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Abstracts of Scientific Papers

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Oral Case Reports

Laparoscopic Induction of Endometriosis: Development of a New Surgical Model

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Endometriosis is a painful disorder of women and nonhuman primates where endometrium-like tissue exists outside the uterus. It currently affects approximately 10% of childbearing-age women, 20% to 50% of women with subfertility, and 40% to 60% of women with dysmenorrhea. There are few medical therapies for the disease, and those that exist have a high recurrence rate and/or lead to undesirable side effects such as bone density loss and hot flashes and can only be used for a limited duration. Development of medical therapies has lagged because there are few physiologically relevant animal models. Previous attempts to develop nonhuman primate surgical models for the disease were based upon Sampson hypothesis and included invasive techniques such as surgical diversion of cervix into abdomen or supracervical ligation to impede normal menstrual outflow. A successful baboon model has been developed that involves transcervical collection of menstrual blood with subsequent laparoscopic seeding of the material into the abdomen. The utilization of the baboon in endometriosis research is limited by cost and housing constraints associated with their large adult size. This study sought to develop a minimally invasive laparoscopic method for the induction of endometriosis in the macaque that would yield lesions similar to those observed in women. Surgical menstrual seedings were timed to the second day of mense and were repeated monthly for a total of 3 seedings. Thereafter, the abdomen was inspected laparoscopically and animals were graded for stage of the disease, similar to grading done in women. Reproductive tracts and all endometriotic lesions were collected at the conclusion of the study for histologic confirmation of the disease. Using this surgical technique, macroscopic and microscopic endometriosis was induced in 5 of 5 artificially cycled rhesus macaques. This pilot study showed laparoscopic transuterine collection and immediate seeding of menstrual endometrium can reliably induce endometriosis in the rhesus macaque. The induced, early stage endometriosis in macaques observed in this pilot study parallels development of the disease in women and provides a new animal model of the disease, which is a valuable resource for future preclinical studies.

Paradoxical Venous Air Embolism in a Rhesus Macaque

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A singly housed 8-y-old male rhesus macaque (*Macaca mulatta*), with a headcap, cylinder and bilateral eye coils underwent surgery to move a cranial well. Surgery was largely uneventful with steady physiologic parameters. Eight hours after induction attempts were made to wean the animal off the ventilator. After 2 h of manual ventilation and doxapram administration there was no indication of recovery. Manual ventilation was halted and the animal expired. Consultation with a human neurosurgical anesthesiologist resulted in a presumptive diagnosis of paradoxical venous air embolism. Venous air embolism (VAE) is the entrainment of air that occurs when a vein is held open to the atmosphere and venous pressure at the operative site is subatmospheric. Paradoxical air embolism is when the passage of the air is entrained (vascular air embolism) from the venous side to the left (arterial circulation) via either an intracardiac connection such as an ASD, VSD, or probe patent foramen ovale, or through AV shunts in the lungs. Entrainment in humans is most commonly associated with sitting position craniotomies (posterior fossa surgery). The stereotaxic unit used in the primate surgery elevated the head from the rest of the body in a way that we believe mimicked the sitting position in humans. All future craniotomies were performed by raising the rest of the body in order to decrease the gradient between the craniotomy site and the heart.

Unilateral Hindlimb Lameness in a 10-Year-Old Rhesus Macaque (*Macaca mulatta*)

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A 10-y-old male rhesus macaque was presented for intermittent nonweight bearing lameness. On physical examination, severe muscle atrophy of the right hindlimb was noted. In addition, there was severe crepitus and limited range of motion (ROM) on extension of the right coxofemoral joint. Arthritis was suspected and antiinflammatory therapy (carprofen 4 mg/kg PO once a day) was initiated. After 2 wk of therapy, no improvement was noted. Radiographs were performed of the affected limb and pelvis. Abnormal findings found on the right side when compared with the left included severe muscle atrophy, multiple areas of radiolucency in the femoral head, reduced cortical thickness in the femur, and an enlarged acetabulum. Chest and abdominal radiographs were also performed, and there was no evidence of pulmonary metastases, or any other abnormalities. CBC and chemistry results were unremarkable. Differential diagnoses included avascular necrosis of femoral head, previous trauma, neoplasia, and osteomyelitis. Surgical intervention was elected and femoral head and neck ostectomy was performed. Biopsy of the excised femoral head revealed end-stage degenerative joint disease. Bacterial culture of the femoral neck was negative. Postoperative pain management included carprofen (3.3 mg/kg PO once a day) and a tapering dose of tramadol. The surgical site healed without complica-

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tions. The initial physical rehabilitation regimen included weekly passive ROM exercise under sedation and additional enrichment to encourage the use of his operated limb. A few months postoperatively, the animal developed a sore on the lateral aspect of the contralateral limb. A larger cage was provided to further encourage mobility. Although postoperative physical therapy is limited for macaques undergoing this type of orthopedic procedure, surgical intervention may improve animal welfare by reducing pain and discomfort.

Osteopenia and Osteoporosis in Castrated and Aged Male Rhesus Monkeys (*Macaca mulatta*)

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While osteopenia and osteoporosis have been the subject of intensive modeling and therapeutic studies in both intact and ovariectomized nonhuman primates, especially rhesus and cynomolgous macaques, there is virtually no information on the effects of castration on bone in males and only limited data on osteopenia in aged males. Most information on castrated primates comes from studies of human eunuchs. The purpose of this report is to present and compare radiographic, photographic, and bone mineral density data using DEXA between the femurs and vertebrae of castrated and intact age-matched male rhesus macaque skeletons from the free-ranging population on Cayo Santiago and to provide additional data on bone in aging macaques from this colony as a natural model for age-related osteopenia in geriatric men. Radiographic evidence will be presented indicating that osteopenia also occurs in the skull of castrated male rhesus monkeys.

Imipenem-Induced Neutropenia in a Rhesus Macaque

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An 8-y-old pregnant female rhesus macaque (*Macaca mulatta*) presented for tarry diarrhea, weight loss, and dehydration. Antibiotic treatment was initiated with baytril and erythromycin pending culture results. Fecal culture was positive for 2 or more Campylobacter spp. Her condition deteriorated the following day with profound lethargy and continued dehydration. Baytril and erythromycin were discontinued, and metronidazole and imipenem/cilastatin intravenous treatments were initiated due to her rapid clinical decline. Imipenem/cilastatin treatment was continued for 3 d (days 2 to 4). Blood work performed on day 6 showed increased liver enzymes and a decreasing neutrophil count. Supportive liver therapy was initiated with SAM-e and milk thistle. Further elevation in liver enzymes, a severe neutropenia, and hepatomegaly were identified on day 9. Differential diagnoses included: hepatitis A, cytomegalovirus, leptospirosis, toxin exposure, and drug reaction. Based on the potential for a contagious disease, the animal was quarantined pending further diagnostic tests. Additional tests for specific pathogens were negative, and a drug reaction to imipenem was considered the

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most likely diagnosis. Limited case reports on imipenem toxicity in humans are consistent with the clinical signs observed in this case, specifically hepatitis and neutropenia. On day 15 the neutrophil count decreased to 130 cells/µL. Given the extremely low neutrophil count, pegfilgrastin, a colony-stimulating factor that specifically binds to hematopoietic cell surface receptors, was administered at a dose of 100 µg/kg. Forty-eight hours following treatment with pegfilgrastin, the neutrophil count increased to 24,110 cells/µL. Subsequently, over the next 2 mo, 3 additional doses of pegfilgrastin were required before the animal was able to sustain appropriate numbers of neutrophils. The animal was fully recovered with a stable neutrophil count 3 mo after the initial onset of diarrhea. This case represents a rare reaction to imipenem and a unique treatment strategy for severe neutropenia in a rhesus macaque.

Effects of Weekly Blood Collection in Male and Female Cynomolgus Macaques

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Blood collection in the laboratory animal setting is an important component of obtaining data for a variety of studies; however, there are various recommendations for safe collection volumes in the literature. Many suggest that 7.5% or 10% of blood volume can be collected weekly, but these recommendations are neither species nor gender specific. There is little information about the maximum amount of weekly blood that can be collected in male and female cynomolgus macaques without causing significant hematologic and clinical abnormalities. We evaluated weekly blood removal of 7.5%, 10%, 12.5%, and 15% of total blood volume for 4 consecutive weeks in male and female cynomolgus macaques. Complete blood counts, serum protein, and body weights were evaluated immediately prior to each blood collection and for an additional 4 consecutive weeks following the last blood collection. Preliminary results indicate that up to 15% of total blood volume can be safely removed weekly for 4 consecutive weeks from healthy, male and female cynomolgus macaques.

Outbreak of Lymphoproliferative Disease in Common Marmosets at the Wisconsin National Primate Research Center

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There has been a significant increase in the incidence of lymphoproliferative disease in the common marmoset (*Callithrix jacchus*) colony housed at WNPRC. Seventeen of the past 20 marmosets euthanized for clinical reasons have been attributed to this outbreak dating from 19 October 2011 to present. The associated clinical signs include weight loss, diarrhea, inappetence, and rare palpable abdominal masses. Gross necropsy findings include mildly thickened mucosa of the small and/or large intestines and rare associated lymphadenopathy. Preliminary histology and immunohistochemistry results are predominantly consistent with nonepitheliotrophic T-cell (CD 3) proliferations and lymphoma. A similar disease process has been previously reported in this colony implicating an Epstein–Barr virus-related γ-herpesvirus typically resulting in B-cell lymphoma. Cross-species transmission of other γ-herpesviruses, including *Herpesvirus saimiri* and *Herpesvirus ateles*, have also been noted to produce lymphoproliferative disease in common marmosets typically of B-cell origin. The present cohort of cases and its preliminary findings are of interest as they show a similar disease course but of T-cell origin. Identification of potential viral causes of this outbreak and further analysis of the histopathologic changes are underway. The presentation will combine premortem clinical findings with gross pathology images, general histopathology, immunohistochemistry, and PCR results to provide a thorough review of this disease event.

Natural Tularemia Infection of Outdoor Housed Rhesus Macaques: Disease Outbreak Investigation

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In the summer and fall of 2010, a series of outdoor-housed rhesus macaques were diagnosed with tularemia. A total of 11 cases were confirmed on necropsy to be positive for *Francisella tularensis*, the causative agent of tularemia. An additional 9 animals with similar clinical signs were identified and responded to empirical antibiotic treatment. A serosurvey of clinically normal macaques housed in the same area found 54.3% (44 of 81) to be seropositive in a population that averages around 800 individuals. A prospective survey of small mammal reservoirs and arthropod vectors was conducted during the same timeframe the following year. Rodent species were trapped and euthanized; carcasses of other species were salvaged when found. Tissue samples and ectoparasites were tested by real-time PCR for the presence of *F. tularensis* DNA. PCR from the 165 rodents, raccoons, cats, and jackrabbits was negative for *F. tularensis*. Fleas, when present, were collected and pooled; all 40 pooled samples were negative for *F. tularensis*. The subspecies of *F. tularensis* was identified by conventional PCR on stored DNA from affected macaque tissue. Amplification using primers for 3 regions of difference were used (RD1, RD3, and RD6) and the results confirmed the subspecies to be holarctica. The widespread seropositivity (54.3%) in the macaque colony when paired with the low incidence of clinical disease (2.5%) in 2010 suggests this strain may have a relatively low pathogenicity in the macaques. In the US, rabbit reservoirs are primarily affected by *F. tularensis* ssp. *tularensis*, while rodent reservoirs typically are affected by ssp. *holarctica*. The local rodent population potentially served to amplify the infection once it was introduced, but the negative PCR results the following year suggest that these species do not serve as a long-term reservoir for disease locally.

Factors Influencing Aggression in Peer Groups of Weaned Long-Tailed Macaques (*Macaca fascicularis*)

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In the captive breeding of primates, "weaning" typically refers to the removal of infants from their mothers, not necessarily equating to the natural weaning process by which an infant gradually becomes nutritionally independent of its mother. The literature contains many examples of the potential negative effects of early weaning, though little is known of the consequences of later weaning. Periodic weaning in breeding facilities frequently

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results in merging infants from different breeding groups into peer groups. At our institution, weaning has typically occurred at around 12 mo of age; however, a revised strategy of later weaning (about 18 mo of age) was accompanied by an increase in aggression. To examine whether group composition and the age at weaning influenced aggression rates we examined 566 groups (10,181 animals: 4801 females, 5,380 males) weaned over a 3-y period (March 2008 through March 2011). Analyses indicated that more aggression occurred when animals were older at weaning ($P = 0.000$) and that there were significant effects on aggression resulting from the number of subgroups per group ($P = 0.03$), the number of males per group ($P = 0.000$) and a significant interaction between the age at weaning and the number of subgroups ($P = 0.002$). These results have enabled us to fine-tune the weaning process with the aim of minimizing the risks of aggression and thereby improving primate welfare.

Novel Assay for Detecting *Mycobacterium tuberculosis* in Nonhuman Primates

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Nonhuman primates (NHPs) used for research purposes are regularly screened for *M. tuberculosis* infection, both as part of transport-associated quarantine and for routine colony health maintenance programs. The current recommended screening method relies on the tuberculin skin test (TST) to identify animals with acute or latent *M. tuberculosis* infection; however, this method is labor intensive, takes 3 d to complete, and has known problems with false positive reactors and anergic response by infected animals. More effective testing with higher sensitivity is needed, while remaining economic in material cost and reducing labor required to perform testing on large numbers of animals. This work describes a more accurate antibody detection test for TB surveillance in NHPs by identifying antigens and using the multiplex format of the peptide microarray for simple high throughput antibody detection assay. A large set of immunoreactive antigens was first identified using peptide arrays derived from open reading frames of the *M. tuberculosis* genome, screening serum samples from TST test positive and negative rhesus macaques. The top immunoreactive peptides were chosen for further analysis based on ability to distinguish positive and negative samples by various analysis methods. Next, a large set of positive (both experimental and naturally occurring infections) and negative (by routine TST) serum samples from rhesus and cynomolgus macaques were run on the peptide arrays to determine sensitivity and specificity. Results from further screening at several NHP colonies with historically negative TST are reported here. Overall, this work identifies novel immunoreactive peptide antigens and an antibody detection assay for *M. tuberculosis* that provide high sensitivity and specificity for colony surveillance programs.

Influence of Levonorgestrel-Releasing Intrauterine Contraceptive Systems on the Baboon Vaginal Microbiome

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Use of levonorgestrel-releasing intrauterine contraceptive systems (LNG-IUS) in humans may alter vaginal microbial populations and susceptibility to pathogens. The impact of LNG-IUS on the vaginal microbiome cannot be easily evaluated in humans. Baboons (*Papio hamadryas anubis*) are a useful animal model for contraceptive trials and reproductive infectious challenge studies. This study evaluated the effects of an LNG-IUS on the baboon vaginal microbiome at baseline and for 6 mo after placement. LNG-IUS were inserted transcervically into 3 captive, reproductively mature, female baboons. The animals were serially evaluated weekly for 4 wk and monthly for 5 mo. Evaluation included physical examination, gram-stained vaginal cytology, and microbial sequencing from vaginal swabs. The animals tolerated the devices well and retained them until device removal at the end of the study. Each animal developed amenorrhea and cervical mucus increased. Gram-stained vaginal cytology was evaluated using Nugent scoring criteria. For the majority of time points, including baseline, Nugent scores were greater than 7, consistent with bacterial vaginosis. The principal finding was decreased Lactobacilli species compared to the human vaginal microbiome. Bacterial DNA was isolated from vaginal swabs for evaluation of microbial diversity by pyrosequencing of the 16S rRNA V3 to V5 hypervariable region. Approximately 59,000 sequences were recovered. Cytologically, the normal vaginal microbiome of the baboon resembles a human bacterial vaginosis state. The LNG-IUS did not alter Nugent scores before or after placement. Since women with bacterial vaginosis may be more susceptible to microbial infection, this model may be useful for future prospective evaluation of LNG-IUS impact on pathogen susceptibility, particularly in the context of a bacterial vaginosis-like state.

Encephalomyocarditis Virus Infection: Confirmed and Suspected Cases in Chimpanzee Sanctuary in Sierra Leone

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Encephalomyocarditis virus (EMCV) infection was diagnosed as the cause of death of 3 chimpanzees and was suspected in 24 other chimpanzee fatalities in a 6-y period (2005 to 2011) in a Chimpanzee Sanctuary (CS) located in Sierra Leone, West Africa. Two distinct phenomena were observed: A) sudden death of 11 chimps, and B) 16 others showed mild clinical EMCV symptoms accompanied by signs of an apparent recovery, but then suddenly started to die. The death toll reached 27 in total and the following observations were reported: EMC virus was isolated from 3 chimps, 6 others had histologic changes similar to EMCV infection and the other 18 chimps had typical clinical presentation and gross pathologic changes similar to EMCV infection. The virus isolated from the dead chimp is serologically distinct from any other serotypes. Samples of rats and bats (potential carriers of EMCV) from CS premises were examined for EMCV conformation, but, surprisingly, all of the results were negative. Despite our efforts to minimize the EMCV infection by controlling the rodent population, fatalities of chimps with similar symptoms continued. In 2011 and 2012, all chimps were vaccinated with EMCV and EMCV booster. In both occasions, serum samples were collected and preserved for their antibody titer analysis and so we can observe the pattern of the disease in the coming years. Unfortunately, 2 chimps showing clinical symptoms similar to EMCV died in Feb/Mar 2012; however, the lab results were negative for EMCV as well as for other regular viruses such as Arena, Lyssa, Filo, Entero, Hanta, RSV, and HMPV. Despite our efforts, the problem continues; either the

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EMC virus is mutating or there are other unidentified diseases that cannot be diagnosed in Sierra Leone.

Acupuncture Treatment in Nonhuman Primates

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Five thousand years ago, acupuncture in its crudest form was first used as a blood-letting therapy. Since that time, techniques have been significantly refined, and today, acupuncture is used to treat a variety of ailments, ranging from osteoarthritis to cardiomyopathy. Acupuncture involves the insertion of thin, sterile needles into defined acupuncture points that stimulate physiologic processes through neural signaling. The majority of acupuncture points correspond to neurovascular bundle locations and motor endplate zones. Numerous scientific studies have proven the benefits of acupuncture, and given this scientific support, we determined acupuncture could benefit the nonhuman primates at our facility. As our colonies age, we are observing an increase in osteoarthritis and have focused many of our acupuncture treatments on this condition. We are currently treating one owl monkey and 3 chimpanzees that have osteoarthritis using acupuncture, and we have developed methods to quantify mobility improvements. We have also used acupuncture as a treatment for cardiac abnormalities and to expedite wound healing. To obtain maximum benefit, we need to perform multiple acupuncture sessions per animal. Sedating nonhuman primates for sequential acupuncture treatments may not always be in the best interest of the animal. In some of the smaller species, we can use gentle manual restraint during acupuncture sessions. We have trained several chimpanzees to voluntarily present and hold for acupuncture treatments in their home enclosures using positive reinforcement techniques. Acupuncture sessions last an average of 10 min, during which time the veterinarian inserts multiple acupuncture needles into specific points. In addition to osteoarthritis, we plan to expand our use of acupuncture treatments to address stress/depression, cardiomyopathy, and diarrhea/constipation. Acupuncture is an innovative treatment technique that we have found to be safe, inexpensive, and most importantly, effective. Our mobility scoring assessments indicate trends towards increased mobility in the animals currently being treated for osteoarthritis.

Pharmacokinetics of Buprenorphine and Sustained-Release Buprenorphine in Macaques

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Buprenorphine is the cornerstone of pain management in nonhuman primates, but the pharmacokinetics of this widely used drug are unknown in nonhuman primates. The premise that the current recommended dosing regimen of buprenorphine provides appropriate analgesia is unsubstantiated. It is therefore conceivable that NHPs do not have adequate pain control from the opioid component of their pain management plan. The purpose of this study was to evaluate the pharmacokinetic profiles of 0.01 and 0.03 mg/kg IM buprenorphine and 0.2 mg/kg SC sustained-release buprenorphine in 2 macaque species (*M. mulatta* and *M. fascicularis*) using mass spectrometry.

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The pharmacokinetics were not statistically different between species and buprenorphine was dose proportional at the tested doses. Buprenorphine had an elimination half-life of 2.6 ± 0.7 and 5.3 ± 2.0 h for the low and high doses, respectively, but the former was constrained by the sensitivity of the analytical method. Sustained-release buprenorphine had an elimination half-life of 42.6 ± 26.2 h. Buprenorphine had an AUC(0-Tlast) of 9.1 ± 4.3 and 39.0 ± 25.1 ng × h/mL for the low and high doses, respectively, and sustained-release buprenorphine had an AUC(0-Tlast) of 177 ± 74 ng × h/mL. Based on a hypothesized therapeutic buprenorphine plasma concentration threshold of 0.1 ng/mL in macaques, these results suggest that buprenorphine dosed at 0.01 mg/kg IM should be administered every 6 to 8 h, but when dosed at 0.03 mg/kg IM, it should be administered every 12 h. These results further demonstrate that a single 0.2 mg/kg SC injection of sustained-release buprenorphine maintains plasma concentrations above 0.1 ng/mL for 5 d in macaques. These findings support a new dosing strategy using sustained-release buprenorphine to improve pain management, decrease animal stress, improve animal welfare, and simplify nonhuman primate postoperative management in laboratory animal and zoological settings.

Adenomatous Hyperplasia of Brunner Glands in Chimpanzees (*Pan troglodytes*)

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Brunner glands are compound, tubular, mucous-secreting glands found in the submucosa of the proximal duodenum, from the pyloroduodenal junction to the sphincter of Oddi. The major role of Brunner glands in digestion is the secretion of alkaline mucous, which neutralizes acidic stomach contents as they enter the small intestines. In humans, Brunner glands infrequently undergo an adenomatous, hyperplastic transformation, forming polypoid structures that have typically been classified as a type of neoplastic lesion. Often associated with renal failure and usually asymptomatic, these structures can cause gastrointestinal bleeding, abdominal pain, intestinal obstruction, bile duct obstruction, or pancreatic duct obstruction. Adenomatous hyperplasia of Brunner glands is also an uncommonly reported finding of the gastrointestinal tract in nonhuman primates. We report on 2 recent cases of acute renal failure in aged female chimpanzees with incidental findings of multiple polyps in the duodenum that were histologically determined to be adenomatous hyperplasia of Brunner glands. Review of prior cases at our institution found additional cases with this combination of findings. We suggest these lesions in aged chimpanzees represent functional hyperplasia associated with marked duodenitis, chronic glomerulonephropathy, and/or renal failure rather than neoplasia.

Ileocecal Intussusception in 2 Chimpanzees (*Pan troglodytes*)

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Intussusception is a condition in which part of the intestine telescopes on itself usually causing swelling, pain, and obstruction of the intestinal tract. We will describe 2 cases of ileocecal intussusception in chimpanzees that presented at our institution in 2012. Both animals presented with lethargy and anorexia. Case 1 was a 15-y-old male and case 2 was an approximately 42-y-old female housed in separate areas. Abdominal radiographs were not diagnostic; however, a classic "dough-nut" shape was readily detectable via ultrasound. Both animals underwent surgical resections of the ileum and cecum. Animal 1 recovered fully, while animal 2 recovered from surgery, but died shortly thereafter. The specific cause of the intussusceptions for both cases remains unconfirmed; however, the animal in case 2 also presented with a persistent eosinophilia and concurrent pinworm infection. Therefore, it is tempting to speculate that a parasitic nidus may be to blame. Common causes in young small animals are parasites, infection, or foreign body. Intussusception in humans is moderately common in very young children and may be associated with rotavirus, but more often is idiopathic. In adult humans intussusception is rare and may be associated with tumor, malignant or benign, Meckel diverticuli, adhesions, or other enteroparesis syndrome. There are few reports pertaining to intussusceptions in nonhuman primates; however, all are consistent in that a parasitic infection was present. Although both of these animals had been repeatedly treated for parasites as a part of the preventative medicine program, it may be that Strongyloides stercoralis, a tenacious infection common to nonhuman primates, may have been a cause of enteroparesis leading to subsequent intussusception. In conclusion, an intussusception is a rarely diagnosed condition in nonhuman primates that may be related to parasitic infection and ultrasound is the imaging methodology of choice in presurgical diagnosis.

Development of an Abdominal Scoring System to Predict Long-Term Outcome for Spontaneous Endometriosis in Aged Female Rhesus Macaques (*Macaca mulatta*)

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Endometriosis affects a large percentage of the female rhesus macaques at our facility. All macaques are currently on long-term research protocols, and treatment is indicated for the majority of cases. There is some debate on whether surgical or medical management is more beneficial for managing endometriosis. We have chosen surgical treatment because of the opportunity to observe complicating factors, as well as the potential to reduce the need for repeated treatments. Our treatment of choice has been abdominal exploratory surgery, usually resulting in ovariectomy or ovariohysterectomy. However, the long-term outcome has varied greatly from case to case. To better predict long-term outcome for surgical cases of endometriosis, we looked at 11 cases of histologically diagnosed disease in a 4-y time period. A scoring system was created based on the appearance of the abdominal contents during surgery. We used the presence of widespread abdominal adhesions, focal adhesions, hemorrhagic cysts (chocolate cysts) and ovarian abnormalities as our criteria. A scoring system of 1 to 3 was created. This scale was given to blinded observers along with the surgery reports, and the animals were scored. With those scores, we then looked at recurrence of menses or clinical signs, need for further medical management (medroxyprogesterone), and survival postsurgery. The lowest scores correlated with complete cessation of clinical signs, while the highest scores correlated with the poorest

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outcomes (acute collapse and death). We then looked at the presenting complaints (palpable mass compared with clinical signs) from each case, along with their scores and end outcome. We found that presenting complaint also correlated well with abdominal score and prognosis. This system will help practitioners make stronger recommendations on surgical or medical management, as well as predict long-term outcomes for animals that undergo surgical intervention for endometriosis.

Assessment of Risk for Mosquito-Vectorless Transmission of Dengue Virus between Nonhuman Primates in a Research Setting

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Dengue is a mosquito vector-transmitted viral disease caused by 4 virus serotypes, dengue virus (DENV) DENV 1, 2, 3, and 4, which cause acute, febrile diseases of varying severity affecting more than 100 million people in the tropics and subtropics each year. Although several dengue vaccines are in clinical trials none are yet licensed for human use. Nonhuman primates (NHPs), especially rhesus macaques, are the animal model of choice for preclinical evaluation of candidate dengue vaccines. After DENV infection rhesus macaques may develop circulating virus (viremia) for up to 12 d, but without disease. As highly social animals, NHPs have additional requirements which must be considered when these animals are used for research, and pair/group housing to enrich animal welfare is desirable whenever possible. Our study is the first to attempt to model the risk for unplanned dengue transmission between pair- or group-housed animals from a bite, scratch, or other incidental contact involving the exchange of body fluids. An experiment was performed in which 2 rhesus macaques were initially infected with a high-titered, laboratory-propagated challenge virus stock. A small amount of sera (0.05 mL) collected during the viremic period from each infected animal was then transferred to 2 dengue naïve "virtual cage-mates" by subcutaneous inoculation to simulate incidental contact resulting in the transfer of body fluids. The testing of sequentially collected blood samples for dengue viremia demonstrated that both contacts became infected, demonstrating that DENV can in fact be efficiently transmitted between animals by incidental blood-blood contact. Therefore, pair or group housing in studies involving DENV challenge may be contraindicated, at least during the viremic period when the animals are potentially infectious.

Abnormal Placental Growth after Pregnancy Termination

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An adult female cynomolgus macaque on a study where an NSAID drug is tested as a contraceptive was diagnosed pregnant. As per protocol, we tried chemical ablation to terminate gestation. Ablation was attempted twice using the progesterone receptor antagonist mifepristone (20 mg IM), followed 48 h later by administration of misoprostol (200 mg PO). Mifepristone blocks progesterone action in the endometrium of the uterus. This interrupts the implantation of the embryo and subsequently causes embryo detachment from the uterus. Misoprostol stimulates uterine contractions that will in turn expel the detached embryo. Ultrasound exams confirmed that the pregnancy termination was unsuccessful and serum samples for hormonal assays were inconclusive. Our next step was an ultrasound guided isotonic uterine/placental infusion. With this procedure we were able to confirm fetal death by myocardial asystole but uterine and placental growth continued. Placental/uterine growth was abnormal in shape, consistency, and size. Surgical intervention was required to remove the retained placental tissue several weeks later. We will discuss possible causes for the failing chemical abortogenic regimens, including media and route used to supply the drugs, the abnormal hormonal changes that the case presented and microscopic and ultrasound pictures will be used to give a chronological picture of the case.

Health Implications Associated with the Use of Aspen Blocks as Enrichment for Rhesus Macaques

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There are a variety of environmental enrichment products available for laboratory nonhuman primates that promote the expression of natural behaviors including exploration, foraging, grooming, and manipulation. It is important to find products that promote species-specific behaviors, and that are durable, easily sanitized, and cost-effective. Two years ago, our institution purchased Aspen chew blocks as a novel enrichment device. A small trial was conducted in 20 animals to assess the safety of the product on animal health and the overall efficacy of the product to provide enrichment. The results of this preliminary trial were promising, no significant hematologic or biochemical changes were observed. A larger trial was started and approximately 160 rhesus macaques from 2 different rooms, both the SPF and conventional colonies, were provided Aspen chew blocks for enrichment. Exposure to this novel enrichment product lasted anywhere from 1 to 42 d, as some animals were relocated during this trial. Recently, numerous animals were reported for the presence of toothpick-like spindle fibers in the stool, emesis, poor appetite, and weight loss. Diagnostics, including a physical exam, radiographs, ultrasound, and/or gastroscopy were performed. To date, a number of animals have required surgery to remove large pseudonest like structures in the stomach, as well as long fibrous wood shavings in the jejunum and cecum. As a result of these phytobezoars, the affected stomachs had multifocal areas of hemorrhage and ulceration. Another striking finding was the severe mucosal thickening, a reaction to the chronic foreign body. Postoperative recovery for these animals has been prolonged and problematic. Wooden environmental enrichment products can promote species-specific behavior through manipulation, chewing, or shredding; however, negative sequelae can result, and these types of products should be cautiously considered.

Unexpected Death in a Term-Pregnant Rhesus Macaque

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A 17-y-old, multiparous, pregnant female rhesus macaque from a breeding colony was found dead in her cage 1 d after her due date. A healthy infant was clinging to her body.

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Necropsy findings included an enlarged left adrenal gland, multiple gastric ulcers (up to 4 mm), subcapsular hemorrhages on both kidneys, and mild mitral valve endocardiosis. The left adrenal gland was 4.5 × 4.5 × 2.75 cm and constituted 0.35% of body weight; the right adrenal gland constituted 0.021% of body weight. Histologically, the left adrenal mass was a pheochromocytoma, and emboli of neoplastic cells were identified within the pulmonary vasculature. Pheochromocytomas secrete excessive amounts of epinephrine or norepinephrine. These catecholamines cause tachycardia, malignant hypertension, hypercalcemia, hyperglycemia, and volume depletion via strong inhibition of the renin-angiotensin-aldosterone system. Histologically, there was equivocal evidence of hypertension (internal elastic lamina splitting, medial thickening) in the afferent renal arterioles, but tunica media hyperplasia of small vessels in other organs was not identified. There was no evidence of hypercalcemia (metastatic mineralization), or of hyperglycemia (pancreatic islet atrophy). The combination of high circulating catecholamines from the pheochromocytoma and high circulating glucocorticoids from parturition likely triggered acute cardiac arrhythmia, resulting in death. There was marked compression atrophy of the left adrenal cortex. The right adrenal gland exhibited multiple extracapsular nodules of cortical hyperplasia; they are considered compensatory for the loss of adrenocortical function in the left adrenal gland. The renal hemorrhages were likely secondary to increased intra-abdominal pressure at parturition. The gastric ulceration may have been a co-morbid condition related to pregnancy or husbandry or myriad other causes. In addition to pheochromocytoma, other causes of unexpected death in macaques include gastric dilation, primary cardiac disease (cardiomyopathy, encephalomyocarditis infection), endometriosis with cyst rupture and hemoabdomen, staphylococcal or streptococcal sepsis, *Clostridium piliforme* infection, and melioidosis (in recently imported animals).

Abdominal Mass and Intestinal Obstruction in Squirrel Monkeys

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Bezoars and intussusception were suspected in 2 Squirrel Monkeys (SQM). Case 1 was a 12-y-old female Bolivian SQM. Case 2 was a 10-y-old female Bolivian SQM. All animals presented with a common clinical signs of diarrhea, weight loss, hypothermia, and a possible movable abdominal mass. Abdominal ultrasound in case 1 revealed an enlarged area associated with the small intestine with unidentifiable margins in the middle quadrant of the abdomen, but it was unable to identify any particular mass in case 2. Differentials included adenocarcinoma, foreign body, fungal or parasitic mass, intestinal over distention, gastrointestinal motility disorder, and ileus. Case 1 and 2 patients were scheduled for fecal occult blood and GI intestinal barium series. During morning observation 2 d later, the animals were noted quiet, depressed, scant stool production, and reduced appetite. The serum chemistry showed hypoproteinemia, increased level of creatine kinase, and hyperglycemia. The GI barium series showed a distended, cavitated area of the small intestine and reduction in the GI transit, with some strictures. The animals did not improve with treatment and were euthanized. Necropsy confirmed that the mass was a tricobezoar and identified multiple strictures along the GI with reddened areas. Histology showed areas of mucosal erosion and ulceration and some traces of hair imbedded in the submucosa and muscularis layer of the GI. This is the first time that trichobezoars have been reported in squirrel monkeys.

Lung Abscess and Hyperthyroidism in a SHIV Infected Rhesus Macaque (*Macaca mulatta*)

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A 13-y-old multiparous female Indian-origin rhesus macaque (*Macaca mulatta*) infected with SHIV 162p3 presented with sinus tachycardia and weight loss without diarrhea suggestive of hyperthyroidism. A complete blood count revealed a leukopenia and mild thrombocytopenia. A serum chemistry panel and urinalysis were unremarkable. A thyroid panel demonstrated increased total thyroxine (T4), total triiodothyronine (T3), free T4 (fT4), free T3 (fT3), and thyroid stimulating hormone (TSH). Based on these results the presumptive diagnosis was secondary hyperthyroidism due to a TSH secreting pituitary adenoma. A contrast-enhanced MRI of the pituitary failed to show evidence of an adenoma. Ultrasound of the thyroid gland and survey chest radiographs were normal. One month later, T4, T3, and fT4 were no longer increased. During the following week, the animal developed a nonproductive cough, pale mucous membranes, and reduced food consumption. Chest radiographs now identified consolidation in the left caudal lung fields. Based on prognosis, the animal was euthanized. The most significant finding at necropsy was a large lung abscess in the left caudal lung lobe that contained a brown/black mucoid material. Thyroid and pituitary appeared normal on gross examination. Culture of the abscess produced *Peptostreptococcus* spp., a gram-positive nonspore forming anaerobic bacteria. *Peptostreptococcus* is a known causative agent for lung abscesses in humans particularly in immunocompromised individuals. In this case, the lung abscess could be attributed to immunosuppression due to the animal's SHIV status. The initial increased thyroid hormones and clinical signs led to the presumptive diagnosis of secondary hyperthyroidism. However, multiple imaging modalities and repeat thyroid testing failed to support this diagnosis. To date, the etiology of the transient hyperthyroidism and clinical signs is unknown. Also, the interpretation of thyroid function tests is problematic given the lack of robust diagnostic testing and limited knowledge of normal thyroid function in nonhuman primates.

When Rectal Procidentia Isn't

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An approximately 3-y-old male rhesus macaque (*Macaca mulatta*) of Indian origin was observed in his social group at our institution with material protruding from the rectum. The animal was born into an outdoor group and, following abandonment by his dam, was raised in the nursery through 188 d of age. He was housed with 10 juveniles being screened for ESPF, and was negative for rhesus rhadinovirus, simian spumavirus, simian cytomegalovirus, and *Macacine herpesvirus* 1. A routine physical was performed on 10 January 2012 and

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no abnormalities were noted. On 20 April 2012 the animal was sedated with ketamine for evaluation of a suspected rectal procidentia. Three to 4 cm of soft tissue protruded from the rectum. The material was grossly contaminated with fecal material and had evidence of extensive mechanical damage. Gentle traction of the material revealed additional soft tissue that was grey and avascular. Abdominal palpation demonstrated a 2- to 3-cm region of thickened intestine in the area of the descending colon. A presumptive diagnosis of rectal procidentia and intussuception was made and the PI contacted. Radiographic and ultrasonographic imaging and exploratory laporatomy were discussed with the PI. Due to concerns of compromising the viral status and prognosis, the animal was transported to necropsy, deeply sedated with pentobarbital, and euthanized. At necropsy, the descending colon contained a 1-cm defect in the wall completely filled by omentum. An 8-cm section of omentum was entrapped in the colonic lumen. The entrapped portion of the omentum was compressed, necrotic, and coated in fibrin and fecal material. Culture of the colonic serosa in the region of the defect grew α-hemolytic *Streptococcus* and *Bacillus* species. The final interpretation was chronic colonic perforation with omental entrapment and necrosis, and focal peritonitis. A review of the clinical history did not reveal previous illness or injury that could explain the cause of the perforation.

Poster Case Reports

Use of Recombinant Proteins as Antigens for Serological Detection of STLV and B Virus Antibodies in Macaque Sera

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Truncated recombinant STLV-p21 (12kD) and B virus glyco-B (79kD) proteins were expressed in insect cells using Gateway and honeybee melittin (HBM) expression system, respectively. The expressed proteins were extracted/purified using detergent extraction, centrifugation and/or nickel chelating column chromatography methods. Purified proteins (antigens) were evaluated by ELISA, SDS-PAGE, and Western blot analysis. Antigens were coated on ELISA plates or coupled to magnetic beads to develop MFIA immunoassay. Purity of the antigens (assays) was evaluated by screening heterologous sera positive for other simian infectious agents including SIV, SRV, and other herpesviruses. Both antigens did not cross react to antibodies against those viruses. Specificity of p21 and glyco-B MFIA and ELISA assays were evaluated by screening sera from SPF and/or superclean macaque colonies with 0 of 87 and 0 of 45 showing positive scores, that is, both p21 and glyco-B assays had 100% specificity. Sensitivity of the recombinant antigen MFIA assays was compared to that using the partially purified whole virus HTLV 1 and 2 and HVP2 lysate assays. Out of 27 STLV tested sera only 2 were negative by lysate MFIA assay which were positive by p21 MFIA and ELISA assays. Both were confirmed positives by HTLV IFA and/or HTLV 1 and 2 Western blot analysis. In a field trial for B virus assays using HVP2 viral lysate and recombinant B virus glyco-B antigens were compared using 625 SPF sera from various institutions. HVP2 MFIA assays showed 5 false positives while the glyco-B assay had only one false positive that were not confirmed by IFA. Both HVP2 and glyco-B assays detected B virus antibodies for 13 confirmed positive sera. Specificity and sensitivity of the developed magnetic bead-based MFIA and ELISA assays was comparable to corresponding MFIA assays using partially purified whole virus lysate assays. Therefore, assays using these developed recombinant antigens can be used for routine serological surveillance of macaque colonies.

Epidemiology of Diarrhea in a Breeding Colony of Rhesus Macaques

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Diarrhea has been the leading cause of morbidity in captive nonhuman primates for over 30 y. It has been reported that prevalence may be as high as 15%, accounting for up to 50% of hospitalizations in primate facilities. Within 1 y, nearly half of those animals treated for diarrhea will experience a recurrence. Given these figures, the epidemic of diarrhea in primate facilities warrants modern investigation. Diarrhea and its sequelae represent a significant health concern in addition to a severe economic burden due to a high veterinary caseload, loss of animals, and research setbacks. Here we describe the pattern of diarrhea in a large breeding colony of rhesus macaques through a retrospective analysis of 12 y of clinical data. We found diarrhea prevalence to be 10% in our outdoor colony with rates differing by age, sex, and annual season. Each year, 12% to 25% of animals with a single case of diarrhea will develop the chronic form. Over 60% of our cases are not associated with pathogens of concern on fecal cultures. Colitis, a related pathology, was found in over 40% of nonresearch deaths. While these figures are staggering, they align well with reports from 20 and 30 y ago suggesting that we will need to be creative in our approach to this clinical syndrome in order to improve animal health and wellbeing.

Lumbosacral Agenesis in a Cynomolgus Macaque (*M. fascicularis*) with Dam Diabetes as Possible Etiology

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At our institution, as the female breeders grow older, following yearly veterinary assessment, several animals are placed on "long term monitoring" plan for geriatric pathologies such as decrease ROM, diabetes, and others. This allows us to monitor closely the animal welfare status of these individuals in their outdoor cage and take necessary measures to attend to them as promptly as possible. On 25 April 2012, one pregnant wild-caught breeder female, tagged as diabetic and with an estimated age of 18 y was presented with dystocia to the veterinary staff. Animal was with open cervix, intact amniotic sac, signs of vaginal bleeding, and emergency ultrasonography revealed live baby. Placental detachment was suspected and decision was taken to perform Caesarean section. Live male baby was recovered and upon primary assessment, it was noted to have: no tail, no patent anal opening (only a pimple), and severely atrophied lower part of the body. Baby was sent for intensive neonatal care in incubator and was euthanized the next day due to poor survival prognosis. Necropsy revealed absence of vertebrae from T12 downwards, presence of a horseshoe-shaped solitary kidney, imperforate anus, and severe muscular atrophy on lower limbs with joints locked in valgus rotation. All of the above points clearly show that this is a typical case of lumbo-

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sacral agenesis, as described in human literature, and this is the first report of such an occurrence in *M. fascicularis*, especially in association with a diabetic dam. In humans, lumbosacral agenesis is an uncommon occurrence and etiology/pathogenesis remains unclear until now, despite strong suspicion that diabetes of the mother might be the trigger.

Fatal Atypical O:3 Yersinia Pseudotuberculosis Infection in Cynomolgus Macaques

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Several fatal cases of Yersinia pseudotuberculosis were diagnosed and confirmed based upon pathology, microbiologic culture and PCR. Within 1 mo of arrival, one animal from a group of 40 cynomolgus macaques was found dead without any prior signs of illness. Over the next 5 mo, 4 additional monkeys were either found dead, or euthanized due to severe clinical signs consistent with yersiniosis. A few of the clinical signs observed included: soft stool/diarrhea (with or without mucus and blood), decreased appetite, hypothermia, bradycardia, and lethargy. Yersinia-related pathology findings included microscopic findings of acute, erosive to ulcerative, necrohemorrhagic enterocolitis, often with large intralesional colonies of coccoid-bacillus bacteria. Stomach and regional lymph nodes also had similar findings. Genotyping by PCR showed an Y. pseudotuberculosis O:3 pattern (gmd-fcl+, ddhC-prt+, manB+, ddhA-B+), but an additional gene, wbyK, was detected and was not typically found within 21 known Y. pseudotuberculosis genotypes. Virulence gene analysis demonstrated that this isolate was a pathogenic strain with inv+, ypmC +, irp1+, yopB+, yopH+, yadA+, lcrF+. This is the second report on discovering wbyK+ O:3 genotype to cause fatal yersiniosis since the first case was reported from farm deer in the US in 2008. As the frequency of wbyK+ O:3 genotype is found more often in different carries, O:3 genotype is proposed to be divided into 2 subtypes: O:3a without wbyK and O:3b with wbyK.

Serological and Molecular Diagnosis of Chagas Disease in Captive Nonhuman Primates in the United States

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Chagas disease caused by *Trypanosoma cruzi* is listed as one of the neglected parasitic infections that have been targeted by CDC as priorities for human public health action. To investigate the endemic status of *T. cruzi* in captive nonhuman primates in the US, samples were collected from different states and diagnosed by anti*T. cruzi* IgM/IgG ELISA and PCR. The seropositive rate was 9.7% and PCR positive rate was 8.3% in Southern states; none was found to be positive in Northern states. Interestingly, *T. cruzi*-specific IgM was detected in both acute and chronic phases, suggesting that long-lasting IgM against *T. cruzi* was present in naturally infected rhesus and cynomolgus macaques. With combined IgM and IgG tests, the sensitivity of *T. cruzi* serodiagnosis was increased not only in early acute phase but also in chronic phase. Molecular heterogeneity of *T. cruzi* will be further characterized by genotyping to help understand the epidemiologic spread of *T. cruzi* among nonhuman primates.

Surgical Management of Coxofemoral Joint Osteoarthritis in an Adult Rhesus Macaque (*Macaca mulatta*)

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An 11-y-old female rhesus macaque (*Macaca mulatta*) was evaluated for severe left leg lameness following a 1-y history of intermittent stiffened gait. Physical examination revealed moderate thigh muscle atrophy, reduced range of motion, and mild crepitus localized to the left coxofemoral joint. Radiographic changes were consistent with moderate to severe osteoarthritis/degenerative joint disease (OA/DJD) with notable femoral head and neck flattening suggesting late stage avascular necrosis as an underlying etiology. Conservative management by way of intraarticular steroid injection was of limited success, providing only 3 mo of improved mobility before apparent lameness returned. A veterinary orthopedic surgeon was consulted, and due to limited improvement with medical management, the decision to perform a femoral head and neck ostectomy (FHO) was made. The surgery occurred uneventfully, and histopathology of the femoral head and neck revealed complete articular cartilage loss, marked multifocal to coalescing areas of fibrosis, and underlying bone resorption consistent with chronic OA/DJD. Four months postsurgery, the animal's condition was substantially improved; left leg range of motion, thigh muscle mass, and weight-bearing ability was approximately 90% that of the right. Radiographs taken at this time confirmed complete femoral head and neck excision with no evidence of ongoing disease. While femoral head avascular necrosis has the potential to severely impact the health and welfare of an animal, the underlying causes are poorly understood in nonhuman primates. Reported etiologies in humans and domestic animal species range from trauma to endocrine and immune disorders. In many instances progression to OA/DJD is imminent without surgical intervention, and to our knowledge, this case is one of only a few to report successful management in nonhuman primates, specifically rhesus macaques through FHO surgery. Long-term monitoring of this animal will provide further insight with regard to management and prognosis following surgery in this species.

Reconstruction of a Scalp Defect in a Rhesus Macaque

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A 7-y-old male rhesus macaque (*Macaca mulatta*) presented with avulsion of an experimentally placed cranial implant. Physical examination revealed a 9 × 4 cm round defect on the scalp. Due to the large size of the wound, traditional methods of closure were deemed inappropriate. Human medicine offers a variety of closure techniques and, through consultation with our Plastic Surgery department, these myriad methods including local flap reconstruction, microvascular free flap reconstruction, and skin grafting were considered. Upon careful examination of the site, the defect was surgically closed with the combination of a harvested skin graft and a local skin flap. Postoperative care included use of a protective bunting dressing for the graft, antibiotics, analgesia, and antiinflammatory medication. The site was successfully closed despite necrosis of the skin graft

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with subsequent granulation of the remaining defect. A second implant was placed within months of the original injury. The surgical technique presented here, which combines 2 different reconstructive options, allows a more timely healing process facilitating both return to research and improved welfare of the animal.

Orbital Cellulitis in a Squirrel Monkey (*Saimiri boliviensis*)

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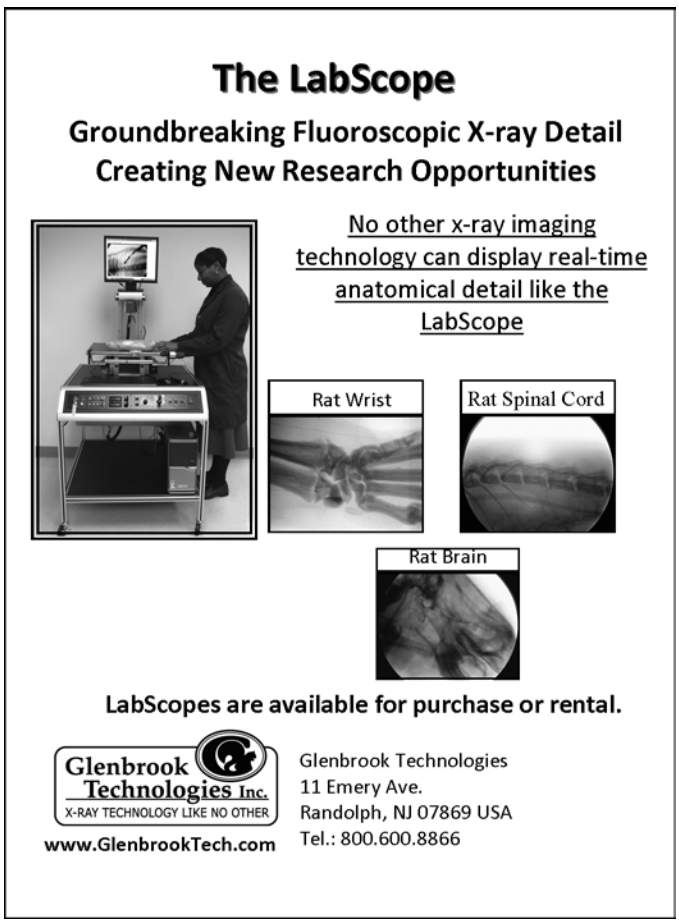
A 15-y-old female Bolivian squirrel monkey presented with acute, severe swelling of the right eyelids. Physical examination revealed eyelid edema, severe chemosis, conjunctival hyperemia, and exophthalmia of the right eye. No dental or systemic abnormalities were detected on physical exam. Pupillary light reflex was normal in the direct and consensual responses. Fundus examination was unremarkable. Ultrasonography showed a swelling of the retrobulbar soft tissues, but no evidence of a distinct mass. Bacterial culture from conjunctival swab recovered Staphylococcus aureus. Viral PCR for Saimiriine herpesvirus type 1 and type 2 were negative. Orbital cellulitis is an infection of the orbital soft tissues posterior to the orbital septum commonly originating from the sinuses, periorbital trauma, or hematogenous dissemination secondary to bacterimia and was diagnosed. Subsequent treatment with systemic antibiotic and NSAID was initiated. The animal recovered from the condition without any complications. To the authors' knowledge, this is the first report of orbital cellulitis in squirrel monkeys.



Physiologic Changes Associated with Physostigmine as a Nerve Agent Simulant

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Physostigmine is a commercially available drug approved for treating conditions such as glaucoma and myasthenia gravis. It is an acetylcholinesterase inhibitor that has also been used as a nerve agent simulant. Historically, our institute used physostigmine in a nonhuman primate model to simulate a nerve agent exposure for chemical casualty care courses. Students learned to recognize and manage a cholinergic crisis in a live patient. Clinically, animals recovered within 45 to 90 min without long-term effects; however, no physiologic data were electronically recorded to identify subclinical perturbations. To determine if there were residual physiologic effects, we used telemetry to monitor blood pressure, a biopotential, temperature, and physical activity and drew blood for acetylcholinesterase levels. Four female rhesus macaques were surgically implanted with telemetry devices. Following surgical recovery and baseline data collection, they were anesthetized (ketamine, 20 mg/kg) and administered a single dose of physostigmine (0.5 to 1.0 mg/kg) intravenously. Approximately 4 min after onset of clinical signs, animals received atropine sulfate (0.1 to 0.2 mg/kg) ± diazepam (0.5 to 2.0 mg/kg) intravenously as an antidote. Blood was collected at 0, 4, and 24 h, and at 7 and 30 d after physostigmine administration. Physiologic values changed significantly shortly after physostigmine administration, but all returned to baseline within 8 h. Acetylcholinesterase decreased significantly by 4 h post physostigmine but rebounded above baseline by 24 h and stabilized at baseline values by 7 d post physostigmine. Physical activity decreased initially, but returned to normal by 24 h post physostigmine. In summary, a single dose of physostigmine caused no lasting physiologic changes.

Use of Novel Telemetry Devices to Collect Individually Discernible Data Sets from Socially Housed Rhesus Macaques (*Macaca mulatta*)

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Animal welfare regulations state that nonhuman primate environmental enhancement plans "must include specific provisions to address the social needs of nonhuman primates of species known to exist in social groups in nature." The intent of these regulations is that facilities will provide social housing (pairs or groups) for social nonhuman primate species. The 2011 *Guide for the Care and Use of Laboratory Animals* also addresses this issue. Both documents provide for single housing of animals for scientific, medical, and social incompatibility reasons. Historically, nonhuman primates assigned to research protocols requiring telemetric monitoring have been singly housed because existing technology did not reliably allow collection of individually discernible data from socially housed animals. We conducted a pilot study to evaluate the ability of a novel telemetry system to collect individual data streams from group-housed animals. Four female rhesus macaques were surgically implanted with telemetry devices that monitored blood pres-

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sure, a biopotential, temperature, and physical activity. Data were continuously recorded while animals were singly, pair- or group-housed. Four individually discernible data streams were recorded under all housing conditions. One unexpected finding was that all 4 separate data streams were recorded for animals even when one or 2 of the cables were transected. Our feasibility study clearly demonstrated this system's utility in monitoring nonhuman primates under social housing conditions. These results foreshadow enhanced animal welfare through nonhuman primate group housing while meeting scientific needs for individual recordings of complex physiologic data for each animal.

Amyloidosis of the Buccal Mucosa in an Aged Rhesus Macaque (*Macaca mulatta*) with Severe Systemic Amyloidosis

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A group-housed, 16-y-old female rhesus macaque (*Macaca mulatta*) presented for lethargy and weight loss. Physical exam findings included dehydration, grade 3/6 systolic heart murmur, and a body condition score of 1.5 out of 5. Clinicopathologic findings included azotemia, elevated alkaline phosphotase, elevated γ-glutamyl transpeptidase, hypocholesterolemia, leukocytosis with mature neutrophilia and left shift, electrolyte abnormalities, and hematuria with pyuria and hyaline and granular casts. A fecal occult blood test was positive. The animal's clinical history included intermittent episodes of diarrhea with weight loss over 1 y, which typically responded to antibiotic therapy and supportive care. Differential diagnosis included gastrointestinal adenocarcinoma, amyloidosis, chronic infectious or inflammatory gastroenterocolitis, and other neoplasia. Postmortem examination revealed marked bile duct dilatation with mucosal petechiae, mitral valve vegetative endocarditis, cecal mucosal hemorrhage, shrunken kidneys with renal pelvic dilation and multiple renal cortical cysts, and a focal erythematous lesion on the buccal mucosa. Histologic evaluation revealed systemic amyloidosis, with amyloid present in the liver, gallbladder, kidneys, spleen, thyroid gland, small intestine, adrenal glands, pancreas, lymph nodes, and buccal mucosa. Amyloidosis has been described in humans, several nonhuman primate species, and other domestic animals. Secondary amyloidosis in humans has been associated with chronic inflammatory diseases, idiopathic colitis, infections, and neoplasia, and in macaque species it has been documented secondary to enterocolitis. The most common locations to find amyloid deposition in nonhuman primates are the kidney, liver, spleen, adrenal glands, intestines, and mesenteric lymph nodes. In humans with widespread amyloidosis it is not uncommon to find amyloid within the oral cavity. Immunohistochemical staining is pending to determine the type of amyloid in this case. This animal had widespread amyloid deposition that was identified in the buccal mucosa, which to the authors' knowledge has not been previously described in nonhuman primates.

Rehabilitation Technique after Finger Fracture in a Baboon (*Papio anubis*)

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Adequate and proper physical therapy (PT) is difficult in nonhuman primates (NHPs) in a captive research environment. Animals in captivity, more importantly NHPs, require the usage of all limbs to maintain a high quality of life. In 2009, a 3-y-old female baboon presented a lame right hand and was diagnosed with a horizontal Salter–Harris fracture of the second metacarpal on the growth plate below the first phalanx of the index finger. Nine days after diagnoses, surgery to place an internal fixation device on the finger's marrow to stabilize and repair the fracture. The invasive surgical decision was made to preserve the finger and its function. To prevent ankylosis of the joint, we developed a novel PT system to exercise her hand. PT gave back lost muscle mass and strength and exercised the fingers to preserve function. We used rope-type dog enrichment toys covered in peanut butter and trail mix to encourage the animal to reach, grab, and pull. This method also encouraged foraging behavior that specifically targets finger movement. After muscle mass recovered, other methods were developed to encourage the animal to pick and pull with just her fingers, as opposed to using her whole hand. In addition, daily enrichment was given in ways to encourage the animal to be more mobile in her stationary cage. Approximately after 5 mo of PT, the veterinarian estimated the animal had gained back 95% function of the second digit of the right hand and regeneration of muscle mass. We proved PT is possible and potentially successful in NHPs and probably underused in other research or captive species. Successful PT programs need to be designed based on species, species-specific behavior, and the individual animal willingness to rehabilitation.

Effect of Antagonism of the NMDA-Receptor by Intravenous Low Dose Ketamine on Obsessive-Compulsive Behavior in Nonhuman Primates

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Obsessive-compulsive behaviors (OCB), such as pacing, over-grooming, and self-mutilation are a common occurrence within captive research nonhuman primate (NHP) colonies. These abnormal patterns of behavior pose a risk to physical and psychologic wellbeing of the NHP and have been associated with, or considered indicative of compromised welfare. Many studies have attempted to describe environmental, physiologic and psychologic etiologies to the conditions, mostly in aim to maintain the animal's welfare but also to enable the production of more accurate research results. Several projects have tried psychotropic pharmaceuticals to see if the undesired behaviors could be controlled. Recent clinical reports from the human neuroscience field show that the use of a low-dose of ketamine (0.5 mg/kg) given over a 1-h period, has marked positive effect on OCB and depression in research subjects. Our project aims at testing if this ketamine regimen will help OCB in NHPs. We tested 4 baboons (*Papio anubis*) and one cynomolgus macaque (*Macaca fascicularis*) that display OCB in different ways. Animals were anesthetized with isoflurane and have not received ketamine within the last 6 mo. As these animals are part of our research colony, thus closely monitored, we have identified the different situations that trigger OCB on each one. The NHPs were video recorded at specific times when OCB triggering situations were expected. Recording sessions were scheduled before any treatment (baseline), after a placebo/saline infusion and after ketamine infusion. Frequency, duration, and intensity level of the OCB were quantified and analyzed. Reviewers were blinded as to the treatment stage of the research subject. Our

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report is a summary of the project's promising findings. To the best of our knowledge, there are no previous reports on this approach to OCB using ketamine in NHPs.

A Study in Telemetry-Implanted Cynomolgus Monkeys to Evaluate Select Cardiovascular Parameters in Animals Restrained in Procedure Cage or Restraint Chair (Pole and Collar)

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The nonhuman primate is a well-established animal model for various types of studies. Manual restraint of nonhuman primates by conventional methods can introduce unwanted variables to measurements obtained during routine data collection. For many decades, industry standards have revolved around the use of drugs, such as ketamine HCl and manual restraint methods, such as hand-catching or pole and collar systems. Stress-induced variables can affect blood values of various parameters, cardiovascular measurements, behavior, and clinical health. The Procedure Cage is a patented animal restraint apparatus designed in Japan by Dr Ryoichi Nagata. The Procedure Cage allows the primary animal enclosure to be maintained as a safe area by separating all procedure activities from the home cage. The USDA mandates research facilities to evaluate alternatives using the principles of the 3Rs. The Procedure Cage is a refinement in restraint technique. This study is being conducted to compare values for select parameters using the Procedure Cage compared with restraint chair. Six telemetry implanted animals are being monitored and data analyzed for ECG, HR, temperature, and BP using a validated telemetry system. On nonrestraint days data is captured for 15 min every 3 h and on restraint days, data is captured from 2 h prior to restraint until 4 h after restraint. In addition, behavior observations are performed once per week to monitor any clinically noticeable changes in behavior. By using the Procedure Cage to restrain nonhuman primates, there is likely to be less stress-induced variables, in addition to the already demonstrated shorter restraint training period and less technician time taken to complete procedures when compared with the other conventional methods.

Successful Retirement of Female Breeding Macaques (*Macaca fascicularis*) in a Large Breeding Colony

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Female macaques are housed in breeding groups of approximately 10 females to one male. Within those groups, lesser ranking females are often traumatized by higher ranking females or the male, and the male may not be allowed to breed the lesser ranking females. Our objectives were 2-fold: to remove the low ranking females suffering trauma in the groups and add productive females. The female breeders were wild caught prior to 2007 and the ages were estimated. It could not be determined if the reduced productivity was due to status in the group or age. The estimated ages of the animals to be removed ranged from 15 to 20 y of age. Returning these animals to the wild was not an ethical or reasonable solution, as the likely result would have been death by competition with other troops and/or capture for the bush meat trade. Euthanasia was also not an option for legal and ethical reasons. Due to space limitations a 2112-m2 enclosure was built. The enclosure contains the trees and natural vegetation present on site (mango, banyan, and bodhi trees). Cabanas and cement pipes were added for shade as well as areas where the animals could find private space. A run-though caging area allowed for routine TB testing and physical exams. Initial population of the compound was 285 females and one male. The overall condition of the animals was noticeably improved within weeks of moving into the enclosure. Some animals with previous hair loss grew back some or all hair. Weakness of limbs observed when animals were in small enclosures improved, as animals were able to climb, run and move in the less restricted environment. At any given time only 3 to 4 pairs groom in the entire compound. The females still have not formed groups within the retirement home but spend the majority of the time sitting individually with distant personal space. The exception to this is that the largest tree has become the nursery where the mothers with their newborn spend most of their time. During the early and later hours of the day the male has been observed to breed a different female frequently and this has resulted in about 20% pregnancy of the female population in only 6 mo of operation.

Evaluation of Reproduction and Raising Offspring in a Nursery-Reared SPF Baboon Colony

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Long-term effects from nursery-rearing nonhuman primates in certain conditions are thought to result in maladaptive behaviors in adulthood. However, the nursery-rearing of baboons is a required husbandry practice for recruitment of conventional, nonSPF baboons (*Papio hamadryas anubis*) into the SPF program at the Baboon Research Resource at our institution. During development of the SPF baboon colony, it was a concern that the first generation of nursery-reared females would exhibit a high rate of abnormal adult behaviors, particularly in areas such as reproduction and raising offspring. Here, we document reproductive data from adult females of the first SPF baboon breeding program of its kind during the program's developmental years, from 2002 to 2011. A total of 34 nursery-reared adult females reached sexual maturity during this time, and the average onset of estrus occurred at 3.27 ± 0.10 y of age. The average age of a female at first conception was 4.23 ± 0.28 y. The first documented pregnancy was conceived in 2007, and the first live birth occurred later that year. By the end of 2011, 22 nursery-reared female baboons had documented pregnancies, and 20 gave birth to at least one infant, with an overall 90.32% live birth rate. This live birth rate was similar to that of age-matched females in the conventional baboon breeding colony (91.74%) of the Baboon Research Resource during the same time period. Several of the SPF females (n = 16) were multiparous, producing at least 2 live infants; no record of twinning or multiple births occurred. Four abortions and one stillborn fetus were documented. Mothering ability was of particular interest with the founding generation of the SPF baboon colony, as all of these females had been nursery-reared from 24 to 48 h after birth until 18 to 24 mo of age, and therefore were not exposed to any intraspecies parental role models to learn natural mothering behaviors. Six mothers were unable to raise

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at least one infant due to maternal neglect, maternal abuse, or abuse inflicted by the dominant male in the mother's social group. Of the infants born, 71.43% were successfully reared by the mother until at least 180 d of age, compared with 81.54% mother-reared success in the conventional colony. Overall, these results suggest the nursery-rearing process during recruitment into this SPF baboon colony did not appear to have adversely affected reproduction.

Model Development: The Liver in Microbial Translocation and AIDS Pathogenesis

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An emerging feature of HIV/SIV pathogenesis is the increased level of microbial translocation that occurs in the later stages of infection. This phenomenon, which most likely occurs via leakage of luminal bacteria and/or their products across the gut wall, likely plays a central role in driving immune activation, which is a well-recognized correlate of HIV/SIV disease progression. We hypothesized that during the early stages of HIV/SIV infection, the liver clears these microbial products, therefore preventing spillover into the systemic circulation. In order to test this hypothesis we developed a novel rhesus macaque model that: 1) catheterized the portal vein, using a previously described technique, without the use of a fluid pump or tether apparatus, 2) measured gut permeability with a unique method in nonhuman primates and 3) collected serial liver biopsies using minimally invasive techniques. This presentation focuses on the model development phase of the study and describes the refinement and optimization that resulted in the final animal model. Furthermore, we will present preliminary proof of concept results that support the success of this model for use in SIV pathogenesis studies that may be applicable to other fields of research.

Videotaped Behavior as a Predictor of Clinical Outcomes in Rhesus Macaques (*Macaca mulatta*)

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Understanding nonhuman primate behavior in the context of animal care and use programs is beneficial for a multitude of reasons including improved health assessment. Accurate clinical assessment can be used to predict clinical outcomes that may aid in determining endpoints. Rhesus macaques (*Macaca mulatta*) are a prey species, and it is thought that they mask their clinical signs in the presence of observers, making it difficult to interpret the severity of their condition on cageside examination. The purpose of this study was to better understand the behavior of critically ill rhesus macaques in the absence of direct observation and determine if subtle behavioral changes can be used as an aid in evaluating their prognosis. Therefore, videotaped observations were collected from critically ill animals and the recorded behavior was analyzed and compared with future clinical outcome. Observations were conducted under 3 conditions: when an observer is present, not present, or recently present. Analysis of current data indicates that animals spend significantly more time in postures associated with pain or illness when an observer is not present or recently present than when an observer is present. In addition, animals that survive spend more time playing, drinking, self-grooming, and turning/shifting when no observer is present or recently present compared with those that do not survive. These preliminary data demonstrate that the use of video to assess clinical signs may be helpful in determining the most appropriate treatment, additional diagnostics, and clinical endpoints in the rhesus macaque.

***Moraxella osloensis* Septic Arthritis in a Rhesus Macaque (*Macaca mulatta*)**

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A 5.5-y-old Chinese-origin female rhesus macaque (*Macaca mulatta*) presented for hindlimb lameness. She was mother-reared in our institution's SPF breeding colony and was seronegative for B virus (*Macacine herpesvirus* 1), simian immunodeficiency virus, simian retrovirus type D, and simian T-lymphotropic virus. Her medical history included social trauma resulting in left tibia osteomyelitis and a surgically repaired right cranial cruciate ligament rupture. Physical examination findings on presentation included thin body condition, mild dehydration, pregnancy, and bilaterally swollen stifles that were warm to the touch, with the right more severely affected. Mild instability, decreased range of motion, and muscle atrophy were observed bilaterally. Hematologic evaluation revealed mild leukocytosis with marked neutrophilia and lymphopenia, moderate anemia, and mild thrombocytosis. Serum biochemistry revealed mild hyponatremia, hypochloremia, hypoalbuminemia, hyperglobulinemia, and moderate hypoglycemia. Arthrocentesis for culture and gram staining revealed *Moraxella*-like organisms. Treatment with enrofloxacin was initiated empirically and subsequently switched to cephalexin based on published case reports. Definitive diagnosis of *Moraxella osloensis* septic arthritis was made via isolation of the organism, cloning, and DNA extraction for sequencing of the 16S ribosomal DNA region. To our knowledge, this is the first reported case of *Moraxella osloensis* septic arthritis in a rhesus macaque.

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