-dose rapamycin treatment blocks mossy fiber sprouting in a dose-dependent fashion. Video monitoring for 9 hours daily for a month revealed that seizure frequency in rapamycin-treated mice (0.13 ± 0.01 seizures/hour, n=64) did not differ significantly from vehicle-control mice (0.14 ± 0.01, n=64). These results suggest that mossy fiber sprouting does not cause temporal-lobe epilepsy and that alternative processes mediate the disease.

Poster #37, Experimental Disease

ANTIGEN CHALLENGE STUDY IN FLAKY TAIL (FT/FT) MICE: AN ANIMAL MODEL OF ATOPIC DERMATITIS (AD)
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Atopic dermatitis (AD) is a chronic relapsing inflammatory dermatitis. In humans, mutations in the filaggrin gene (FLG), a key protein that facilitates formation of an epidermal barrier, is a major predisposing factor for AD. Disruption of barrier function leads to increased percutaneous allergen transfer. Homozygous ft/ft mice have mutations in FLG. The objectives of the study were 1) identify cutaneous disease biomarkers after antigen challenge in ft/ft mice and 2) examine the expression of barrier proteins in predilection sites and non-predilection skin sites. C57BL/6J, heterozygous (ft/+ ) and ft/ft mice were euthanized 14 or 28 days after once daily topical challenge with antigen of the mite (dermatophagoides pteronyssinus) or petrolatum (vehicle). Transepidermal water loss (TEWL) was measured as an indicator of epidermal barrier function. TEWL levels increased (P<0.03) in antigen treated ft/ft mice. At the site of antigen challenge (dorsal skin and pinnae) there were no histological changes in control or treated mice, although the predilection sites (facial skin) of both control and antigen treated ft/ft mice had acanthosis, hyperkeratosis, and chronic inflammation accompanied by increased immunohistochemical expression of (pro)flaggrin and caspase-14. Gene expression of back skin revealed increased (P<0.05) expression of CCL20 in antigen-treated ft/ft compared to either vehicle-treated ft/ft or antigen-treated C57BL/6J mice. Increased CCL20 mRNA expression may be an early inflammatory signal as CCL20 recruits CCR6-positive T cells and immature dendritic cells. The lack of histological inflammatory response at the site of challenge indicates dermal response to antigen challenge may have a site predilection. The utility of TEWL and CCL20 as biomarkers of the disease should be explored further.
**Poster #39, Clinical Case Report/Series**

A SYSTEMIC CHRYSGOSPIRUM INFECTION IN A FREE-RANGING PLAINS GARTER SNAKE (THAMNOPHIS RADIX)

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A free-ranging plains garter snake (Thamnophis radix) was diagnosed post-mortem with Chrysosporium ophiodicola. The snake originally presented alive to the Wildlife Medical Clinic at the University of Illinois with a 1cm x 1cm lesion caudal to the left eye, cataracts in both eyes, dehydrated, and in respiratory distress. The snake was treated with antibiotics and supportive care for 45 days and then euthanized due to lack of improvement. Necropsy revealed multisystemic disseminated granulomas most notably in the lungs. Numerous intraleisional fungal organisms, consisting largely of septate hyphae, were detected histopathologically by Grocott’s methenamine silver stain among clumps of necrotic cellular debris and aggregates of epitheloid macrophages. Chrysosporium sp. was isolated from tissue specimens with formation of mycelial colonies on Sabaroud Dextrose Agar at 25 C. Isolate identity was confirmed by 18S ITS DNA sequencing with 99% homology to Chrysosporium ophiodicola. Chrysosporium has already been identified as an emerging infectious disease of eastern massasauga rattlesnakes (Sistrurus catenatus catenatus). Because the Chrysosporium only seemed to affect the localized region of the cranial lesions in the rattlesnakes, this report of a systemic infection in a free-ranging garter snake suggests this disease has multi-species involvement with various clinical manifestations.

**Poster #40, Clinical Case Report/Series**

VIMENTIN EXPRESSION IN CANINE PROSTATE CARCINOMA: A POTENTIAL INDICATOR FOR DISTANT METASTASIS

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Epithelial to mesenchymal transition (EMT) has been shown to play an important role in the metastasis of carcinomas, and vimentin expression can be used as an indicator of EMT. Vimentin expression has been demonstrated in canine prostate carcinoma, but no study has compared the degree of vimentin expression in prostate carcinomas without metastasis versus carcinomas with metastasis. We examined canine tissue samples from 5 cases with benign prostatic hyperplasia (BPH), 2 cases of prostate carcinoma without metastasis and 6 cases of prostate carcinoma with metastasis. Immunohistochemistry was performed on these samples, including pancytokeratin (AE1/AE3), cytokeratin 8/18 (CK 8/18), vimentin and uroplakin III (UPK III). All of the primary tumors and all metastases expressed AE1/AE3 and CK 8/18, but not UPK III. Vimentin was expressed to varying degrees in primary tumors with metastases and associated metastatic lesions, but rarely if at all in non-metastatic tumors. All cases of BPH exhibited staining with AE1/AE3 and CK 8/18, but not with vimentin or UPK III. These results show that EMT may be a factor in the metastasis of canine prostate carcinomas.
CHARACTERIZATION OF THE CLINICO-PATHOLOGICAL FEATURES AND OUTCOME IN CASES OF SEVERE ANEMIA IN UK CATS
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In cases of severe feline anaemia, it can often be difficult to identify a cause despite performing a defined clinical diagnostic process. This study’s aim was to investigate severe anaemia in cats to determine outcome, including diagnosis, treatment, and survival data. A review was performed of all samples submitted to the University of Glasgow Clinical Pathology department from cats with a haemoglobin concentration < 5 g/dL over a 16 month period. Clinical histories were retrospectively obtained from submitting practices. Seventy-six cats of 119 severely anemic submissions were included in the study, while the remainder were excluded due to lack of clinical history. The mean hematocrit of the 76 cats was 12.23% (3.4-17.0%) 54 of which were classified as non-regenerative. Screening for feline pathogens was not performed in all cases and yielded few positive results. This included 2 cats positive for FeLV antigen (n=47), 2 FIV antibody-positive animals (n=48) and one cat positive for Candidatus Mycoplasma haemominutum (n=16). Mortality was high with 56 cats deceased within 6 months after initial presentation. A definitive diagnosis was reached in only 23 cats. The most common diagnoses were renal failure (n=6) and neoplasia (n=6). Three cats each were categorized as haemorrhage and FIP, and 1 case each of FIV or FeLV related disease, chronic bacterial enteritis/hepatitis, cholangiohepatitis, and myelodysplasia. Of the 20 cats surviving to 6 months, 13 had been on immunosuppressive treatment for presumptive immune-mediated haemolytic anaemia. The findings of this study indicate that many cats with severe anaemia remain undiagnosed and are deceased by 6 months. This supports the need for further research into the underlying causes of severe feline anaemia.

USING RNA SILENCING FOR WEST NILE VIRUS PATHOGENESIS AND VACCINE STUDIES
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Our laboratory is using novel methods to understand the pathogenesis of West Nile virus (WNV) and explore new strategies for targeted, rational vaccine design. We are taking advantage of microRNAs (miRNA), the natural role of which is to post-transcriptionally silence protein expression. This type of epigenetic transgenic control has recently been exploited both in vitro and in vivo for multiple viruses. Because WNV is a positive, single-stranded RNA virus, we have taken advantage of tissue-specific miRNA silencing and we have cloned viruses with added target sequences specific to miRNAs present in neurons and myeloid cells. Using our 3 week-old CD-1 mouse model of WNV encephalitis, we have shown that while wild type virus kills 70-90% of mice, mortality is completely prevented in mice infected with the neuron-specific miRNA target-containing virus. Viral infection of the nervous system is absent in mice infected with the neuron miRNA target-containing virus as confirmed by plaque assay and immunohistochemistry. We are also stabilizing these miRNA target sequences in the viral genome to prevent mutation which could result in a reversion to virulence. We have inserted the miRNA target sequences into one, two, or three different locations in the 3’ noncoding region of an infectious clone of WNV and have compared their replication kinetics to those of wild type virus, both in vitro and in vivo. With these cloned viruses, we can better understand the pathogenesis of WNV and design safer, more targeted vaccines.