Projects funded in 2011

**Pharmacokinetics and efficacy of liposomal extended-release buprenorphine in a rat model of neuropathic pain**

Dr. Dale Bjorling  
Department of Surgical Sciences

Animals do not like frequent injections and it may be difficult for owners to give dogs and cats pills at home. Morphone-like medications (opioids) are used to treat pain from many causes, but may be abused by people or accidentally ingested by children. Buprenorphine is an opioid drug commonly used in animals. It is one of the few drugs that can be used to treat pain in cats. Our laboratory has developed a formulation of buprenorphine that lasts for 2 weeks in rats using liposomes (LE-Bup). Liposomes are small, artificial membranes that form into hollow spheres. Drugs may be loaded into these hollow spheres, and the liposomes leak the drug slowly into the body. We will test the release rate of more LE-Bup formulations in rats, and determine their effectiveness at treating rats in a standard model of pain from nerve injury. This study would provide preliminary data to develop LE-Bup for clinical use in animals and people.

**In vivo evaluation of acoustoelastic strain gauge in the normal equine superficial digital flexor tendon**

Dr. Sabrina Brounts  
Department of Surgical Sciences

The superficial digital flexor tendon (SDFT) is a commonly injured soft tissue structure in performance horses. Injury of this structure happens to occur mainly in the mid-portion of the SDFT. Prognosis for return to full athletic function is guarded due to the fact that horses are placed back into work to soon and re-injury of the tendon occurs. Therefore it is important to be able to assess quantitatively the mechanical property of tendons under load before the horse returns to full athletic use. At the University of Wisconsin a novel technique called “Acoustoelastography (AE) was developed, which interrelates the ultrasound wave propagation to the local tissue biomechanical stiffness. Pathological diseased tendon has less stiffness than normal healthy tendon. AE can assess this in virtually real-time without knowing/recording tissue loads or performing extensive numerical analysis on images. The goal of this project is to determine whether AE can measure mechanical properties and strains non-invasively in normal equine tendons and secondly establish a reproducible method of applying AE to the equine SDFT in vivo. The ability to evaluate the degree of tendon injury via its function would revolutionize diagnosis, monitoring, and treatment of musculoskeletal injury. By identification of weak areas within the tendon before overt changes in tendon anatomy are appreciated, rehabilitation programs could be specifically tailored for the patient reducing the rate of re-injury. In addition, a more specific prognosis for soundness after return to a high level of athletic competition may be determined. Degenerative tendon changes may be detectable earlier, allowing identification of high-risk animals before a career ending injury occurs.
Radiographic anatomy of juvenile bovine limbs
Dr. Randi Drees
Department of Surgical Sciences

The University of Wisconsin-Madison, Veterinary Medicine Teaching Hospital receives referral patients from farms around Wisconsin and even farther afield. Young calves and older cattle patients are frequently radiographed to assess the source of lameness and swelling of their limbs. With the radiographic technology available at the VMTH, we can obtain detailed radiographs of the affected limbs. The reference images available are quite old and are based on images which are much less detailed than those we can obtain today. Our objective is to take radiographs of calves at different points during their development, in order to have an improved reference of normal juvenile bovine limbs. We can then use these images to help diagnose disease in our patients, and also to improve learning resources for our students and a reference for veterinarians in practice.

Efficacy of taurine supplementation as a treatment for canine urinary incontinence
Dr. Heidi Kellihan
Department of Medical Sciences

Twenty percent of spayed female dogs will develop some degree of urinary incontinence, which is the unconscious leaking of urine during sleep or activity. This disease significantly impacts quality of life for these patients and their owners. New therapies are needed that are proven to be effective and safe. One novel therapy is taurine, an amino acid supplement that has many important functions in the body, although all of its physiological roles are not fully understood. Taurine has been safely used in dogs and cats for years for the treatment of heart disease caused by taurine deficiency. We have observed resolution of incontinence in canine patients supplemented with taurine, suggesting that taurine may be a reasonable, alternative therapy for incontinent dogs. The objective of this study is to evaluate the response of incontinent dogs to treatment with taurine, as compared to placebo, in a randomized, blinded clinical trial.

Low temperature blood-free perfusion for prolonged cardiac arrest in small dogs
Dr. Jon McAnulty
Department of Surgical Sciences

The goal of this research is to study methods to utilize very low temperature methods for achieving long term cardiac arrest in small animals. The significance of this research is in development of methods that will allow easier and more successful methods for cardiac surgery in the dog than is currently available with conventional cardiac bypass techniques. The specific studies proposed are an extension of previous work and are targeted at successful implementation of these methods in small dogs which is anticipated to represent the majority of the cases for which these surgeries are needed in the clinic. Small dogs represent a specific challenge with respect to down sizing the pump circuits, fluid volumes and alteration of methods protocols to achieve similar success as seen in larger dogs. We anticipate that success in these studies will lead directly to application of these methods in patient animals.
In vitro biomedical evaluation of four surgical techniques for fusion of the equine distal and tarsometatarsal joints
Dr. Samantha Morello
Department of Surgical Sciences

Osteoarthritis of the distal hock joints is a debilitating cause of lameness in many equine athletes. The disease process results in significant pain for the animal, part of which is believed to arise from instability of the joints. We aim to evaluate the stability of the hock after various surgical treatments designed to promote ankylosis of these distal joints. In particular, we are evaluating the implantation of Kerf-cut cylinders, devices which have been used in both human and equine surgeries to stabilize regions of the spine. The potential exists to implant these devices in horses via a minimally invasive approach saving time and money. We aim to show that the implantation of these cylinders will improve the biomechanical stability of the distal hock joints and thereby may reduce lameness and facilitate fusion. It is hoped that this background study will provided us with enough data to conduct a clinical trial.

Arthroscopic assessment of stifle synovitis in the dog
Dr. Peter Muir
Department of Surgical Sciences

Cruciate rupture is the most common cause of lameness in dogs. Ruptures usually occur during normal activity and are not associated with accidental injury. Traditionally, knee arthritis was thought to be a consequence of joint instability after rupture of the cruciate ligament. However, recent work suggests this paradigm is incorrect and that development of cruciate rupture is a consequence of inflammatory knee arthritis. Consequently, it has been proposed that cruciate rupture develops because of rheumatic disease characterized by chronic inflammation of the joint lining or synovium. The health of the cruciate ligament tissue is closely related to the joint environment, as the ligament is surrounded by joint fluid and covered by the joint lining. Although synovitis is typically found in affected dogs, it is difficult to assess severity of inflammation clinically, particularly in therapeutic clinical trials. Minimally invasive surgery with a rigid fiber optic arthroscope provides a magnified view of the joint lining, with little patient risk. In human beings, the arthroscopic appearance of the synovium is highly correlated with histologic inflammation of the synovium. This study will determine whether there is an association between quantitative arthroscopic scoring of synovial inflammation and histologic markers of synovial membrane inflammation. Arthroscopy promises to be a useful tool upon which individual treatment plans may be based and responses to therapy may be monitored. This knowledge will be used in clinical trials evaluating use of disease-modifying medical therapy for affected dogs.

Epidural analgesia is extended when dexmedetomidine is added to bupivacaine in dogs undergoing hindlimb orthopedic procedures
Dr. Lesley Smith
Department of Surgical Sciences
Epidural administration of opioids (e.g. morphine) or local anesthetics (e.g. bupivacaine) provides analgesia of varying durations for hindlimb and lower abdominal procedures. Epidural analgesia is used commonly at the UW VMTH for dogs that undergo hindlimb orthopedic surgery. Use of epidurals for post-surgical pain management is also common in general practice. Bupivacaine and morphine are the most common drugs chosen for epidural use in veterinary medicine. Studies from human medicine suggest that alpha-2 agonist drugs, including dexmedetomidine, have benefits when added to the epidural analgesics, including better quality of analgesia and an extended duration compared to when single drugs are used alone. In addition, morphine is a controlled substance, whereas dexmedetomidine and bupivacaine are not controlled, thus are routinely available to general practitioners. No scientific studies have been reported in veterinary medicine on the analgesic use of epidural dexmedetomidine. The goal of this study is to compare the duration of epidural analgesia attained from bupivacaine alone, bupivacaine + morphine, and bupivacaine + dexmedetomidine. Our hypothesis is that addition of dexmedetomidine to the epidural will provide longer and more effective analgesia than when bupivacaine is administered alone or in combination with morphine. If our hypothesis proves correct, dogs that receive epidural dexmedetomidine and bupivacaine will have lower pain scores and will require less additional analgesia in the post-operative period. Results of this study would provide valuable information to veterinarians in both general and referral practice about the duration and comparative analgesia of these drugs when administered epidurally to dogs.

**Characterization of beta catenin expression and pathway activity in canine malignant melanoma**
Dr. Tim Stein
Department of Medical Sciences

Canine oral melanoma is a highly aggressive cancer associated with a poor overall survival due to local disease recurrence as well as spread to other organs. Similar to advanced melanoma in humans, canine oral melanoma is poorly responsive to conventional anti-cancer therapies. The lack of sustainable disease control warrants investigation of novel therapies, preferably targeting features specific to the tumor and different from normal cells. Perturbation in a cellular signaling pathway - the Wnt/β-catenin pathway - has been implicated in the progression of human melanoma. Our preliminary data indicate β-catenin (a protein) is expressed in canine oral melanomas, and we propose to further evaluate this pathway’s potential to serve as a therapeutic target. We hypothesize that the Wnt/β-catenin signaling pathway will be active in a subset of canine oral melanomas. The results of our study will indicate whether further research is warranted to determine the prognostic and therapeutic relevance of the Wnt/β-catenin signaling pathway in canine oral melanoma.

**Health Assessment of Endangered Whooping Cranes in the Central Flyway**
Dr. Barry Hartup
Department of Surgical Sciences and International Crane Foundation

The North American whooping crane (Grus americana) was successfully returned from the brink of extinction, but remains highly endangered. Despite highly publicized reintroductions, the only self-sustaining flock remains the original migratory population that breeds in Wood Buffalo National Park, Canada and winters at the Aransas National Wildlife Refuge in coastal Texas. This population remains at
risk: total mortality for the 12 months following April, 2008 equaled 57 birds (21% of the population of 266 cranes). A newly authorized study will involve capture, marking and tagging of whooping cranes from this population with conventional and satellite telemetry for the next 3 years. My study is designed to provide health assessments from whooping cranes during the last 2 years of captures at the Aransas NWR. Together with development of a dataset of marked individuals and detailed telemetry, follow-up investigations of migration health risks and mortality factors will be possible, where previously only scant opportunistic information was available. The results of this investigation will be used to develop science-based strategies to prevent losses of whooping cranes in the decades to come and contribute to the recovery of the species.