Orthopaedic Research Center

Arthros

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The Dedication and Open House of The Gail Holmes Equine Orthopaedic Research Center

November 1, 2002

The Dedication and Open House of the Gail Holmes Equine Orthopaedic Research Center on Friday, November 1st, 2002 was the culmination of years of hard work on the part of researchers and overwhelming generosity on the part of donors. Over 200 people attended the Dedication ceremony and toured the new building and the renovated Orthopaedic Research Laboratory. It was a wonderful opportunity for CSU's Orthopaedic Research Program supporters to see the new facilities and meet the dedicated researchers, graduate students, staff and volunteers. Visitors were also able to check out displays of completed and current research projects. This event illuminated the incredible results that occur when the researchers and donors work together towards a single goal—

Plush toy horse, "Glory," is the first patient in the new surgery room.

improving the musculoskeletal health of horses and humans.

The new Gail Holmes Equine Orthopaedic Research Center features a surgery room with windows into the conference room, four offices, a treatment room with a high-speed treadmill for exercising horses, two wings of deluxe horse stalls and multiple turnouts. The $2 million needed to build this Center

The new Gail Holmes Equine Orthopaedic Research Center and remodeled Orthopaedic Laboratory.

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Message from Dr. McIlwraith

We have had a great year, both in productivity from the Research Center and financial support of the program. Our highlight this year was the opening of our new facilities. We have moved into The Gail Holmes Equine Orthopaedic Research Center and are enjoying the beautiful facility. The renovation of our older building into an extensive basic laboratory facility also turned out really well, and we now have the space and equipment to address the important research questions with state-of-the-art modalities and techniques.

It is also a particular pleasure to welcome Dr. Donna Wheeler and her Orthopaedic Bioengineering team into our building. Interdisciplinary research is critical for us staying ahead, and the support of the College of Engineering and the Vice President for Research and Technology to make this work is greatly appreciated.

In addition to our continued acquisition of grants and support funding for salaries, we have had three other very notable gifts this year. The first is a $3 million endowment from Barbara Cox Anthony to create the Barbara Cox Anthony Endowed University Chair. We are so grateful to Mrs. Anthony for her fantastic generosity.

We also have received $500,000 from Ken and Virginia Atkinson to purchase a state-of-the-art MRI machine and, most recently, have received an additional $500,000 from Alice Walton to complete a building to house the MRI. Alice has also committed to donating $100,000 per year for five years for personnel support. We still need some more endowment money to ensure permanent positions for two critical

faculty members, but our progress this year has been terrific.

I must also add a comment on the personnel and productivity within our laboratory, of which I am particularly proud. Our senior investigators, Drs. Dave Frisbie, Chris Kawcak and Clark Billinghurst, have continued to do and supervise excellent research, as well as continue to obtain grant funding. We have had two PhD students finish their programs this year, and both are producing exciting and useful research. We wish Dr. Louise Southwood and Dr. Fahd Al-Sobayil the best in their future careers. Drs. Sophie Morisset and Troy Trumble also defend their PhD work within the next two months.

The other area that impresses me so much is the work of our research associates and student hourlies. Heather Colhoun, working with Dr Frisbie, keeps an incredible team together for our surgeries and our horse care. The morale of our team always impresses me when we are working together, as we pursue the common goal of making things better for the horse.

Wayne McIlwraith
Director

Two Orthopaedic Research Center Graduate Students Receive PhD Degrees

Congratulations to Drs. Louise Southwood and Fahd Al-Sobayil, both graduate students at the Orthopaedic Research Center who received their PhD degrees during 2002.

Dr. Louise Southwood is now a faculty Assistant Professor doing large animal emergency and critical care at New Bolton Center, University of Pennsylvania. Her future plans are to get Board Certified in Emergency and Critical Care, continue some of the research that she began as a PhD student in fracture healing and, hopefully, apply some of the techniques to gastrointestinal diseases in horses. Dr. Southwood is also expecting a baby in June 2003.

Dr. Fahd Al-Sobayil will soon return to his native Saudi Arabia to work as an Assistant Professor in the College of Agriculture and Veterinary Medicine at King Saud University—AlQasseem branch, where he will teach and work in the veterinary hospital. He also plans to potentially work at a private clinic. The focus of Dr. Al-Sobayil's PhD work was examining biomarkers in exercised horses compared to exercised horses with osteoarthritis (see page 5 for the full article).

$3 Million Gift Donated to the Orthopaedic Research Center

Mrs. Barbara Cox Anthony donated $3 million to the Colorado State University Orthopaedic Research Center, as well as an additional $3 million to the Animal Cancer Center. The Centers are known internationally for their cutting edge research into veterinary and human health. This gift will provide the "people money" that both Centers need to attract and retain the best scientific minds.

"This is an easy investment to make. The veterinarians who are engaged in the kind of research that will ultimately benefit both animal and human health are deserving of our support," said Mrs. Barbara Cox Anthony, President of the James M. Cox, Jr. Foundation. "These are marvelous facilities conducting important and extraordinary work. The Orthopaedic Research Center and the Animal Cancer Center are engaged in scientific pursuits that are making a significant impact on the world of medicine."

The $3 million donated to the Orthopaedic Research Center will create an endowed University Chair in Orthopaedics. The earned interest generated by this account will support a salary and benefits for a scientist, as well as provide a small operating budget for research projects. This is a vitally important gift to the Orthopaedic Research Center, since 90 percent of the innovative research done at Colorado State University is funded through private individuals, companies and competitive research grants.

"This is a tremendous boost to our research programs," stated Dr. Wayne McIlwraith, the Director of the Orthopaedic Research Center. "The success of our programs revolves around our people, and to support these people, we need permanent funding."

Over the past 17 years, the research done by the orthopaedic team at CSU has not only benefited horses, but has also advanced human orthopaedic treatments. The Orthopaedic Research Center is dedicated to conducting research on treating and preventing musculoskeletal problems occurring in equines and humans. Current projects include using gene therapy to treat arthritis, defining fluid markers that predict orthopaedic disease and using computer joint modeling to prevent fractures. The Orthopaedic Research Center scientists are collaborating with human-based health foundations on several projects to benefit both horses and people.

Dedication

continued from page 1

was raised through private donations. Gail Holmes and Herbert Allen contributed a significant portion of this and have been instrumental in raising the remainder of the funds necessary for the new facility.

While the new Research Center was under construction, the adjacent Orthopaedic Research Laboratory underwent extensive remodeling. Previously unusable space has been transformed into laboratories, office space and a conference room. The Orthopaedic researchers share the remodeled area with Orthopaedic Bioengineering. A third of the $900,000 needed for this remodeling was donated by private individuals.

The new Gail Holmes Equine Orthopaedic Research Center, along with the remodeled laboratory, will allow the researchers to achieve a whole new level of research into preventing and treating musculoskeletal problems. Please feel free to call Katie Ruggle at 970-491-4165 to set up a tour of the new facilities.

Gail Holmes unclips the lead ropes to officially open the new building. From left: Dr. Wayne McIlwraith, Director of Orthopaedic Research; Dr. Albert Yates, CSU President; Gail Holmes; Dr. Lance Perryman, Dean.

Study Participants Needed

The researchers are still looking for horses to be involved in the Dynamix shoe study. If you have a horse with navicular disease and wish to participate, please contact Dr. Jeff Alldredge at 970-491-4413.

New Equine Magnetic Resonance Imaging (MRI) Center to be Built at the Orthopaedic Research Center

Diagnosing a problem is the first step in solving the problem. This is especially true in joint disease and injury. The Orthopaedic Research Center will soon have an important new tool for identifying musculo-skeletal problems, monitoring therapy and creating joint models that could help predict, and therefore prevent, injuries before they occur—an Equine Magnetic Resonance Imaging (MRI) Center. Construction on an addition to the Orthopaedic Research Center to house a new MRI scanner will begin in Spring, 2003.

What is Magnetic Resonance Imaging?

Magnetic Resonance Imaging (MRI) is the gold standard for identifying joint disease in humans and is the best technique for non-invasively assessing a joint. A human orthopedic patient rarely has surgery without an MRI scan performed prior to surgery. Unlike X-rays, MRI allows the clinician to see soft tissues and cartilage in the joints, thus allowing them to better plan surgery. MRI is also used to monitor patients after surgery.

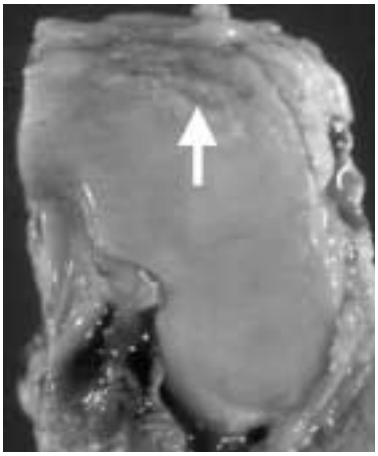
Equine veterinarians are at a disadvantage when describing joint disease to horse owners. Magnetic Resonance Imaging will allow equine veterinarians to better characterize diseases such as navicular disease, bone spavin, osteochondrosis and osteoarthritis. However, human machines have been very limiting for imaging equine joints - until now. Researchers in the Orthopaedic Research Center at Colorado State University, along with Dr. Charles Ho, a noted expert in the field of orthopaedic MRI, have identified a Magnetic Resonance Imaging scanner that would work well for horses.

The Future of Imaging

This equine MRI suite, which was made possible through the generosity of Ken and Virginia Atkinson and Alice Walton, will have a high-field machine to be used on anesthetized horses, which will produce very clear, high resolution images, and a low-field machine which will be able to be used on standing horses. Future modifications will hopefully allow images to be taken as high as the stifle joint—a major breakthrough in the field of imaging.

The MRI scanner will image soft tissues, such as articular cartilage, ligaments and tendons. The horses would be anesthetized, placed on a custom made table, and then put into the bore of the machine.

The MRI Center will not only help horses admitted to the Orthopaedic Research Center. Drs. Chris Kawcak, Richard Park and Wayne McIlwraith also plan to provide an MRI consulting service for cases all around the world. The MRI Center will open up a whole new field of study in equine medicine that could be the greatest advance in equine orthopedics in recent years.



The figures below demonstrate the power of MRI to improve diagnosis of joint disease. On the left is a picture of damage to the radial carpal bone of a horse (arrow). In the middle is an X-ray of the same area, showing the suggestion of damage at the site (arrow). On the right is an MR image of the same joint showing with absolute certainty the presence of damage (arrow).

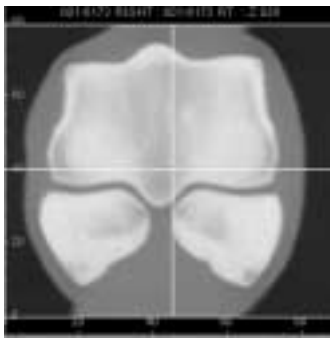
Diagnostic Imaging in Equine Orthopaedics

The Use of Computed Tomography (CT), Radiography (X-Rays), and Magnetic Resonance Imaging

Radiography

The use of X-rays has become a permanent fixture in human and veterinary medicine as a tool to visualize everything from fractures to abdominal contents. X-rays work on the basis of light energy. A

photon, which is basically a small packet of energy, is created by the X-ray tube. The photon beam emitted is focused on the patient while a cassette with photographic film lies beneath the patient. Each tissue type absorbs a different amount of energy from the photon beam, and denser tissues absorb more photons allowing less energy to pass through the patient. The amount of energy passing through the patient is detected in the film cassette beneath the patient. Just as with regular camera film, the areas that received more light photons become black when developed. Bone and metal appear the whitest, or most radiodense. Fat and air are the darkest, or radiolucent.



Computed Tomography

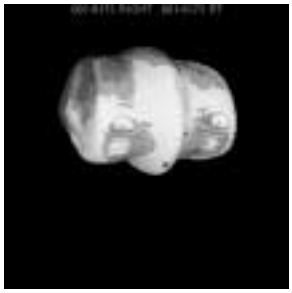
A Computed Tomography scan (CT-scan, CAT-scan) uses many X-ray photon beams fanned out in a circle to create a slice through the patient's body. Equine patients lie on a "couch", which is actually a movable table, and are moved into the circular gantry where they encounter the X-ray beams at specific measured increments. The result is several slices of equal width, usually 2-10 mm, that are viewed in succession to give a more realistic picture of the shape, size and position in space of specific anatomical structures. For this reason, CT can be more useful than standard X-rays in determining the extent or presence of fractures, especially in cases of subtle lamenesses. CT also has the ability to create images in different planes than what the original slice was taken. This is called orthogonal viewing, and helps to further depict the three-dimensional nature of structures such as bony contours.

Magnetic Resonance Imaging (MRI)

MRI is a new and very popular method of imaging the body. It works on the principle that any atom can create an external magnetic field. MRI is the picture of how weak magnetic fields created by tissue chemistry alter a known magnetic force when applied. Since each tissue has a specific chemical makeup, the magnetic resonance produced by tissues is very individualized. Thus, MRI is capable of producing superior soft tissue visualization compared with other imaging techniques. (See related article on page 4).

Three-Dimensional CT

It is now possible to create three-dimensional reconstructions of bone from the original CT scan. Peripheral computer models are created using a specialized computer program that runs on a PC platform. The program reads the CT data and creates three-dimensional images by "stacking" the CT slices together. Individual bones can be isolated from joints, or entire joints can be modeled. Here at the ORC, work is being done to determine bone density patterns by mapping colors that correlate to specific densities on the surface of the CT models. This enables veterinarians to detect changes in bone density earlier than would be evident on X-rays.



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Recent Biomarker Studies

Markers—Differentiating Between Exercise and Disease

The Orthopaedic Research Center recently completed a study, which was the focus of Dr. Fahd Al-Sobayil's PhD work, to determine if synovial fluid (the fluid in joints) and serum biomarkers could differentiate between horses with osteoarthritis in an exercise program and horses without osteoarthritis in the same exercise program. Since almost all markers change with exercise, the hypothesis was that the markers would change more dramatically with osteoarthritis and exercise than exercise alone.

Conclusions

The researchers were successful in proving that the markers did change more dramatically in the horses with osteoarthritis and exercise than with exercise alone. The study had some other interesting results as well:

Aggrecan and collagen are components in cartilage—collagen is like a sponge, and aggrecan is like the water that fills the "sponge," which squeezes out when pressure is put on the cartilage. There has been debate over which component degraded first in osteoarthitis. In this study, aggrecan changes preceded collagen changes.

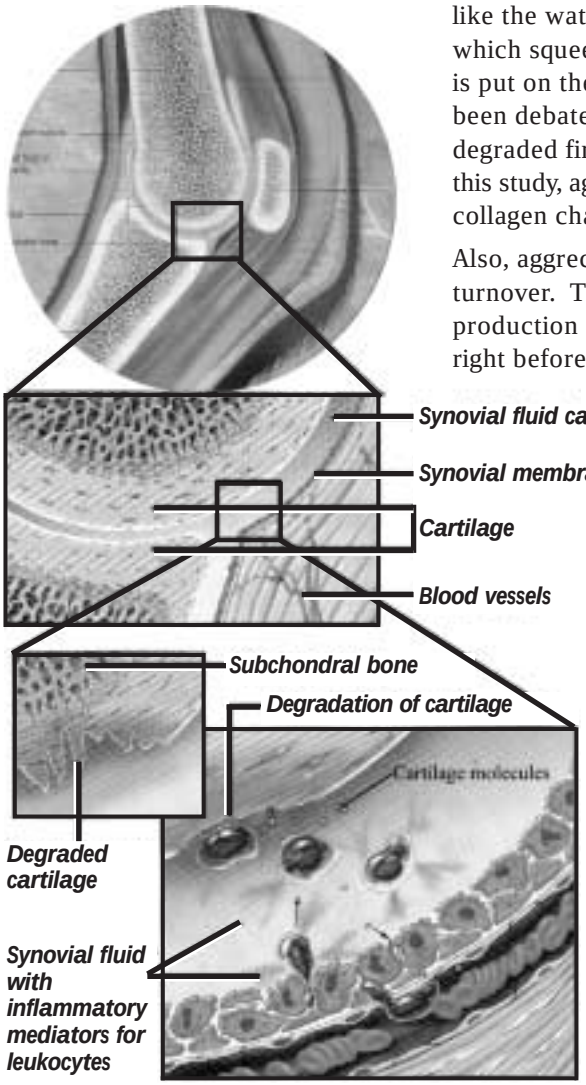
Also, aggrecan synthesis preceded turnover. This means that the production of aggrecan increased right before the cartilage began to degrade—the body was attempting to rebuild the cartilage.

Another long-debated point has been whether cartilage or bone is the first to sustain damage. In this study, cartilage changes preceded bone changes.

Further Research

The Grayson Jockey Club Research Foundation has provided the Orthopaedic Research Center with funds for another study involving racehorses. The purpose of this study was to use what we have learned about biomarkers and their relationship to exercise and arthritis and extend it into a "real life" situation.

Two hundred and fifty 2-3 year old racehorses were followed for 10 months. This study is being done by Drs. Billinghurst, Frisbie and Kawcak (and Research Associate Megan Knowlton) in collaboration with Drs. Rick Arthur, Vince Baker, Jeff Blea and Wade Byrd at Santa Anita and Hollywood Park racetracks in Southern California. Veterinarians performed monthly exams on each horse, and monthly blood samples were taken for biomarker analysis. Various diagnostic tests were also done to identify any suspected lesions. Biomarker assays are currently underway, and we are hoping to show the ability to predict lesions in race-horses through the analysis of blood samples.



This diagram shows the inside of a joint and what happens with the biomarkers when there has been cartilage damage.

The biomarkers are released into the blood where we can detect them through a blood sample.

Lab technicians then analyze the blood and any other tissues or fluids for biomarker changes.

Can Horses Help Humans?

Studies conducted at the Orthopaedic Research Center impact more species than just horses. One example of the work being done at the Center to help humans, as well as horses, are the investigations into microfracture therapy.

The Similarities Between Horses and Humans

Horse cartilage is very similar in thickness to human cartilage, and horses suffer from cartilage injuries and diseases similar to humans. Research in horses contributes to both human and horse health.

What is Microfracture?

Dr. Richard Steadman developed this arthroscopic technique in the mid 1980's to help heal the cartilage damage that often occurs in active people, particularly world-class athletes such as Picabo Street, Tommy Moe, Joe Montana and Terrell Davis.

Surgeons use a small 'pick' to make numerous holes in the bone underneath the cartilage (subchondral bone).

Why use Microfracture?

Articular cartilage, which protects the underlying bone from damage during movement, has no blood supply.

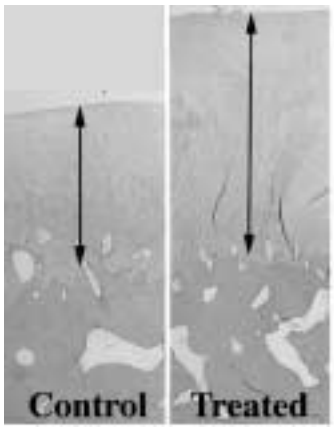
When traumatized, articular cartilage attempts to repair itself but cannot. Some scientists believe this is because there is no blood to carry in growth factors and repair cells.

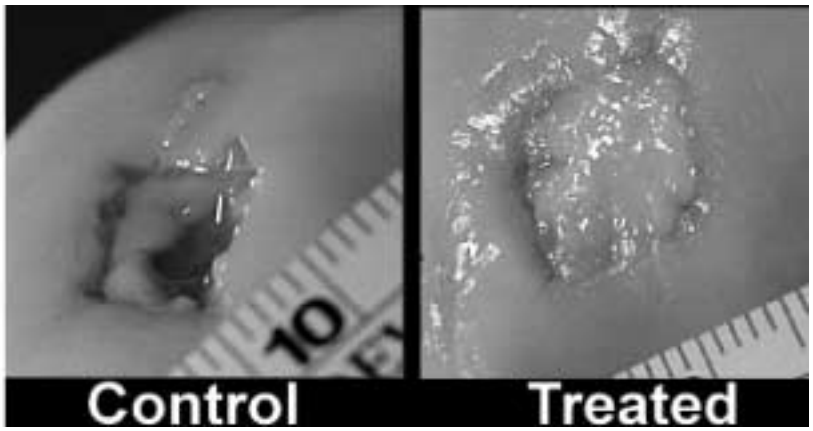
Microfracture increases blood flow to the wound by tapping holes into the rich blood supply of the subchondral bone below the lesion, thereby releasing repair cells and growth factors into the cartilage defect and joint in general.

Horses Helping Humans

Studies at the ORC conclusively proved that the amount of repair tissue made following the microfracture technique is significantly greater compared to that which formed following other standard techniques.

Before studying microfracture in horses, surgeons did not remove the calcified cartilage (tissue between the articular cartilage and the subchondral bone) from a lesion. Work with horses showed that articular cartilage healed significantly better when the calcified cartilage layer was removed.





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Sky Jack

In January 2001, Sky Jack had won five out of six lifetime starts, including the California Cup Classic. He had just won the Native Diver Handicap (G3) on December 3, 2000, by seven lengths and was named Horse of the Meet and Leading Handicap Horse at Hollywood Park. Unfortunately, he was sidelined by bone chips in his right knee.

Dr. Wayne McIlwraith of the Orthopaedic Research Center removed the chips in January of 2001. Sky Jack's devoted owners, Rene and Marjorie Lambert of Ren-Mar Thoroughbreds, along with his trainer, Doug O'Neill, ensured that the grey gelding had a long time off from training to fully heal. Their patience paid off as, after 14 months off the track, Sky Jack re-entered the racing world with a bang. A letter from Sky Jack's owners says it all:

August 30, 2002

Dear Dr. McIlwraith,

The expertise with which you performed surgery on Sky Jack, along with your competent staff, has enabled him to come back on the racing scene with unprecedented success. Since his return to racing in February, he has won the "Mervyn Leroy Handicap," "The 2002 Hollywood Gold Cup" and was named "Horse of the Meet" for the 2002 Spring/Summer meet at Hollywood Park.

We are very grateful for the dedication and skill that you have given to the Thoroughbred industry. We would like to thank you on behalf of ourselves, our staff and, of course, Sky Jack, in aiding in his current and future success!

Sincerely,
Rene and Marjorie Lambert
Ren-Mar Thoroughbreds, Inc

Orthopaedic Research Center Advisory Member Dies

Saudi Arabia's Prince Ahmed bin Salman bin Abdulaziz, an Orthopaedic Research Center Advisory Board Member and a generous supporter of the research program, died from a heart attack on July 22, 2002, at age 44. His unexpected death came only two months after winning the Kentucky Derby with War Emblem, a victory which he had dreamed about since seeing the Kentucky Derby on television as a child. War Emblem's trainer, Bob Baffert, stated, "His passion for horses was incredible—he lived and breathed them." Prince Ahmed is survived by his wife and five children, including 5-year-old triplets.

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Racetrack Surfaces

Introduction

The high rate of occurrence of lameness and injury at the racetrack is a major problem the equine racing industry faces. The cause of these injuries, which often compromise or end the competitive careers of countless equine athletes on an annual basis, has been the focus of several studies in recent years.

Elements including conformation, unsoundness and hereditary factors are important components in causing these injuries; however, there is reason to suspect that racetrack surfaces may be partially responsible.

Upon impact of the horse's hoof on the ground, the musculoskeletal loading is determined by the rate and amount of penetration of the hoof into the ground. It is estimated that the force between the horse's leading front hoof and the ground at the gallop can reach approximately 175 % of the horse's body weight. The force conveyed to the cannon bone is about 3-4 greater than the force acting on the hoof due to the fetlock joint's lever type action.

Research has suggested that different racing surfaces may change concussive forces which are felt by the horse's leg and the presence of a less suitable racetrack surface could significantly impact the risk to all horses running on the surface.

Research

Comparisons of different surfaces such as weak, medium and strong soils as well as of dirt, sand, wood and rock have been made. In each case, research indicates that, as the stiffness of the racing surfaces increase, loading forces of the limbs increase as well.

Dr. McIlwraith of the ORC is currently participating in a collaborative study with Dr. Raoul Reiser from Human Health and Exercise Science at CSU, Mick Peterson from Mechanical Engineering at the University of Maine, Dennis Moore and Steve Woods, racetrack superintendants at Santa Anita, Hollywood Park and Los Alamitos racetracks. The study is being funded by the AQHA.

The goal of the study is to develop equipment to test and ensure that racetracks have a consistent effect on the loading of the horse from track to track.

Conclusion

Providing consistent racetrack surfaces will take variations in tracks off the list of factors that cause injury and move it onto the list of things that can be done to further reduce and prevent injuries.

Once the equipment is available and racetracks are able to be tested to ensure consistency of surface properties, additional studies can be conducted to determine optimal surface conditions that maximize performance and minimize the chance of injury.

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Arthros is an annual CSU Orthopaedic Research Center publication.

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.

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Opportunities for Private Giving

It is an exciting time for the Orthopaedic Reseach Center!
The Gail Holmes Equine Orthopaedic Research Center and lab are open, and the scientists are making enormous strides in advancing the treatment and prevention of orthopaedic problems. The support of the individuals, foundations, and corporations who recognize the quality of the program and understand the importance of the Center's research made all of this possible.

To all those who have donated to the Orthopaedic Research Center—thank you. Your support is invaluable. Hopefully, you will continue to make it possible for the researchers to improve the health and quality of life for both humans and horses.

There are a variety of ways for an individual or group to make a tax-deductible charitable contribution.

Outright Gifts

Cash: Cash, usually given in the form of a check made payable to the Colorado State University Foundation, is available for the Orthopaedic Research Center to use according to your wishes.

Securities: Stock certificates are delivered either directly to the Foundation with endorsed stock powers or through an intermediary such as a bank or broker.

Gifts-in-Kind: Whole or partial interest in valuable items such as art, antiques, computers, laboratory equipment, horses, coin collections, or jewelry can be donated.

On-line Gifts: Credit card gifts can be made on-line through a secure, confidential form accessible from the Web page.

Planned Gifts

Bequest: A specific percentage of the full estate, or the entire estate, is left to the Colorado State University Foundation in your will.

Life Insurance: The Foundation is named beneficiary in your life insurance policy, or ownership of a policy is transferred to the foundation.

Charitable Gift Annuity:
An annuity contract obligates the foundation to pay you or other designated beneficiaries a fixed sum annually for life. A deferred payment annuity enables payments to begin after a specified number of years.

Charitable Remainder Trust:
A gift of a specific amount is placed in a trust managed by a specified financial institution. You turn over control of the funds, but still retain a life income from the funds. After you and any other beneficiaries die, the remainder of the funds comes to the foundation. These trusts may take effect while you are alive or may be created by your will.

Charitable Lead Trust: A gift of a specified amount is placed in a trust for a specific period. During that time, the Foundation receives the income from the trust. When the period of the trust ends, the principal is returned to you or a beneficiary. Typically, you are not taxed on the income received by the foundation during the life of the trust.

Real Estate

A gift of real estate may be made as either an outright gift or a planned gift.

There are many ways to help the Orthopaedic Research Center. If you have any questions about making a gift or wish to discuss financial matters concerning your contribution, please contact Paul Maffey, Director of Development, College of Veterinary Medicine and Biomedical Sciences, at (970) 491-3932 or e-mail r.paul.maffey@cvmbs.colostate.edu.

Thank you.

ORTHOPAEDIC RESEARCH CENTER

I would like to support the work of the Orthopaedic Research Center.

*Name*_____

*If joint gift, spouse's full name*_____

*Home Address*_____

*City/State/Zip*_____ *Home Phone ( )*_____

☐ *Enclosed is my/our check in the amount of $* _____
(Please make check payable to the Colorado State University Foundation.)

*Please charge this gift of $*_____
to my/our ☐ *Mastercard* ☐ *Visa*

*Card Number*_____

*Expiration Date*_____ *Name on card* _____

*Cardholder Signature*_____

☐ *I/We prefer to give through a pledge in the amount of $*_____

*I/We will pay $*_____ *per year for* _____*years*

in the month of _____. *(Not over five years, please)*

☐ *Enclosed in my/our first payment.*

☐ *This gift will be matched by my employer.*

A matching gift form: ☐ *is enclosed.*
☐ *will be sent separately.*

Please return completed form (with check, if applicable) to: Colorado State University Foundation, P.O. Box 1870, Fort Collins, Colorado 80522-1870.

Contact Paul Maffey, College of Veterinary Medicine and Biomedical Sciences, if you have any questions or need additional information. Phone (970) 491-3932.