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The Value of Aquatic Therapy in Managing Equine Osteoarthritis



Horse undergoing aquatic therapy in the underwater treadmill at the Gail Holmes Equine Orthopaedic Research Center.

Underwater treadmill exercise has become increasingly popular for the rehabilitation of equine musculoskeletal injuries; unfortunately, there has been no scientific evaluation of its effectiveness for the treatment of OA and its associated alterations in musculoskeletal function in horses. The purpose of this study was to define the proposed mechanisms of action of aquatic therapy and to determine its efficacy in the treatment of equine OA.

Osteoarthritis (OA) is one of the most debilitating musculoskeletal disorders among equine athletes. It is a common cause of poor performance, early retirement, and reduced life expectancy. Medical and surgical management of equine associated lameness disorders cost more than \$700 million within the

United States in 1998. Osteoarthritis is a progressive disease characterized by joint pain, inflammation, synovial effusion, limited range of motion, and a progressive deterioration of articular cartilage. The ensuing disease process affects not only the articular cartilage but also the surrounding articular tissues, including subchondral bone, joint capsule, synovial membrane, and periarticular soft tissues. As the disease progresses, characteristic pathologic changes occur including fibrosis and thickening of the joint capsule, articular cartilage fibrillation and erosion, and osteophyte formation, which all lead to functional impairments. Unremitting joint pain and inflammation often cause adaptive muscle guarding and altered

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Letter From Dr. McIlwraith

Welcome to the 2011 edition of *Arthros*. Our newsletter highlights some of our important findings in the last year including a ground breaking study on aquatic rehabilitation in equine osteoarthritis, the results of our study in cutting horses on the significance of yearling radiograph changes, and some clarification on some differences with platelet-rich plasma products. We also introduce our new Equine Sports Medicine Service, as well as the two new Equine Sports Medicine residents.

Further details of our research productivity for the last two years will be available in our 2010-2011 Orthopaedic Research Center and Orthopaedic Bioengineering Research Laboratory report which is being published now. If you would like a copy and do not receive one by the end of January 2012 please contact Paula Vanderlinden at the ORC.

The newsletter also contains information on new staff, a new faculty position, as well as a new lab manager, in addition to the residents and graduate students. Thanks to the ability and hard work of our faculty and staff we continue to make progress in a number of areas. Thanks to our donors, as well as research funding agencies, we have been able to continue with all our programs and research efforts. We will continue to justify your investment in what we do here.

Best wishes,



Wayne McIlwraith
Director



Aquatic Therapy

continued from Page 1

weight bearing to protect the affected limb from further discomfort and injury. Compensatory muscular adaptations are characterized by inefficient muscle activity leading to muscle weakness, joint instability and altered limb loading. Maladaptive musculoskeletal responses may produce additional gait alterations and predispose other articulations to an increased risk of injury (i.e., compensatory lameness). In humans, compensatory changes in posture and movement exacerbate the initial joint injury, which cause further alterations in limb biomechanics and contribute to the progression of OA. Similar compensatory mechanisms such as delayed muscle activation, muscle weakness, restricted joint range of motion, and a redistribution of limb loading are likely to also occur in horses.

Physical rehabilitation has become an effective treatment option for improving deficiencies and weaknesses associated with primary joint injuries, as well as reducing harmful compensatory gait abnormalities in humans. Rehabilitation programs that address OA and musculoskeletal injuries often incorporate some form of aquatic exercise. Therapeutic aquatic interventions can be used to optimize the treatment of sensory and motor disturbances in order to achieve the functional restoration of full athletic performance. Aquatic therapies, such as underwater treadmill exercise have also been reported in humans to increase cardiovascular endurance, improve muscle strength and timing, decrease limb edema, improve range of motion, decrease pain, and reduce mechanical stresses applied to the limb. Exercising in water provides a medium in which the effects of increased buoyancy, hydrostatic pressure, and the viscosity of water along with the ability to alter both temperature and salinity combine to play an important role in musculoskeletal rehabilitation. The increased resistance and buoyancy

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inherent in aquatic exercise increases joint stability and reduces weight bearing stress on muscles and joints. The immersion of the distal limb in water applies a circumferential compression of equal magnitude that increases with depth below the surface of the water, increasing extravascular hydrostatic pressure, which in turn promotes circulation and reduces edema.

Up until now, equine investigations into aquatic therapy have focused mainly on the horse's cardiovascular and respiratory responses to exercising in water. Equine swim training programs report an improvement in cardiovascular function, a reduction in locomotor disease, and an increase in the development of fast-twitch, high-oxidative muscle fibers, reflecting improved aerobic capacity. In addition, fine-wire EMG electrodes have been used to demonstrate the increased muscle intensity of the equine thoracic limbs during a pool swimming exercise program compared to overground walking. A recent equine study assessed changes in stride parameters while walking in various depths of water. Underwater treadmill walking with water at the level of the ulna resulted in a longer stride length with a reduced stride frequency, compared to walking in water at the level of the pastern joint.

A project was established by the Equine Orthopaedic Research Center to investigate the functional, biomechanical, and cellular effects of aquatic therapy on diminishing the progression of OA using an experimental model within the equine middle carpal joint (knee). Results from this study provide an objective assessment of the pathologic characteristics associated with OA and the clinical and disease-modifying effects



A horse is hosed down prior to entering the underwater treadmill.

allied with aquatic therapy. This study was the Ph.D. project of Dr. Melissa King working with Drs. Haussler, Kawcak and McIlwraith together with Dr. Raoul Reiser of the Department of Health and Exercise Science.

Multiple variables were assessed in this study including clinical lameness exams and knee joint range of motion, magnetic resonance imaging, weight bearing forces and muscle activation patterns, alteration in balance control and assessment of cellular changes within the joint. The analysis of the biomechanical data revealed that the amount of weight bearing that each horse applied to the front limbs remained symmetrical in those horses exercised in the underwater treadmill. However, the control horses (no underwater treadmill) demonstrated unequal front limb loading as the limb with induced knee OA bore significantly less weight than the non-OA limb. Similarly, the muscle activation patterns within select front limb muscles remained symmetrical between the front limbs in the aquatic therapy horses, while the control horses had a significant delay in muscle activation of the OA affected front limb. Clinically, range of motion within the knee of the horses exercised in the underwater treadmill was significantly improved one week

after starting underwater treadmill exercise and this improvement continued throughout the remainder of the study. At study conclusion the range of motion within the OA affected knee in those horses exercised in the underwater treadmill had returned to the measurement taken before creation of OA, which was not the case for the control group. MRI demonstrated less scarring within the OA affected knee of horses exercised in the underwater treadmill

compared to the control horses OA affected knee. In addition, there was a significant reduction in the amount of inflammation present within the synovial lining of those horses exercised in the underwater treadmill; however, this was not the case in the control group. Lastly, this study demonstrated that underwater treadmill exercise significantly improves overall balance control under varying stance conditions in horses with knee OA.

To our knowledge this is the first controlled study that has evaluated the effectiveness of underwater treadmill exercise to reduce morbidities associated with knee OA. Aquatic therapy for the management of knee OA demonstrated enhanced balance control, both clinical sign and disease-modifying improvements, evenly distributed front limb weight bearing and symmetrical timing of select front limb musculature. Overall, results from this study indicate that underwater treadmill exercise is a viable therapeutic option in managing OA in horses. Furthermore, this work provides a considerable contribution to the field of equine rehabilitation as it is one of the first studies to provide evidence-based support for equine aquatic therapy.

David Frisbie Receives AAEP President's Award



Dr. David Frisbie accepts the 2011 President's Award from the American Association of Equine Practitioners.

Dr. David Frisbie received the President's Award at the 2011 American Association of Equine Practitioners' meeting.

The President's Award honors an AAEP member who has demonstrated a dedication to the association during the past year by contributing a significant portion of time and expertise to benefit the health and welfare of the horse.

The current AAEP President (Dr. Bill Moyer) chooses the recipient. He selected David for all his excellent work as Chair of the AAEP Educational Programs Committee both for his innovations and his efforts in this important role. This is an excellent and appropriate honor.

Congratulations, David!

New Study Supports Small Volume Bone Marrow Aspirates for Mesenchymal Stem Therapy

For the past six years, the faculty of the Orthopaedic Research Center have investigated the potential of bone marrow-derived mesenchymal stem cells (MSCs) to heal orthopaedic injuries. The process of generating MSC treatments starts with the harvest of a bone marrow aspirate from the injured horse. While we have long believed that a 5 ml aspirate from a single site is sufficient to produce an MSC treatment, other laboratories have advocated harvesting as much as 50 ml of bone marrow. In order to address this discrepancy among laboratories, Drs. John Kisiday, David Frisbie, Laurie Goodrich, and Wayne McIlwraith compared the yield and differentiation potential of MSCs obtained from 5 ml and 50 ml aspirates taken from the same horse.

Bone marrow was harvested from the sternum and ilium from 6 donor horses. Five ml and 50 ml aspirates were taken from different sites (such as the

left or right ilium). Five ml aspirates could be quickly harvested from the ilium (1-2 minutes) or sternum (10-30 seconds), whereas 50 ml aspirates required approximately ten times longer to harvest. The MSC yield from 5 ml aspirates was not significantly different from 50 ml aspirates; however, the amount of materials and laboratory manipulation for 50 ml aspirates were three times greater than for 5 ml aspirates. Differentiation of MSCs into bone and cartilage were not different between large and small aspirates. Based on the efficiency of bone marrow collection and processing, we concluded that 5 ml aspirates are preferable to 50 ml aspirates.

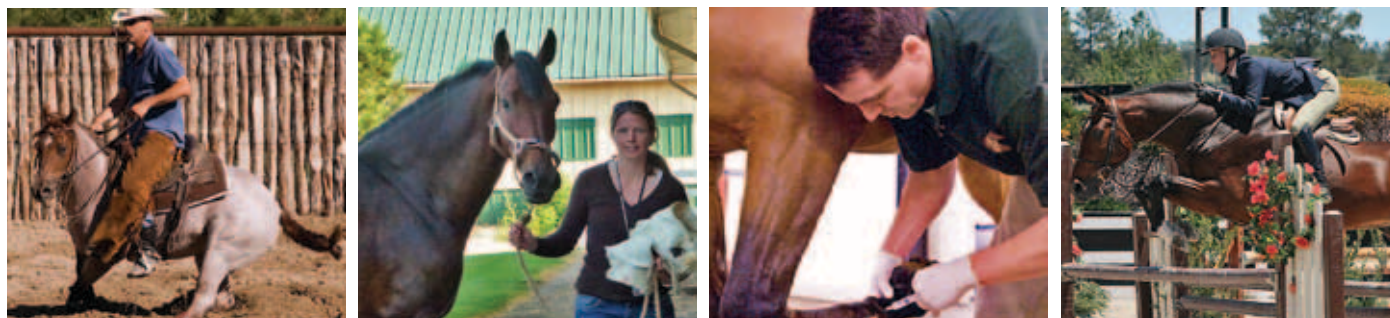
While the primary objective of this study was to evaluate the effect of aspirate volume on MSC yield and differentiation, a secondary comparison between samples from the ilium and sternum demonstrated a higher MSC yield and stronger differentiation into cartilage for cells from the ilium. Taken



Aspirating bone marrow from ilium (pelvis).

together, our data indicated that small volume aspirates from the ilium allow for the most efficient processing of MSCs with the highest differentiation potential. While differentiation into cartilage and bone cells are considered general markers of therapeutic potential, we hope to extend the results of this study by considering other behavior by which MSCs promote healing in clinical cases, such as the synthesis of growth factors.

New Equine Sports Medicine Service



The discipline of equine sports medicine has advanced significantly in recent years due to the development of new diagnostic and therapeutic techniques. Although much of the advancements in equine sports medicine have been pioneered by the Colorado State University Equine Orthopaedic Research Center (EORC) and the CSU Veterinary Teaching Hospital (VTH), state-of-the-art medical care was previously restricted to in-house hospital patients only. EORC faculty have collaborated with the VTH to develop an ambulatory Equine Sports Medicine service (ESM), targeting equine athletes throughout Colorado. The primary goal of the service is to support the equine athlete; from birth, through adolescence, competition, injury, rehabilitation, and retirement.

The ESM service provides a conduit through which our specialists can reach out to clients and referring veterinarians. The service offers clients throughout Colorado state-of-the-art diagnostics and treatment for musculoskeletal, respiratory, cardiovascular, and medical issues on an ambulatory basis. Services include lameness and follow-up examinations, digital radiography, digital ultrasound, extracorporeal shockwave therapy, laser therapy, joint injections, therapeutic management of back pain, and regenerative therapies (IRAP, PRP, and bone marrow-derived stem cells). All surgical cases are referred to the Equine Surgery service at the VTH to provide consistent, thorough follow-up of post-surgical cases. The ESM service strives to return the equine athlete to athletic

performance, by rehabilitating the entire horse, not just the injured region.

By providing advanced diagnostic and therapeutic services to the industry in an ambulatory setting, CSU is enhancing teaching by providing students a practical, efficient experience. Currently, students in the PVM program only experience sports medicine practice outside of CSU or in the clinic setting of the VTH. Establishment of the ESM service allows students the opportunity to experience the challenges and

The ESM service strives to return the equine athlete to athletic performance, by rehabilitating the entire horse, not just the injured region.

rewards of practicing sports medicine in a practical setting under the strict guidelines of the newly established American College of Veterinary Sports Medicine and Rehabilitation (ACVSMR), similar to the strict guidelines of colleges such as the American College of Veterinary Surgery and the American College of Veterinary Internal Medicine. This service allows students to follow a case from start to finish, clinically assess treatment outcomes and monitor the progression of injury healing.

The ESM service is the first within the ACVSMR. Four faculty members in the EORC are charter members of ACVSMR, and recognized that an equine sports medicine service would provide a resident with experience to fulfill the

requirements for board certification. The American College of Veterinary Sports Medicine and Rehabilitation residency at CSU was approved in May 2010, and as of July 1, 2010, the EORC began providing training to the first American College of Veterinary Sports Medicine and Rehabilitation resident at CSU. A second resident began training July 15, 2011. As a clinical entity, ESM provides cases for prospective and retrospective clinical study of disease, diagnostic techniques, and treatment efficacy.

The ESM staff includes two faculty clinicians and one technician. The service is managed by Dr. Chris Kawcak, D.V.M., Ph.D., Diplomate ACVS and ACVSMR, who has managed the ambulatory service in the EORC and is currently Equine Section head in the VTH. Additionally, Dr. Melissa King has been hired as a clinician for this service. She brings 10 years of experience in private practice and has recently completed her Ph.D. in Equine Sports Medicine and Rehabilitation through the EORC. She is one of only a handful of clinicians in the world to have expertise in equine rehabilitation. She is qualified to take the American College of Veterinary Sports Medicine and Rehabilitation board certification examination this coming spring, bringing two American College of Veterinary Sports Medicine and Rehabilitation certified clinicians to the ESM service.

For more information about the Equine Sports Medicine service, or to schedule an appointment, please contact the ESM coordinator at (970) 556-3931.

The Frequency of Radiographic Abnormalities in Young Cutting Horses

Radiograph repositories are commonplace in yearling Thoroughbred sales as they provide a means for veterinarians and potential owners to evaluate radiographs prior to bidding on or purchasing sale horses. Due to the success of this program in

This study found a high frequency of young cutting horses with radiographic abnormalities based on pre-sale screening radiographs.

Thoroughbreds, the National Cutting Horse Association followed suit in 2005 by introducing radiograph repositories at Western Bloodstock cutting horse sales. Although the frequency of radiographic abnormalities has been well documented in breeds such as Standardbreds and Thoroughbreds, it has not been evaluated in Quarter

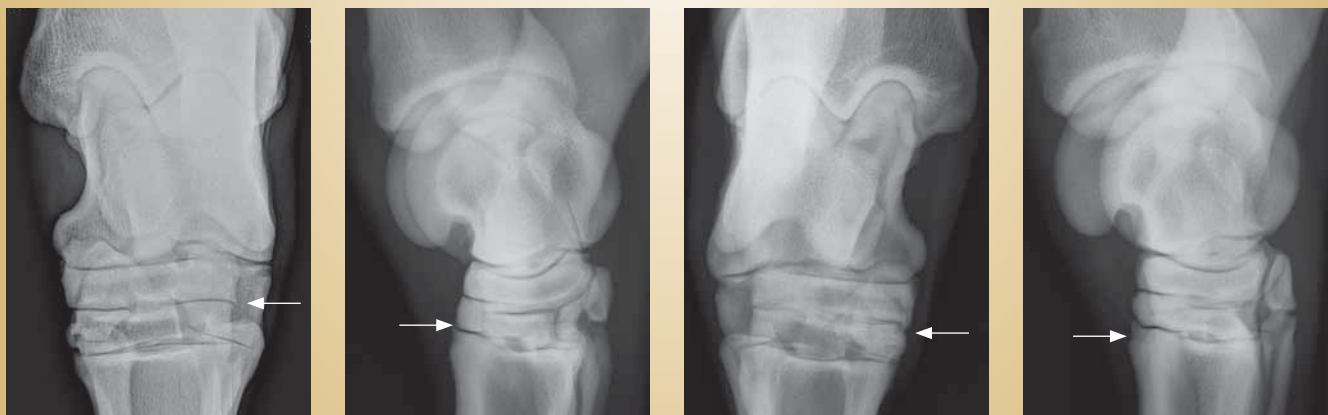
Horses or cutting horses. Furthermore, the correlation between certain radiographic abnormalities and future performance was also unknown.

The purpose of this first study was to determine the frequency of radiographic abnormalities in the stifles, hocks, fetlocks and knees (carpi) in this group of young cutting horses. The study was performed by Dr. Erin Contino as part of an MS degree project working with Drs. Park and McIlwraith.

In total, this study evaluated 8,857 repository radiographs from 458 horses. There were 278 yearlings and 180 2 year olds. The majority of horses had stifle (454 horses) and hock (438 horses) radiographs included in the repository which indicates that these are areas of concern in cutting horses. Overall, 408 (89.1 percent) horses had at least one radiographic abnormality recorded from the stifle, hock, fetlock, or knee.

In the stifle, the most common abnormality was change in the medial condyle (the weight bearing surface) of the femur which is the most common location for subchondral bone cysts. Changes to this region were recorded in 188 of 454 (41.4 percent) horses. In the hock, abnormal radiographic findings were recorded for 304 of 438 (69.4 percent) horse. Most of these changes were found in the distal hock joints which is a common location for osteoarthritis.

In conclusion, this study found a high frequency of young cutting horses with radiographic abnormalities based on pre-sale screening radiographs. Importantly, this work enabled additional research to determine which radiographic abnormalities may negatively influence a horse's ability to perform as a cutting horse (this study is also published in this issue of *Arthros*).



A Osteophytes (bone spurs) within the distal hock joints were recorded by joint and bone involved and graded by size. From left: A very small osteophyte (Grade 1) on the distolateral aspect of the central tarsal bone (A), a small osteophyte (grade 2) on the proximal dorsolateral aspect of the third metatarsal bone (B), a medium

C osteophyte (grade 3) on the distomedial aspect of the central tarsal bone (C), and a large osteophyte (Grade 4) on the proximal dorsolateral aspect of the third metatarsal bone (D) are shown with arrows. Reproduced with permission from Contino et al (2011).

The Relationship Between Radiographic Changes and Performance Outcomes in Cutting Horses

Radiographic repositories are becoming increasingly popular in multiple disciplines as a screening tool prior to sale. However, the importance of the radiographic findings must be objectively assessed relative to potential significance. While studies have been done to correlate survey radiographic findings with performance

The findings of this study can be used to help veterinarians make more objective assessments of survey radiographic findings prior to sale.

outcomes in Thoroughbreds, no such published study exists in Quarter Horses. This study was done by Dr. Myra Barrett with Drs. McIlwraith, Park, and Contino.

The goal of this study was to better clarify the potential significance of radiographic changes on repository radiographs relative to performance. The aim was to allow veterinarians and their clients to make more objective, informed decisions prior to purchase about the potential implications of various radiographic changes.

This study follows on from the previous study by Drs. Contino, Park, and McIlwraith that evaluated radiographic changes of 438 Quarter Horses. The changes documented in the first study were compared to objective performance outcome parameters. The parameters were: 1) likelihood of competing; 2) likelihood of earning money as a three year old, four year old, and as a three and four year old combined; 3) average amount of money earned as a three year old, four year old, and as a three and four year old combined. Mailed questionnaires and phone calls to owners of horses that did not earn money were used to try to determine why the horse had no recorded earnings.

When the tarsometatarsal (TMT) and distal intertarsal (DIT) joints were examined together, the presence of small (grade 2) osteophytes, which affected 19 percent of the horses, was associated with reduced chance of competing, earning money, and mean money earned. Very small and small osteophytes of the third and central tarsal bone assessed individually at the level of the TMT and DIT also had some significant effects in multiple performance outcome categories. The presence of thickening of the dorsal cortex of hind second phalanx as well as osteophytes at this location was associated with an increased likelihood of earning money. Several other potentially significant findings are reported but affect a relatively small number of the horses included in the study. The most important finding was that radiographic

changes of the medial femoral condyle (MFC) of the stifle were not significantly associated with performance outcome.

In summary, many radiographic changes were found to be not associated with performance outcome. The most significant finding was that lesions of the MFC in the stifle were not associated with decreased performance. However, some mild changes were associated with decreased performance and some radiographic changes were correlated with improved performance outcome. The findings of this study can be used to help veterinarians make more objective assessments of survey radiographic findings prior to sale. This research helps lay the groundwork for further investigations of the significance of survey radiographic findings in individual breeds and disciplines.



Platelet-Rich Plasma: Do the Products Differ?

Drs. John Kisiday, David Frisbie, and Wayne McIlwraith, in collaboration with Drs. William Rodkey and Richard Steadman of the Steadman Philippon Research Institute, recently had an article entitled “Effects of platelet-rich plasma composition on anabolic and catabolic activities in equine cartilage and meniscal explants” accepted for publication in the journal *Cartilage*. This study was motivated by the widespread clinical usage of platelet-rich plasma (PRP), a growth factor-rich therapeutic that is generated from the patient’s own blood. Clinicians have used PRP to treat joints by way of intra-articular injection, although the effect of PRP on cells within articular cartilage and the meniscus is poorly understood. Given these unknowns, the goal of this study was to test the response of articular cartilage and meniscus cells to PRP in a highly-controlled laboratory setting.

The high levels of growth factors in PRP are derived from blood platelets. To create PRP, blood is subjected to an initial spin that pulls down the red blood cells but leaves the platelets in the plasma supernatant, the latter of which is harvested as PRP. This single spin results in a 60 percent concentration of platelets relative to whole blood. The platelet

concentration may be increased further by applying a second spin that retains the platelet population while reducing the volume of plasma. While both “single” and “double” spin PRP preparations are used clinically, it has been commonly advocated that a concentrated platelet population, and thereby higher growth factor concentration, that results from double spin preparations, is more therapeutic than single spin PRP.

This hypothesis was tested by exposing equine articular cartilage and meniscal explants to single spin (including Arthrex ACP™) and double spin (including Harvest SmartPrep™) PRP preparations and measuring anabolic and catabolic responses. In general, single spin PRP stimulated higher tissue synthesis than did double spin PRP. Furthermore, gene expression of an enzyme that is known

to degrade articular cartilage and the meniscus was more highly expressed in double spin PRP than in single spin PRP. These data reject the hypothesis that increases the concentration of platelets in PRP is beneficial for articular cartilage and the meniscus; furthermore, these findings suggest that high platelet concentrations for intra-articular injection should be considered with caution.



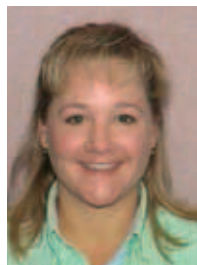
Centrifuge used to spin the blood as part of the process leading to the harvest of PRP.



Anticoagulant is drawn into a double syringe (left). 9mls of blood is drawn into syringe (center). Both syringes are centrifuged and the ACP is drawn into the smaller syringe (right). Images provided courtesy of Arthrex, Inc.

New Staff and Graduate Students

Dr. Melissa King



Melissa King joins us as a clinical instructor in Equine Sports Medicine as well as assuming positions of Director of the Gait Analysis Center and the ORC veterinarian.

Melissa graduated from Colorado State Veterinary School in 1997. After graduating she did a one year internship at Rood and Riddle Equine Hospital in Lexington, KY. Upon completion of her internship Melissa returned to northern Colorado to begin her career as an equine ambulatory clinician focusing on equine lameness. After practicing for 10 years Melissa sold her ambulatory practice to pursue a Ph.D. in equine lameness and rehabilitation. Having recently completed her Ph.D. (with details of this research elsewhere in the newsletter) we are very happy to have persuaded Melissa to move into a faculty position with us.

Dr. Christina Lee



Christina Lee received her BS in animal science at UC Davis in December 2002, during which time she worked in Dr. Sue Stover's lab for Dr. Hill collecting

data to investigate correlations between equine suspensory apparatus injury with suspensory apparatus failure and metacarpal condylar fractures. She then entered graduate school at UC Davis in 2003 in the Molecular, Cellular and Integrative Physiology graduate group working in Dr. Clare Yellowley's laboratory. For her dissertation studies, Dr. Lee investigated the effects of oxygen tension on the expression of proteins associated with bone remodeling and hypoxic regulation of gene expression in osteoblastic cells. In 2007 Dr. Lee came to Colorado State University to work at the

Orthopaedic Research Center as a Post-Doctoral Fellow under the mentorship of Dr. David Frisbie and Dr. John Kisiday to develop an in vitro model to investigate the cellular and molecular responses of chondrocytes to cartilage injury. In early 2011 she transitioned from her postdoctoral position into her current role as Laboratory Manager and Research Coordinator for the Orthopaedic Research Center.

Dr. Dora Ferris



Dora Ferris started an Equine Sports Medicine residency at the ORC in July 2010. She initially joined the ORC in July 2008 as the staff veterinarian responsible for

the clinical management of research horses, overseeing treadmill training of the horses, assisting with clinical cases and aiding research associates. She received her DVM from Washington State University's College of Veterinary Medicine in 2007 and she completed an internship focusing on equine lameness and surgery at Oakridge Equine Hospital in Edmond, OK prior to coming to CSU.

Dr. Erin Contino



Erin Contino joined the ORC as an Equine Sports Medicine resident in July 2011. Erin is originally from Concord, California, Erin but moved to Fort Collins to

attend CSU, graduating in 1999 with a bachelor's degree in Equine Sciences. In 2009, she completed a master's degree in Equine Radiology with Drs. McIlwraith and Park researching abnormal radiographic findings in yearling and 2-year-old cutting horses. After graduating from CSU with her DVM degree she did an internship at Pioneer

Equine Hospital in California and is now returning for the Equine Sports Medicine residency.

Trinette Ross



Trinette Ross is an instructor and advisor for the undergraduate Equine Sciences Program and is also the Equine Teaching and Research Center Event Coordinator

at CSU. She received her undergraduate degree from Montana State University and then completed an MS degree at Texas A&M University. Trinette is now a Ph.D. student at the ORC (Advisor, Dr. McIlwraith) evaluating the effect of omega 3 fatty acids in equine osteoarthritis model.

Colorado State University's 13th Annual Stallion Auction to benefit Equine Research

Jan. 11-14, 2012

Online bidding opens at 11 a.m., Jan. 11, 2012, and closes at 11 a.m., Jan. 14, 2012 (all times MST).

Bid Online!

Go to www.csuequineortho.com and click on the Stallion Auction link. Bids do not include chute fees, booking fees, or associated reproductive and veterinary costs. Winning bid amounts in excess of published stud fees may be tax-deductible.

How You Are Helping

Proceeds will go to the outstanding equine research programs at Colorado State University's Orthopaedic Research Center and Equine Reproduction Laboratory. With your bid, you can help these programs improve the musculoskeletal and reproductive health of horses.

Questions? Call (970) 297-4165 or e-mail Paula.Vanderlinden@ColoState.edu. Stallions and minimum bids listed at www.csuequineortho.com.

Visiting Speakers 2010-2011

We had a number of renowned speakers visit us in the last year. These visitors all gave excellent seminars on their work to our group.

Dr. Linda Sandell

Linda Sandell, PhD, Mildred B. Simon Professor and Director of Research, Department of Orthopaedic Surgery, Professor at the Washington School of Medicine visited CSU in August 2010. Dr. Sandell is one of the preeminent figures in molecular and cell biology of cartilage and is currently president of the Osteoarthritis Research Society International. Her seminar title was "Genetic Influences on Cartilage Repair in Mice." This research work by Dr. Sandell and colleagues has shown that different strains of mice can have marked differences in their ability to heal a cartilage defect confirming that there are inherent genetic factors that can affect ability for repair.

Dr. Chris Little

Dr. Chris Little, Director of the Raymond Purves Bone and Joint Research Laboratories, University of Sydney at the Royal North Shore Hospital, presented a special seminar during his visit to the CSU Orthopaedic Research Center in September 2011. Dr. Little spoke on, "Treating Osteoarthritis – Changing Perspectives Based on Pre-Clinical Models." Dr. Little is an Associate Editor of the journal of OARSI, *Osteoarthritis and Cartilage*, and is an internationally known researcher in osteoarthritis, as well as a board-certified equine surgeon. Dr. Little has evolved from an equine surgeon to cutting edge research in laboratory animal models that identifies novel target for therapy in osteoarthritis.

Dr. Frank Barry

Dr. Frank Barry, Director, National Centre for Biomedical Engineering Science, Professor of Cellular Therapy, Regenerative Medicine Institute, National University of Ireland, Galway, presented a special seminar on "Stem Cell Therapy: The Stem Cell-Host Response." Dr. Barry is world renowned as a leader in adult derived mesenchymal stem cells and his institute's research demonstrating generation of meniscus and decrease of osteoarthritis with intra-articular MSC therapy was the inspiration for our recent work on intra-articular MSC administration for clinical cases of soft tissue injury in joints as well as our experimental demonstration of enhancement of cartilage repair.

Dr. Barry's seminar was followed with a strategic planning session with faculty of the ORC regarding future collaborative research on the important aspects in equine stem cell therapy.

Dr. Liz Regan

Dr. Liz Regan, MD, PhD, Assistant Professor, Department of Medicine National Jewish Medical and Research Center presented the seminar, "Interplay of Inflammation and Antioxidant Defenses in OA Joints" in June 2011. While we have been aware of the importance of free radicals in osteoarthritis, Dr. Regan's work has increased the sophistication of different antioxidant roles in OA joints.



Arthros

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Our Purpose:

To find solutions to musculoskeletal problems, especially joint injuries and arthritis in horses and humans.

Our Philosophy:

To offer the best treatment of clinical cases possible, with continued and critical assessment of our results; to use these results to change our treatments; to point our research toward prevention of problems we cannot treat effectively or that cause permanent clinical damage.

Our Goals:

To find new methods to heal joints already damaged; to use state-of-the-art research techniques to find ways to prevent the occurrence of joint diseases and musculoskeletal injuries; to find methods of early treatment to prevent permanent damage when joint disease does occur.

2010 Equine Orthopaedic Research Center Supporters

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James M. Cox Jr. Foundation

President's Society –
\$25,000 - \$99,999

Ms. Gail Holmes, Double Dove
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Racing Hall of Fame

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Intra-Articular Mesenchymal Stem Cell Therapy Improves Cartilage Repair

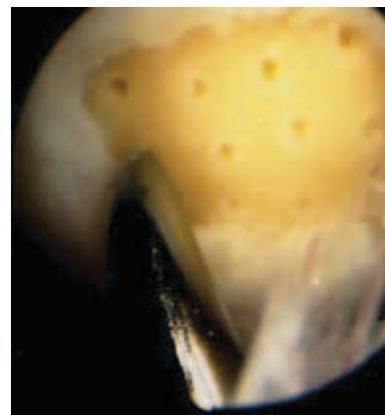
In a study just published in the November 2011 issue of *Arthroscopy: The Journal of Arthroscopic and Related Surgery*, Drs. McIlwraith, Frisbie, Kisiday, Werpy, and Kawcak in collaboration with Drs. Bill Rodkey and Richard Steadman of the Steadman Philippon Research Institute evaluated intra-articular injection of bone marrow-derived mesenchymal stem cells (BMSCs) to augment healing of microfractured defects compared to defects treated with microfracture alone.

One month after creating full thickness microfractured cartilage defects in the femorotibial joint one randomly selected joint received an intra-articular injection of either 20x10⁶ BMSCs with 20 mg of hyaluronan (HA) or 20 mg of HA alone (control standard of care). Horses were confined for two weeks, hand walked up

until four months and then subjected to strenuous treadmill exercise simulating race training until completion of the study at 12 months.

Arthroscopic examination confirmed a significant increase in repair tissue firmness and the overall score of the tissue and there was a trend for better overall repair tissue quality. Immunohistochemical analysis showed significantly greater levels of aggrecan and repair tissue treated with BMSC injection.

This was a critical finding as previous 12 month studies after microfracture have shown normal levels of one of the two critical components (Type II collagen) but only 50 percent levels of aggrecan. Aggrecan provides compressive stiffness to the articular cartilage and is critical in long term viability of repair tissue.



Arthroscopic view of a microfractured defect in a medial femoral condyle. The BMSCs were administered intra-articularly together with 20 mgs HA 4 weeks after creation of the defect.

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