RESEARCH REVIEW 2012

New and Potential Discoveries in Equine Medicine

UCDAVIS VETERINARY MEDICINE

Center for Equine Health
School of Veterinary Medicine
University of California, Davis

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New and Potential Discoveries in Equine Medicine

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Center for Equine Health
School of Veterinary Medicine
University of California
One Shields Avenue
Davis, California 95616-8589
Telephone: (530) 752-6433
Fax: (530) 752-9379
www.vetmed.ucdavis.edu/ceh
www.facebook.com/ucdavis.ceh

Published by the Center for Equine Health

Michael D. Lairmore, DVM, PhD, Dean, School of Veterinary Medicine

Claudia Sonder, DVM, Director, Center for Equine Health

Barbara Meierhenry, Senior Editor, Center for Equine Health

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Director's Message

IF YOU ARE READING THIS summary of equine research studies conducted through the Center for Equine Health, you have probably been compelled in some way to make a difference for a horse.

This ***Research Review*** is made possible by the many donors who have stepped forward and invested in knowledge. Over the past 40 years, the Center for Equine Health has worked collaboratively with the UC Davis School of Veterinary Medicine to discover new diagnostic and therapeutic tools for preventing and treating disease and prolonging the bond that exists between horses and humans. The return on investment is improved equine health and well being.

The Center for Equine Health is the only research center of its kind in this country that works directly with a School of Veterinary Medicine to produce evidence-based science that changes outcomes. Teams of scientists and clinicians are able to approach disease at a molecular level and translate that information to equine patients. We are making strides in equine genetics, regenerative medicine, orthopedics and neonatal medicine, to name a few. We are collaborating in some cases with physicians and environmental scientists to promote a one-health approach to medical progress. Many of the discoveries made in horses have direct implications for human health, especially in the area of regenerative medicine. The use of the body's own stem cells to facilitate healing and repair is being actively studied and implemented in clinical trials in humans and horses. Be sure to read our update of the regenerative medicine program (pp. 12-13), as much progress has been made since its inception in 2006.

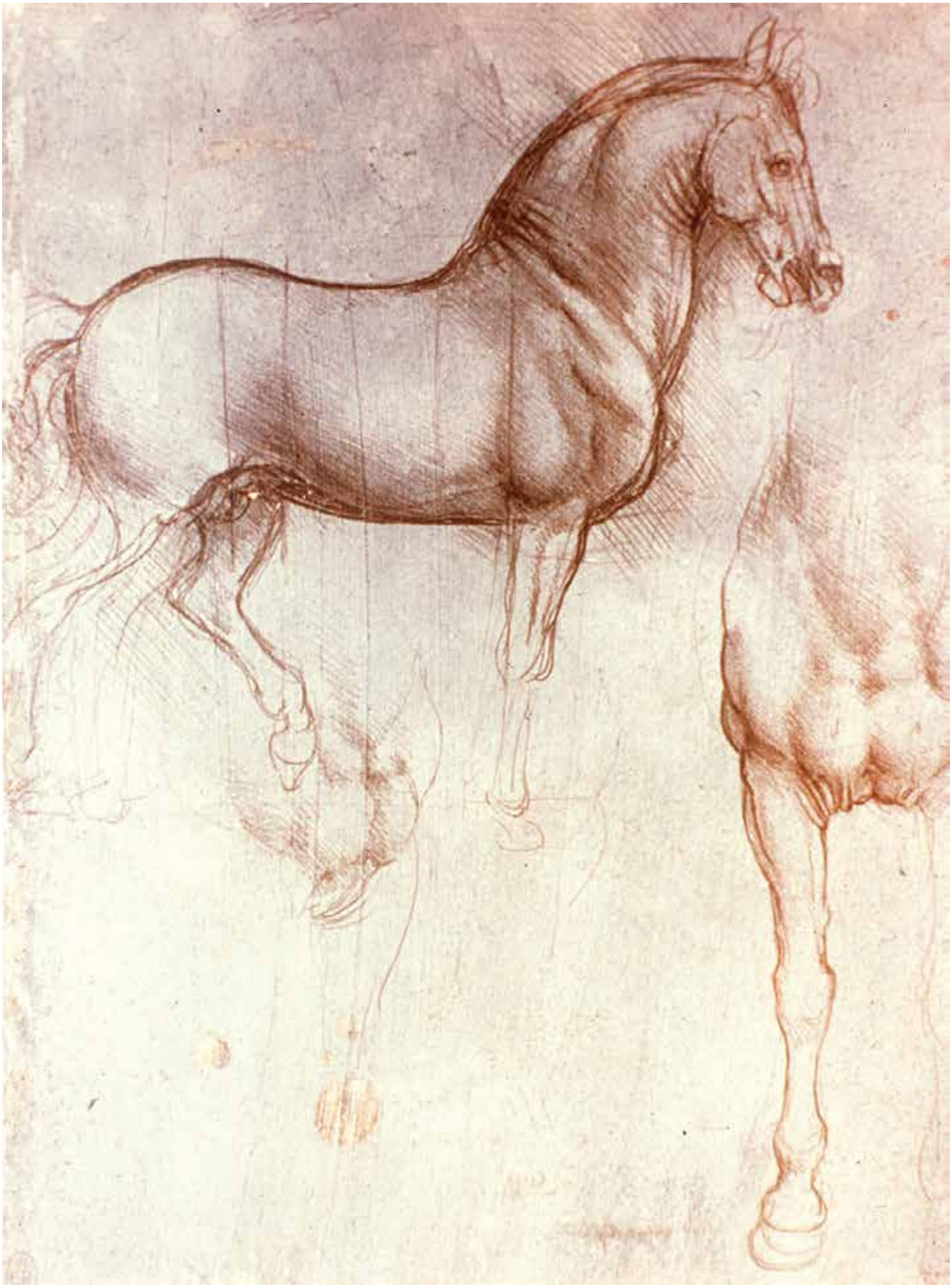
As with all study, investigation leads to new questions. Thus, many of the research projects described in this ***Research Review*** are ongoing. As technology advances, we have the ability to look at data in ways that lead us down different paths. The equine genome is complicated and UC Davis is working feverishly to fill in the knowledge gaps that will allow us to significantly improve and advance veterinary medicine.

Dr. Claudia Sonder with Cash, a long-time CEH resident and teaching assistant.

The Center for Equine Health has a goal to identify research priorities for each of the equestrian disciplines and deliver those needs to the dedicated team of scientists who can solve the problems. To do so, we need the input and the support of those who share our desire to do the best we can for the horses that have impacted our lives so greatly.

The American Horse Council's motto this year is well founded: ***A healthy horse, a healthy industry***. The age of biological medicine is upon us and our reliance on pharmacology will likely decline as we develop ways to stimulate the body to heal itself and identify risk factors for injury. Investment in veterinary medicine will foster the research that will allow all of us to adapt to the changes ahead and stand tall as stewards of the horse. I encourage you to join in the effort!

Claudia Sonder, DVM
Director, Center for Equine Health



Danika Bannasch, DVM, PhD
VM: Population Health and Reproduction

Jeff Blea, DVM
Southern California Equine Foundation

Dori Borjesson, DVM, PhD, DACVP
VM: Pathology, Microbiology and Immunology

Joseph Dowd, DVM, PhD
Equine Veterinarian

Gregory L. Ferraro, DVM
VM: William R. Pritchard Veterinary Medical Teaching Hospital

Kent Fowler, DVM, PhD
California Department of Food and Agriculture

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VM: Surgical and Radiological Sciences

Heather Knych, DVM, PhD
VM: Equine Analytical Chemistry Program

Irwin K. M. Liu, DVM, PhD
Equine Veterinarian

Kent Lloyd, DVM, PhD
VM: Associate Dean, Research

N. James MacLachlan, DVSc, MS, PhD, DACVP
VM: Pathology, Microbiology and Immunology

Stuart Meyers, DVM, MS, PhD, DACT
VM: Anatomy, Physiology and Cell Biology

Brian Murphy, DVM, PhD, DACVP
VM: Pathology, Microbiology and Immunology

Cecilia Penedo, PhD
VM: Veterinary Genetics Laboratory

Sarah Puchalski, DVM
VM: Surgical and Radiological Sciences

Nicola Pusterla, DVM, PhD, DACVIM
VM: Medicine and Epidemiology

Claudia Sonder, DVM
Center for Equine Health

Fern Tablin, VMD, PhD
VM: Anatomy, Physiology and Cell Biology

Johanna L. Watson, DVM, PhD, DACVIM
VM: Medicine and Epidemiology

Clare Yellowley, DVM, PhD
VM: Anatomy, Physiology and Cell Biology

CEH Scientific Review Committee

The Scientific Review Committee evaluates all research proposals submitted for funding, critiquing and occasionally suggesting redesign of a study before funding is awarded.

CEH Focused Research Initiatives

These initiatives were founded by the generous contributions of private individuals and/or organizations concerned with the health and well-being of animals, especially horses.

The Center for Equine Health has established several focused research initiatives to concentrate resources, expertise, cutting-edge technology and state-of-the-art equipment in certain areas of scientific research. These initiatives are conducted under the auspices of the CEH and were founded by the generous contributions of private individuals and organizations concerned with the health and well-being of animals, especially horses.

Established in 1988, the **J. D. Wheat Veterinary Orthopedic Research Laboratory** focuses on equine musculoskeletal diseases. In 1997, the Dolly Green Research Foundation of Southern California provided a $1 million endowment in Dr. J. D. Wheat's name. Dr. Wheat was a professor emeritus and a founding faculty member of the UC Davis School of Veterinary Medicine whose visionary leadership helped develop this orthopedic research laboratory. The Dolly Green Foundation, having recognized the orthopedic laboratory's contribution to the welfare and protection of the equine athlete, wanted to protect the work of ensuing generations of scientists and to honor one of its founding scientists.

Performance horses incur a wide variety of athletic injuries that are unique to their particular athletic pursuit. Scientists are working hard to discover risk factors, preventive measures and effective treatments for each. The orthopedic laboratory has expanded its scope to include companion animals, livestock, and wildlife species. Under the direction of Dr. Susan Stover, the orthopedic laboratory's vision is to (1) improve sport horse and companion animal welfare, (2) understand causes of injury and disease, (3) develop better methods for diagnosing, treating, and preventing injury and disease, and (4) provide education to ensure that equestrian sports, pleasure riding and companion animals may be safely enjoyed.

Over the past few years, researchers in the J. D. Wheat Veterinary Orthopedic Research Laboratory have achieved some major accomplishments that will significantly benefit horseracing:

- Discovered the specific sites of stress remodeling that precede and precipitate proximal sesamoid bone fractures (the most common cause of catastrophic fetlock injury) in racehorses.
- Determined which radiographic abnormalities for 2-year-old Thoroughbreds in-training-sales are associated with poor race performance.
- Demonstrated marked increases in pastern bone stresses that occur when the fetlock approaches the maximum extent of fetlock extension.
- Characterized the diagnostic imaging features characteristic of scapular fractures in racehorses.
- Demonstrated the diagnostic usefulness of bone scan for prevention of humeral fractures in racehorses.

- Characterized a method using ultrasound for detection of scapular stress fracture in racehorses.
- Determined the periods of time in racehorses' careers when racehorses are at highest risk for catastrophic scapular fracture.
- Determined differences in fetlock extension and how the hoof interacts with the surface between dirt and synthetic surfaces.
- Discovered changes associated with fractures of the lumbar spine (lower back) in racehorses.
- Developed continuing education technical notes on humeral and scapular stress fractures.
- Documented jockey injuries in California and recognized the high proportion that resulted from catastrophic racehorse injury.
- Demonstrated that horses affected with silicate associated osteoporosis (bone fragility syndrome) have markedly weak bone material in the cannon bone.

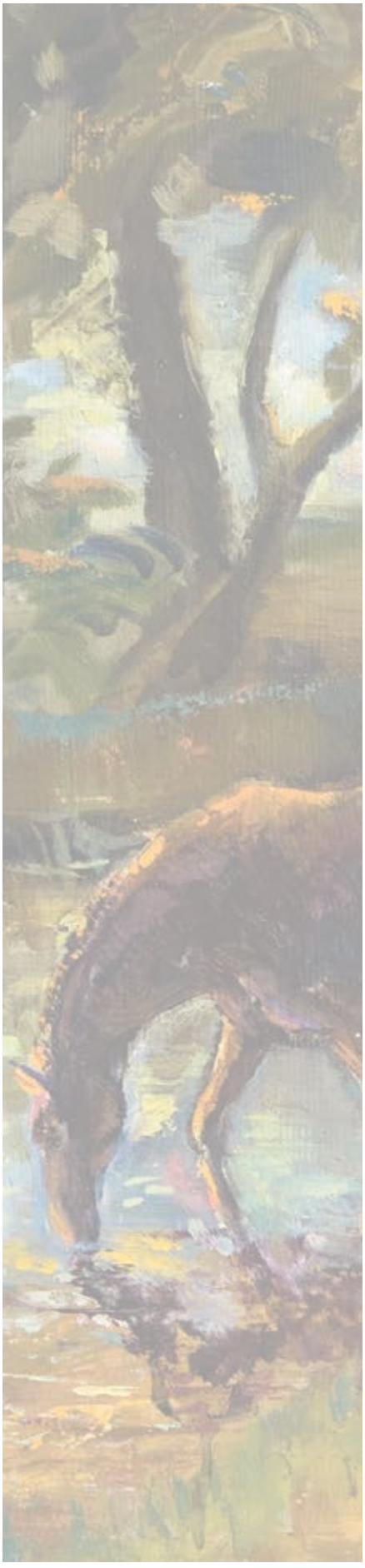
Great strides have been made in discovering the causes of catastrophic injury in racehorses and deleterious impact on jockey welfare. We have an even better understanding of the events leading to bone fracture and better techniques to detect stress fractures in live horses. We can identify race surface and exercise factors that place horses at increased risk for catastrophic injury and provide horseshoe recommendations to prevent suspensory apparatus injury. But the challenge continues in order to make horseracing a safe sport for horses and people.

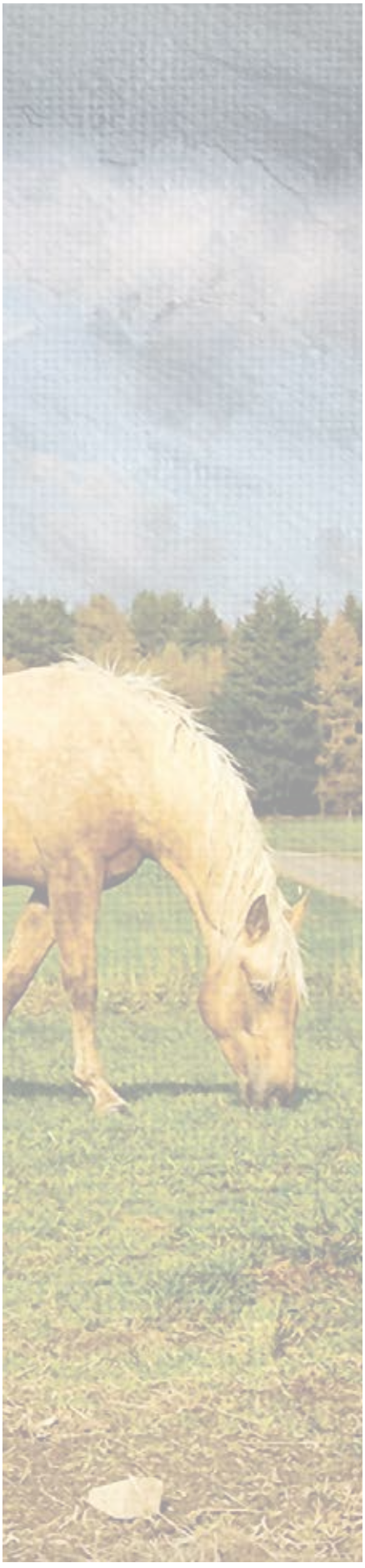
To contact the J. D. Wheat Veterinary Orthopedic Research Laboratory, visit their website at ***www.vetmed.ucdavis.edu/vorl***, or contact Dr. Susan Stover at ***smstover@ucdavis.edu*** (telephone 530/752-7438).

In January 2001, the **Bernice Barbour Communicable Disease Laboratory** (BBCDL) was established to conduct research devoted to investigating the mechanisms by which infectious diseases are produced. The Bernice Barbour Foundation, Inc., was established by the late Bernice Wall Barbour of New Jersey, who devoted her life to making the lives of animals happier and healthier. The Foundation's trustees are concerned that the increasing voracity of infectious agents poses a serious threat to the well-being of all creatures. The BBCDL was established to address this problem.

Infectious communicable diseases pose one of the major threats to worldwide health in the 21st century. Currently, the capacity of many infectious oganisms to adapt and mutate far exceeds the medical community's ability to respond with new strategies for control. The resilience of these pathogenic microbes, combined with the rapidity with which humans and animals currently circumvent the globe, present today's biomedical scientists with a most difficult challenge.

— Continued on page 10





The BBCDL employs an innovative approach to accomplish its goals. Instead of studying specific diseases in isolation, the laboratory provides a research umbrella under which scientists from varying disciplines work together as a team to study disease-causing microbes throughout the world. The BBCDL's work focuses on three critical areas of infectious disease research: (1) the microorganism's life outside the host, (2) the pathogenic mechanisms used by microorganisms to invade the host and cause disease, and (3) the defense mechanisms used by hosts against microorganisms.

Some major accomplishments to date include:

- Conducted studies of hemorrhagic fever viruses (responsible for bluetongue virus and African horse sickness) to try to distinguish the relative contributions of viral and host factors to vascular injury with a long-term goal of designing strategies for therapeutic intervention.
- Determined that host-macrophage-derived cytokines induced by bluetongue virus infection are most likely critical to enhanced paracellular permeability and increased vascular permeability, rather than direct effects of the virus itself on endothelium. Furthermore, that coagulation disturbances are central to the pathogenesis of hemorrhagic fever, thus the data are all consistent with a pathogenesis that centers on a virus-induced "cytokine storm", where it is the host's protective response to the virus, not the direct effects of the virus, that ultimately causes these catastrophic diseases.
- Evaluated the pathogenesis of hemorrhagic fevers in bluetongue-infected sheep in South Africa to assess temporal alterations in coagulation and production of cytokine mediators relative to onset of clinical signs of vascular injury.
- Began field epidemiological investigations of *Culicoides* insect vectors in California to address concern that orbiviral diseases could become even more widely distributed and to define the potential vector species that currently are present in California and what viruses they transmit.

To contact the Bernice Barbour Communicable Disease Laboratory, visit their website at ***www.vetmed.ucdavis.edu/ceh/BBCDL***, or contact Dr. James MacLachlan at ***njmaclachlan@ucdavis.edu*** (telephone 530/752-1385).

Viral diseases of humans and animals are becoming increasingly important to the maintenance of worldwide health. The changing demographics of the horse industry, particularly the international movement of sport performance horses, clearly places horses in an especially high-risk category for both infection and transmission of any new and/or emerging viral disease. With initial funding support provided by Dr. Bernard and Mrs. Gloria Salick, the **Equine Viral Disease Laboratory** was dedicated in April 1999 to facilitate the diagnosis, control and study of the global spread of viruses that have the potential to cause disease in horses and humans. Subsequent core laboratory support for specific infectious disease research has been provided recently by the Harriet E. Pfleger Foundation, the Bernice Barbour Communicable Disease Laboratory and the Center for Equine Health. The mission of the Equine Viral Disease Laboratory is to promote equine

health by undertaking research on diseases of the horse caused by viruses. Specific objectives are to provide state-of-the-art diagnostic expertise, reagents and technology dedicated to the horse, and to facilitate transfer of this technology and expertise to appropriate partners within this and other universities, in the state and federal governments, and in international health organizations.

Under the direction of Dr. N. James MacLachlan, the Equine Viral Disease Laboratory is leading the international effort to develop better diagnostic technology to identify diseases. The laboratory is working to improve vaccines to prevent these diseases and is coordinating efforts to better monitor and control them. It disseminates information on a regular basis and provides a facility that is a global hub for the interaction of scientists involved in the study of disease.

Some major accomplishments since the laboratory's inception include:

- Pioneering work in the characterization of Equine Arteritis Virus (EAV) and Equine Viral Arteritis (EVA), including development of improved assays to expedite accurate diagnosis of EVA infection in horses and a new-generation vaccine for immunizing horses against EVA.
- Comprehensive epidemiologic studies to examine the impact of West Nile Virus on horses in California.
- Extensive study of herpesvirus-induced respiratory disease of young Thoroughbred horses to determine the precise role of these viruses in the occurrence of respiratory disease in yearlings.
- Development of a recombinant vaccine for African Horse Sickness Virus.

Future goals for the Equine Viral Disease Laboratory are to broaden diagnostic capabilities through strategic partnering with pre-eminent groups nationally and internationally in order to address every major viral disease of the horse. The laboratory will continue cutting-edge research on viral diseases of the horse that are important to the regional industry. There will be a focus on new diagnostic and immunization technologies, characterization of the epidemiology and pathogenesis of important viral diseases of the horse, and identification of new and emerging viral diseases of the horse.

To contact the Equine Viral Disease Laboratory, visit their Web site at ***www.vetmed.ucdavis.edu/evdl***, or contact Dr. James MacLachlan at ***njmaclachlan@ucdavis.edu*** (telephone 530/752-1385).

The Center for Equine Health's **Stem Cell Regenerative Medicine Group** was established in 2007, fueled by the high level of veterinary intervention required to re-establish soundness in performance horses. The program has continued to grow and has made remarkable progress in basic research, translational* research and therapeutic use of these cells for a wide variety of equine disorders and injuries. The group has maintained collaborative partnerships with other stem cell scientists from the university's **College of Biological Sciences**, **Department of Biomedical Engineering**, and the **School of Medicine's Institute for Regenerative Cures**.

The initial emphasis of the program was to target the potential of mesenchymal stem cells (MSCs) for orthopedic repair, including bone healing and tendon and ligament repair. We continue to expand our use of MSCs to treat equine patients with these disorders and are currently completing a retrospective study to determine how well our therapy has worked on a variety of these injuries.

We have also developed additional research and clinical teams in both equine and small animal medicine. We now have strong scientific teams in the following areas:

- Tissue engineering – heart valve replacement; small vessel repair; cartilage repair
- Liver disease – tracking stem cells to the liver; evaluating stem cells for the treatment of portosystemic shunt in dogs
- Oral disease – mandibular repair and the treatment of chronic, severe oral inflammatory diseases in cats
- Spinal cord injury – a unique "neural" stem cell derived from canine skin is isolated, expanded and will be injected into dogs with spinal cord injury
- Ophthalmic disease – inflammatory and immune-mediated eye diseases in dogs and horses
- Gastrointestinal disease – inflammatory bowel disease in dogs
- Wound healing – MSCs embedded in matrix to augment wound healing in horses

Each of these areas of research will have a major impact on the health and medical care of animals and humans in the near future.

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* Scientific research that helps to make findings useful for practical applications. In human medicine, translational research is described as "from bench to bedside" or from laboratory experiments through clinical trials to point-of-care patient applications.

Areas of Future Funding Needs in Equine Regenerative Medicine

Infectious, Inflammatory and Immune-Mediated Diseases in Horses

Currently, MSCs are being investigated for the treatment of sepsis and pulmonary diseases in humans, including chronic obstructive pulmonary disease. MSCs alter inflammatory cell function and they also respond to bacterial pathogens. Studies will be needed to determine how equine MSCs interact with the cells that respond to bacterial infection (neutrophils) and how MSCs function in inflammatory airway diseases in horses.

Laminitis

MSCs increase blood flow and decrease inflammation. It is these qualities that make MSCs such a promising therapy for inflammatory and vascular diseases like laminitis. Although we have successfully used MSCs to treat laminitis, it is unclear how the cells function to help heal this condition. Studies are needed to determine what kind of stem cells are best for the treatment of laminitis, how best to administer the cells, and how they heal this unique tissue.

Potential Uses for Stem Cells in Equine Medicine

CEH Awards

The CEH has adopted an active role in the recruitment and development of the next generation of veterinary scientists. The equine industry will need many highly skilled and talented individuals to advance the medical management and care of horses. The CEH has stepped forward to meet this challenge by developing programs that will attract and support individuals who have demonstrated their affinity and dedication to equine medicine.

2011 James M. Wilson Award

The 2011 James M. Wilson Award was presented to Dr. Amanda Arens for her work on equine bone fragility syndrome. The Wilson Award is given each year to an outstanding equine research publication authored by a graduate academic student or resident in the UC Davis School of Veterinary Medicine. Dr. Arens' publication, *Osteoporosis Associated with Pulmonary Silicosis in an Equine Bone Fragility Syndrome*, was honored with the Wilson Award.

Dr. Amanda Arens with Sailors Sweet Sue

Horses from certain regions in California are developing a bone fragility disorder that results in bony deformities and spontaneous fractures. This study aimed to describe visible, radiographic and microscopic postmortem findings in affected horses and to assess any associations between the bone disorder and pulmonary silicosis (a chronic lung disease), heavy metal, and trace mineral abnormalities.

A postmortem evaluation of nine horses with the disorder and three unaffected horses was conducted. Bones and soft tissues were evaluated visibly and microscopically. Bone, lymph nodes, and lung tissue were evaluated radiographically. Tissues were evaluated for silicon levels, the presence of crystalline material, heavy metals, and trace minerals. All nine affected horses had osteoporosis and clinical or subclinical lung disease due to pulmonary silicosis (8/9) or pneumoconiosis due to dust inhalation (1/9). All affected horses had radiographic low bone density and microscopic toxic silica dioxide polymorphs including cristobalite, tridymite, quartz, and mixed silicates. Lung and liver tissue from affected horses had elevated levels of elemental silicon. Osteoporosis was highly associated with the presence of pulmonary silicosis. No abnormalities in heavy metal or trace minerals were detected.

This evaluation indicated that most horses with the bone fragility disorder have systemic osteoporosis associated with pulmonary silicosis. The actual cause and mechanism of the bone disease is unknown. However, this study provides circumstantial evidence for a silicate-associated osteoporosis.

2012 James M. Wilson Award

The 2012 James M. Wilson Award was presented to Dr. Carrie Finno for her work on neuroaxonal dystrophy (NAD), an inherited neurologic disease that affects all breeds of horses. The Wilson Award is given each year to an outstanding equine research publication authored by a graduate academic student or resident in the UC Davis School of Veterinary Medicine. Dr. Finno's publication, *Electrophysiological Studies in American Quarter Horses with Neuroaxonal Dystrophy*, was honored with the Wilson Award.

Horses affected with this disease appear to be normal at birth but develop signs of neurologic disease, including incoordination and an abnormal posture (standing with limbs crossed or base-wide) during the first two years of life. Some horses will also develop an abnormally quiet or dull mentation, often appearing sedated. Equine degenerative myeloencephalopathy (EDM) is considered a more severe variant of equine NAD and therefore, the disease is termed NAD/EDM.

Although there is strong evidence that NAD/EDM is inherited, it appears that dietary vitamin E plays a role in the development of the disease. When foals are predisposed to developing NAD/EDM due to their genetic makeup and they do not receive enough vitamin E during the first year of life, they appear to develop more severe neurologic abnormalities than foals with the same genetic "risk" that received enough vitamin E.

Dr. Carrie Finno with Smart N Cody

Dr. Finno received her DVM in 2004 from the University of Minnesota, where she also completed an internship in large animal medicine and surgery. During that time, she developed a strong background in equine genetic research. She then completed a residency in large animal internal medicine at UC Davis and obtained her board certification in internal medicine in 2008. Most recently, she obtained a PhD in comparative pathology, for which she performed clinical and genetic investigations of equine NAD. She is currently continuing her research into the genetics of equine NAD at the University of Minnesota.

CEH Focused Research Endowments

Perpetual funding sources for specific areas of equine research are essential to the current and long-term success of the CEH.

Through the University of California's managed endowment system, the Center for Equine Health has established perpetual funding sources for specific areas of equine research. These endowments are essential to the CEH's current and long-term success. So far, 15 such endowments have been established, ranging from $10,000 to more than $1 million. The endowments are described below.

Individuals interested in supporting the CEH may contribute to one or more of these endowments or work toward creating a new one in an area of equine medicine that is of interest to them personally. There is currently a need for a reproductive endowment to fund future study in this important field. For more information regarding the endowment programs, contact Dr. Claudia Sonder at **(530)752-6433** or send an e-mail to **csonder@ucdavis.edu**.

Director's Endowment
Provides general funding for CEH research, educational or welfare activities most critical to the needs of the horse in any given year. This endowment also provides the foundation for all future CEH endeavors.

Performance Horse Endowment
Focuses on the medical problems of the mature show and event horse. Also funds long-term, in-depth studies of problems that preclude horses from performing athletically as they age. Areas of study include colic, nutrition, cardiopulmonary health, degenerative orthopedic processes and infectious disease.

Equine Athletic Performance Laboratory
Provides for the development of analytical methods for accurately evaluating the athletic conditioning and performance capability of individual horses. Once these analytical techniques are fully developed, the goal of the program will be to provide an objective evaluation of the ability of drug agents and training methods to enhance performance and decrease the risk of injury in competitive horses.

J. D. Wheat Equine Orthopedic Research Laboratory
Provides for investigation of the underlying causes of bone fractures, their prevention, and new methods of fracture repair. (Originally established by the Southern California Equine Foundation, Inc., with funds provided by the Dolly Green Research Foundation.)

Bernard and Gloria Salick Equine Viral Disease Laboratory
This endowment supports a program dedicated to international scientific investigations of emerging equine viral diseases. Its goal is to identify and control viral diseases of the horse that can affect the international movement, commerce and health of competitive equine athletes.

Animal Rescue and Disaster Medicine Endowment
Focuses on developing improved techniques for the rescue of large animals during natural disasters. The fund also supports research into various medical conditions of the animals and the development of improved treatment regimens.

Lucy G. Whittier Endowment for Equine Perinatal and Infectious Disease
Dedicated to improving the health and medical treatment of newborn foals and their dams and to conduct research on infectious diseases associated with foals.

Polly and Bill Swinerton Director's Endowment
This fund supports the activities of the CEH Director to advance the facility's teaching, research and service missions.

Peray Memorial Endowment
Provides funding for resident house officers of the UC Davis Veterinary Medical Teaching Hospital (VMTH) to conduct equine respiratory disease research.

John P. Hughes Memorial Endowment
Provides funding for VMTH resident house officers to conduct clinical research in any area of equine medicine or surgery.

Dan Evans Memorial Endowment
This endowment provides funding for VMTH resident house officers to conduct research in any area of equine medicine and surgery that is relevant to the development of their specialty board certification.

Equine Enduring Legacy Endowment
This fund provides for the development of new treatment methods and techniques in equine medicine or surgery. It supports the application of experimental treatments to horses that may have untreatable or life-threatening conditions, as well as the conduct of clinical research trials to aid in the development of new therapies.

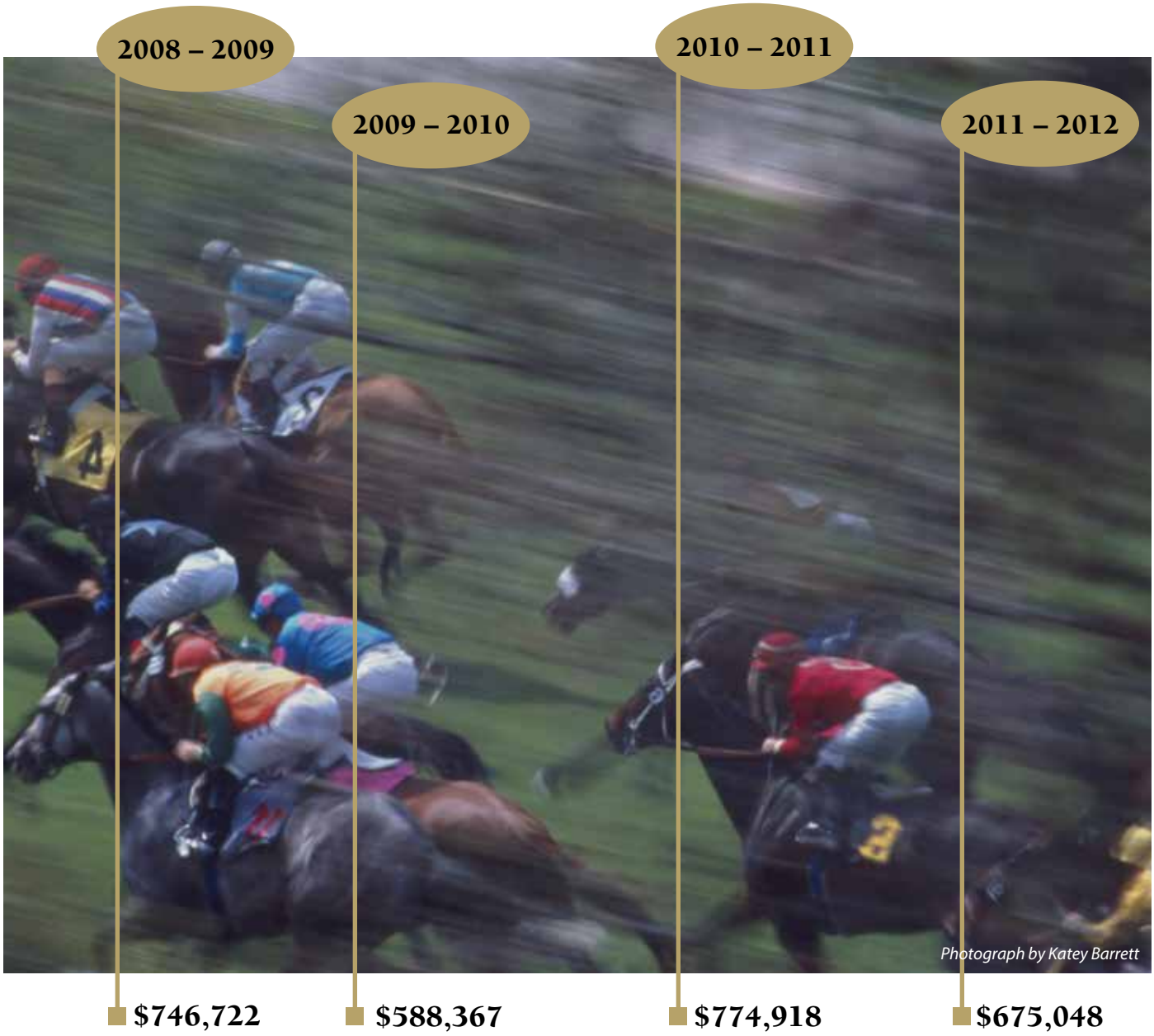
Marcia MacDonald Rivas Research Endowments
These funds are available to teaching and research personnel, including all faculty at the Assistant Professor level, Lecturers, and MSP Professionals with less than five years of employment in the School of Veterinary Medicine. New and junior faculty members are preferred, as are equine-related projects.

Juliette Weston Suhr Fellowship Fund
This fund provides annual fellowships for postgraduate veterinary students who are interested in conducting research in the areas of exercise-related cardiopulmonary and metabolic disorders.

William and Inez Mabie Family Foundation Endowment
This is a permanent endowed fund to support the Center for Equine Health in its operational, educational and research efforts. Endowment is distributed at the discretion of the CEH Director for advancing the health, well being, performance or veterinary care of horses through research and/or education. The endowment is conditional on receiving an additional $1.8 million in private matching gifts within six years. The second endowment is intended to secure the CEH director's position so that future leaders can be recruited and maintained.

Photograph by Katey Barrett

Simulcast Racing Contributions



In 1987, the Satellite Wagering Act (Senate Bill 14) designated one-tenth of one percent of California's simulcast racing handle to be used for equine research. In 1994, Senate Bill 518 was passed, designating the redistribution of the simulcast racing percentage. One-third of the simulcast money is now designated for research, while the other two-thirds is designated for the Equine Analytical Chemistry Program which has three components: (1) a full-service, routine drug testing program, (2) a forensic toxicology program, and (3) a pharmacology research and methods development program. The latter includes the development of new tests and documentation of drug testing effects on racehorse performance. In 2001, the Account Wagering Bill (AB 471) was passed, directing simulcast contributions made through televised wagering to UC Davis equine research and drug testing programs.

Completed RESEARCH STUDIES

Regenerative Medicine

Studies in regenerative medicine have been funded by grants from Dick and Carolyn Randall, the Harriet Pfleger Foundation, and other generous donors.

Evaluation of Deterioration in Mesenchymal Stem Cells Isolated from Equine Bone Marrow, Fat and Placental Tissue

Funded by Dick and Carolyn Randall

In equine veterinary medicine, cellular therapy is increasingly used for tissue repair. Primary mesenchymal stem cells (MSCs) are typically obtained from the horse's own bone marrow, fat or placental tissues. A common challenge is that cell-based therapies require large cell numbers. As such, MSC expansion is important because the original cell harvest often contains limited numbers of MSCs.

MSCs are capable of extensive replication under culture conditions. However, the molecular changes that result from long-term cell culture and expansion are unknown. Long-term culture will eventually lead to cellular aging (senescence) and potentially increase the risk of genetic and cellular alterations, which could be associated with spontaneous cell transformation and aberrant growth. It is important to understand whether MSCs derived from fat, bone marrow and placental tissues have similar growth patterns, expansion and cellular aging so as to select the best source of cells.

Cellular aging is associated with characteristic changes in cell shape followed by permanent growth arrest. Cell replication involves DNA molecules called telomeres. As cells age, these telomeres become progressively shorter. Aging cells will also accumulate markers such as lysosomal β-galactosidase and change their gene expression of extracellular matrix components such as osteonectin.

In this study, we compared the onset of deterioration (senescence) in MSCs isolated from equine bone marrow, fat and umbilical cord tissue using the markers of aging described above. We found that MSCs from bone marrow, fat and placental tissue cultured long-term all exhibited characteristics of growth arrest, alterations in cellular structure, telomere shortening and accumulation of lysosomal ß-galactosidase. However, there was a significant difference in the onset of deterioration between bone marrow, fat and placental cells, with cells isolated from bone marrow deteriorating at much earlier passages during subculturing.

How does this research benefit horses?
The results of this study suggest that mesenchymal stem cells isolated from equine bone marrow should not be subcultured beyond six or seven passages for research and clinical purposes, and that cells from fat and placental tissue may be expanded to high numbers for tissue banking.

Investigators: Martin Vidal, Naomi Walker, Eleonora Napoli, and Dori Borjesson
Study ID: 08-66

Evaluation of Intra-Arterial and Intravenous Regional Limb Perfusion of Mesenchymal Stem Cells in the Normal Equine Distal Limb Using ^{99m}Tc-HMPAO

Funded by an anonymous donor to the Center for Equine Health

Stem cell-based therapy has been used in recent years for the treatment of equine orthopedic and soft tissues injuries and controlled trials suggest that bone marrow-derived mesenchymal stem cells (MSCs) improve tissue quality. The main route of stem cell delivery thus far has been to inject the MSCs directly into the lesion. Recent reports suggest, however, that MSCs are capable of concentrating and engrafting in injured tissues after systemic application. Therefore, equine practitioners have begun to embrace the use of regional limb perfusion with MSCs.

The purpose of our study was to evaluate intra-arterial (IA) and intravenous (IV) regional limb perfusion of MSCs in the distal limb of the horse using scintigraphy. We found that regional limb perfusion of the distal limb results in good persistence of MSCs in the perfused area for at least 24 hours using either the intra-arterial or the intravenous technique. Both techniques led to a good diffusion of the MSCs to the carpal and metacarpal areas, but the intra-arterial perfusion technique resulted in a more reliable distribution of the cells in the pastern and foot area. The pneumatic tourniquet was 100% efficient at preventing diffusion of the MSCs. Other tourniquet types were not efficient.

How does this research benefit horses?
Alternative routes of administration would be beneficial for the treatment of lesions that cannot be accessed directly or in order to limit needle-induced iatrogenic damage to the surrounding tissue. This technique is currently available for clinical cases at the Veterinary Medical Teaching Hospital with lesions that appear to be well vascularized on ultrasound exam. Follow-up of these cases is indicated. Future work is needed to determine the fate of MSCs after their attachment to the endothelium and whether these perfusion techniques help equine MSCs to home to injured tissues.

Investigators: Albert Sole, Mathieu Spriet, Larry Galuppo, Kerstien Padgett, Dori Borjesson, Erik Wisner, Robert Brosnan, and Martin Vidal
Study ID: 09-52

The Center for Equine Health's Stem Cell Regenerative Medicine Group combines the talent, skill and knowledge of more than two dozen research and clinical faculty from different academic departments within the School of Veterinary Medicine, the College of Biological Sciences, the College of Engineering and the School of Medicine's Institute for Regenerative Cures. Together, the knowledge and experiencve of all these scientists represent leadership, creativity and optimism for developing stem cell therapies to treat not only horses, but humans and other animals.

♦ Medicine

♦ Orthopedics

♦ Reproduction

Growth Factor Content of Equine Platelet-Rich Plasma

Horses often suffer athletic injuries to tendons and ligaments. The healing process in these tissues is slow and prone to re-injury, limiting the animal's return to useful performance. Platelet-rich plasma, known to contain growth factors that should augment tissue repair, is now being used to treat these injuries directly in hopes of a better outcome, but the method to ensure maximal growth factor supplementation at the site has not been optimized.

In this study, we experimented with different injection techniques and activation substances to optimize the levels of growth factor contained in a PRP product. An ELISA was used to quantify growth factor levels of the different preparations. We found that platelets prepared using the tube method had higher platelet concentrations than those of the Harvest Smart Prep but that growth factor concentrations did not vary between the two preparation methods. Shear force from either 21- or 25-gauge needles did not result in increased growth factor release. Treatment with either 10 or 20 μg/ml collagen results in increased growth factor release.

How does this research benefit horses?
The results of this study showed that injection of unstimulated PRP released extremely low levels of growth factors and that development of a standardized PRP activation protocol for clinical application in horses is needed to ensure that maximal growth factors are available to the lesion requiring treatment.

Future Work
The study of PRP and other therapeutic biological treatments are ongoing at UC Davis as veterinarians seek treatments that will preserve athleticism.

Investigators: Fern Tablin, Jamie Textor, and Jeff Norris
Study ID: 08-18

Study of Different Feeding Protocols on the Intragastric pH of Normal Horses Using a Continuous Measurement Device

Gastric ulceration is a common problem in all type of horses. A stomach pH > 4 is required for ulcer healing. The housing of horses in a stable is a predisposing factor for ulcer formation since it modifies their eating habits from grazing all day to eating twice a day. Food material in the stomach buffers acidity and increases the pH. However, grazing all day may predispose to obesity.

In this study, we determined whether the use of a grid feeder modifies the gastric pH of horses, the amount of food consumed and the amount of time horses spend eating. We found that gastric pH changes based on the type of feeder used and that it may be affected by the amount of time horses spend eating.

How does this research benefit horses?
This study showed that by changing feeding methods, gastric ulcers may be prevented. Increasing the amount of time horses spend eating may have a beneficial effect.

Investigators: Jack Snyder, Jorge Nieto, and Sawsan Yamout
Study ID: 09-10

Investigation of a New Technique for Magnetic Resonance Imaging of Equine Tendons

Although magnetic resonance imaging (MRI) of tendons has many potential clinical applications in the horse, musculoskeletal MRI has been slow to evolve as a mainstream imaging modality. One reason is the poor signal obtained from tendons with conventional techniques. Recently, several publications in the human medical literature have recommended imaging tendons at a specific orientation to the main magnetic field, the so-called "Magic Angle", in order to increase the signal obtained from the tendons. The increased signal intensity results in better visualization of tendon anatomical detail leading to more accurate diagnoses.

In this study, we tested the "Magic Angle" technique on equine tendons and ligaments and compared it with imaging obtained by the conventional MRI technique. In addition, we calculated a specific magnetic resonance parameter of normal tendon—the T1 value—using the magic angle effect and defined the normal range of T1 values for specific tendons. We then measured the T1 value of abnormal tendons.

Magic angle imaging allowed calculation of the T1 value of each tendon. The normal range of T1 values for the different tendons of the metacarpus has now been established. Abnormal tendons had an elevated T1 value, similar to that reported for humans. Certain chronic lesions were apparent using magic angle imaging but not conventional imaging, but acute lesions were better defined with conventional imaging.

How does this research benefit horses?
Magic angle imaging is beneficial in detecting early tendon lesions through elevation of the T1 value of tendon and in improving the characterization of chronic lesions. However magic angle imaging should be used in combination with conventional imaging as focal acute lesions were better defined with conventional imaging.

Future Work
T1 mapping and study of early extracellular matrix response to injury could lead to the development of biomarkers for early tendon and ligament damage. Finding early evidence of strain before serious injury will benefit equine athletes.

Investigators: Mathieu Spriet, Erik Wisner, and Lucy Anthenill
Study ID: 08-06

Connective Tissue Signaling as a Marker for Tendon Injury

Tendon injuries in equine athletes are common, difficult to treat and associated with prolonged lay-up periods. The diagnosis of tendon injuries has improved with recent advances but is still reliant on specialized diagnostic imaging equipment such as ultrasound and MRI. Earlier diagnosis of tendon injury by a simple stall-side test would allow horse owners to withdraw horses from training at an earlier time point, potentially preventing serious tendon injury, decreasing lay-up time and decreasing the incidence of re-injury. We hypothesize that digital (tendon) sheath fluid in horses with injury of the deep digital flexor tendon (DDFT) will have elevated levels of the tendon-specific biomarker Tenascin-C.

In this study, we measured and compared tendon sheath Tenascin-C levels in clinically normal horses and in horses with tendon injury to determine whether this hypothesis was correct. We found that a significant difference in Tenascin-C concentration existed between horses with and without tendon injury. Horses with tendon injury within the digital tendon sheath had higher concentrations of Tenascin-C in the associated tendon sheath fluid. The alteration in Tenascin-C was detected using commercially available ELISA kits. Tenascin-C was identified in tissue samples of abnormal tendons using immunohistochemistry. This data provides impetus for further investigation of this biomarker as an early diagnostic test for tendon injury.

Tenascin-C, with further characterization, may provide a means of developing a minimally invasive, inexpensive test for the identification of tendonitis in performance or pleasure horses, potentially preventing serious tendon injury.

How does this research benefit horses?
This study provides critical cornerstone information regarding the utilization of Tenascin-C as a novel biomarker candidate for the identification of early tendon injury. Tenascin-C, with further characterization, may provide a means of developing a minimally invasive, inexpensive test for the identification of tendonitis in performance or pleasure horses, potentially preventing serious tendon injury.

Investigators: Sarah Puchalski, Nick Huggons, Leah Raheja, Robin Bell, Larry Galuppo, and Richard Tucker
Study ID: 08-14

Evaluation of a Diode Laser-Induced Equine Superficial Digital Flexor Tendinopathy Model

Funded by the Alamo Pintado Foundation

Equine tendon and ligament injuries remain a therapeutic challenge in performance horse practice. Many different treatment modalities have been used to enhance healing with variable but mostly marginal success rates, with the rate of injury recurrence varying from 23 to 43% in sport horses and up to 53 to 67% in racehorses. With the advent of new biological treatment options such as mesenchymal stem cells, growth factor technologies and tissue scaffolding materials, the need for an appropriate tendinopathy model to test these therapeutic options has recently been challenged.

Many controlled trials have used the long-established collagenase-induced tendinopathy model. However, lesions from this model can be highly variable in their size and extent from the site of injection, and have been suggested to poorly represent clinical injuries. Recently described surgical techniques have the advantage of creating large, well defined core lesions, yet they require general anesthesia and histopathologically, the surgical techniques failed to create an obvious inflammatory response. Coblation technology based on radiofrequency energy is costly and the lesions appeared to be unpredictable in size and location.

UC Davis looked at diode lasers as a possible tool to induce superficial digital flexor tendinitis that can be controlled in size and resemble naturally occurring cases. Further studies are necessary to develop a consistent, repeatable tendinitis model.

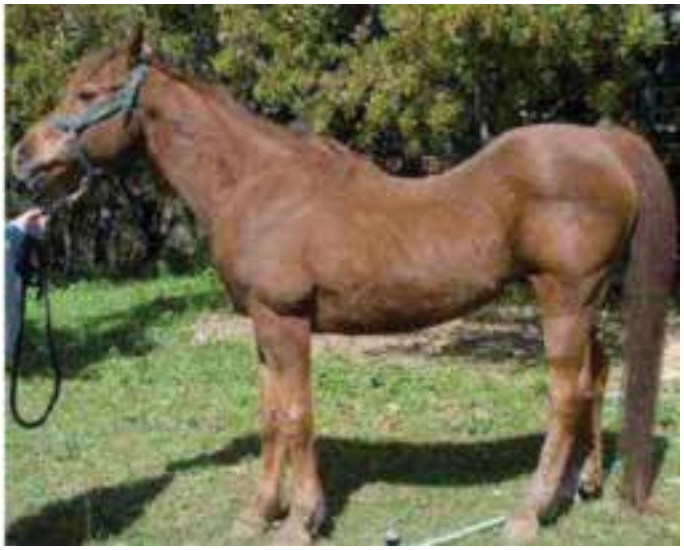
Investigators: Martin Vidal, Stuart Vallance, Mary Beth Whitcomb, Brian Murphy, Mathieu Spriet, and Larry Galuppo
Study ID: 08-50

Assessment of Blood Tests and Use of Ultrasound for the Diagnosis of Osteoporotic Bone Disease in Horses

Bone fragility syndrome (BFS), otherwise known as silicate-associated osteoporosis, is a progressive, debilitating, and ultimately fatal bone disease affecting horses. Although bone scan, physical exam and scapular ultrasound abnormalities have been described for this disease, the exact findings that lead to a diagnosis have not been clearly defined. Thus, there is a need to define the criteria for a diagnosis as well as a need to assess the accuracy of the less expensive tests, such as physical exam, ultrasound, and blood tests for disease diagnosis. Finally, in order to monitor disease progression and response to treatment and to conduct future clinical studies, it is necessary to establish a scale of clinical findings associated with disease severity.

We have now developed severity indices that provide a framework to capture the progressive spectrum of disease manifestations. Studies of bone fragility syndrome are ongoing at UC Davis as researchers work to develop an affordable, fieldside diagnostic test for this insidious disease.

This study had several objectives: (1) to determine the diagnostic method (bone scan, physical exam or ultrasound) that best equated with a positive diagnosis for bone fragility syndrome; (2) to develop indices of disease severity using bone scan and physical exam findings; and (3) to compare the physical exam findings, ultrasound findings and blood concentrations of two bone markers between horses with and without the bone disease as diagnosed by bone scan.



Horse with bone fragility syndrome. Note the characteristic bowing of the shoulders and swayed back. Flared nostrils are a sign of respiratory disease.

We found that scintigraphy is still the most definitive diagnostic modality for bone fragility syndrome at all severity levels, and that a physical exam and scapular ultrasound are accurate at moderate to severe disease levels. We have now developed severity indices that provide a framework to capture the progressive spectrum of disease manifestations. Markers of bone resorption and formation that were evaluated were not useful for diagnosing BFS in individual horses.

How does this research benefit horses?
Clearly defined criteria for diagnostic test results provide veterinarians with a needed diagnostic protocol for bone fragility syndrome. The severity indices may be useful for assessing disease progression and response to treatment.

Future Work
Studies of bone fragility syndrome are ongoing at UC Davis as researchers work to develop an affordable, fieldside diagnostic test for this insidious disease. Please contact Dr. Claudia Sonder at the Center for Equine Health if you wish to support future efforts to develop diagnostic and therapeutic options.

Investigators: Susan Stover, Ian Gardner, Sarah Puchalski, Mary Beth Whitcomb, Robin Bell, and Amanda Arens
Study ID: 09-01

Ability of the Progestin 5α-Dihydroprogesterone to Stimulate the Uterus and Maintain Early Pregnancy in the Mare

Numerous progestins in addition to progesterone are produced in the mare during pregnancy and become the dominant progestational compounds circulating in the mare's blood during the latter half of pregnancy. Low circulating levels of progesterone during most of gestation in the mare and undetectable progesterone levels in some megaherbivores, such as the elephant, have lead to speculation that other endogenous progestins may maintain pregnancy. The bioactivity of these endogenous progestins, such as 5α-dihydroprogesterone, is unknown, and therefore their relative importance in maintaining pregnancy remains unclear.

In this study, we investigated whether 5α-dihydroprogesterone (5α-DHP) has a progestagenic effect on the endometrium as well as the ability to maintain early pregnancy. We found that administration of 5α-DHP in ovariectomized mares induced activation of the uterine epithelium, as evidenced by increased height of glandular and luminal epithelium, nuclear size, gland density and secretion of lipocalin (P19), a progesterone-responsive protein. In addition, early pregnancy was maintained in 7 of 9 mares receiving 5α-DHP injections despite induced luteolysis (regression of progesterone-producing tissue) at 14 days and resulting loss of endogenous progesterone.

How does this research benefit horses?
To our knowledge, this is the first report of progestagenic effects of 5α-DHP in any species. The discovery that 5α-DHP is sufficient to maintain early pregnancy and embryonic development in the mare advances our understanding of the unique nature of equine early pregnancy maintenance. Along with an assay specific for 5α-DHP developed for this study, this new knowledge may provide avenues for evaluating the progestagenic state and health of pregnancies in the mare as well as therapeutic and/or prophylactic options for management of high-risk pregnancies.

Investigators: Alan Conley, Barry Ball, and Elizabeth Scholtz
Study ID: 07-01

Evaluation of the Production and Effects of the Progestin 5α-Dihydroprogesterone in the Cycling and Early Pregnant Mare

Progesterone has long been accepted as the single hormone necessary to maintain pregnancy in mammals. However, no progesterone can be found in the circulation of mares in the second half of gestation. Another progestin, 5α-dihydroprogesterone (5α-DHP), which binds the equine progesterone receptor with high affinity, increases to high concentrations in the second half of gestation. Results from our previous work indicate that 5α-DHP has a direct progestagenic effect on the mare's uterus and circulates at levels sufficient to maintain early pregnancy and embryonic development, confirming for the first time that 5α-DHP is an active progestagen in the horse. Still, little is known about its production or metabolism in the mare.

Researchers are working on ways to quantify 5α-DHP in the pregnant mare to create an association between DHP levels and maintenance of pregnancy. Ultimately, this information could be used to monitor the health of a pregnant mare more specifically.

In this study, we investigated several aspects of 5α-DHP: whether it stimulates progesterone responsive glandular secretions in the mare's uterus, whether its concentration differs during the nonpregnant estrous cycle from that of early pregnancy, and whether 5α-reductase (the enzyme responsible for converting progesterone into 5α-DHP) is present in the mare's corpus luteum and which form(s) of the enzyme predominates during the estrous cycle vs. early pregnancy.

We demonstrated that 5α-DHP is a potent progestagen in the mare—the first such observation in any mammal—and is not only capable of sustaining pregnancy in the absence of progesterone, but of stimulating endometrial growth and differentiation. 5α-DHP is produced in the placenta in late gestation but is likely produced in the circulation of cyclic mares, and mares without a developed placenta, from progesterone secreted by the ovary (corpus luteum). 5α-DHP may prove to be a more potent progestagen in mares than progesterone itself, a more important hormone for the maintenance of equine pregnancy therefore and a possible marker or predictor of pregnancy loss in the horse.

How does this research benefit horses?

The rate of pregnancy loss prior to day 30 is estimated to be as high as 20% in normal mares and as high as 80% in subfertile mares. The economic impact of early pregnancy loss in the mare is undeniable and progestin supplementation is often recommended to prophylactically treat mares who may suffer early pregnancy loss, even though studies to date have been unable to correlate early embryonic death with maternal progesterone levels. Knowledge of the role of 5α-DHP in early pregnancy will improve the current understanding of pregnancy recognition and pregnancy maintenance, providing a basis for further diagnostic, prophylactic or therapeutic options for early pregnancy loss.

Future Work

Researchers are working on ways to quantify 5α-DHP in the pregnant mare to create an association between DHP levels and maintenance of pregnancy. Ultimately, this information could be used to monitor the health of a pregnant mare more specifically.

Investigators: Alan Conley, Barry Ball, Scott Stanley, and Elizabeth Scholtz
Study ID: 10-01

Evaluation of a Novel Reproductive Hormone (Anti-Müllerian Hormone) as an Aid for Diagnosis of Ovarian Tumors in Mares and Retained Testes in Stallions

Granulosa-cell tumors are the most common ovarian tumor in mares and the current method for hormonal diagnosis of this tumor fails to detect approximately 20% of mares with this condition. Likewise, the method currently used to detect the presence of a retained testis in a previously castrated horse relies on multiple blood samples for testosterone and may not be as reliable for the diagnosis of a retained testis. We believe that serum concentrations of anti-Müllerian hormone (AMH) are elevated in mares with granulosa-cell tumors and in geldings with retained testes, and assay for serum AMH can be used for the diagnosis of these conditions.

In this study, we developed and validated a specific radioimmunoassay for determining anti-Müllerian hormone in the horse. We also determined concentrations of AMH in the blood of mares with granulosa-cell tumors and in previously castrated stallions with retained testes. We found that serum AMH concentrations in mares with confirmed granulosa-theca cell tumors were elevated compared with normal cycling mares or pregnant mares. Concentrations of serum AMH in horses with retained (cryptorchid) testes were significantly higher than in geldings.

How does this research benefit horses?

Our validated assay for serum AMH concentrations in horses offers a more sensitive method for detecting granulosa-theca cell tumors in the mare compared with the existing assay for inhibin. This test is currently available at the William R. Pritchard Veterinary Medical Teaching Hospital. Similarly, serum AMH concentrations offer an additional method to detect the presence of a retained (cryptorchid) testis in a previously castrated gelding. Further studies on serum AMH concentrations in horses will provide new insights on infertility in both the mare and stallion.

Future Work

The Equine Reproduction Service at UC Davis has pioneered much of the research that has enhanced assisted reproduction options and treatment of reproductive disorders. An investment in future knowledge will go a long way toward improving reproductive outcomes in horses.

Investigators: Barry Ball, Alan Conley, Irwin Liu, and Juliana Almeida
Study ID: 09-02

The Equine Reproduction Service at UC Davis has pioneered much of the research that has enhanced assisted reproduction options and treatment of reproductive disorders. An investment in future knowledge will go a long way toward improving reproductive outcomes in horses.

Resident
RESEARCH STUDIES

In an effort to encourage residents to conduct equine studies, the Center for Equine Health provides funding through specialized endowments for selected research by residents at the UC Davis School of Veterinary Medicine's teaching hospital. These studies help residents learn to design and conduct research studies of merit. In many cases, these pilot studies are later expanded into larger research projects based on the study results.

Resident research is vital to the success of the equine research program and to creating veterinary leaders of the future. Funding for resident research is currently lacking.

The Effects of Combining Antibiotics and Hyaluronic Acid on Equine Stem Cells

Funded by The Patterson Foundation

It is a common practice in the veterinary field to combine pharmaceuticals for treatment of orthopedic injuries in the horse. As mesenchymal stem cells (MSCs) gain mainstream approval for clinical use, veterinarians have been combining MSCs with other medications, including antibiotics and hyaluronic acid. It is not known if this practice compromises the health and survival of the stem cells.

In this study, we wanted to determine whether incubation of equine bone marrow mesenchymal stem cells with the antibiotics gentamicin and amikacin or hyaluronic acid altered the immediate characteristics of the stem cells prior to injection, including pH and viability *in vitro*. We also wanted to determine whether prolonged exposure altered the proliferative potential (ability to expand) of the cells.

We found that combining mesenchymal stem cells with the antibiotics resulted in rapid cell death. However, the stem cells remained >80% viable when combined with hyaluronic acid. All additives immediately decreased pH compared with penicillin/streptomycin but remained constant over time. Stem cell proliferation was not altered when combined with hyaluronic acid.

How does this research benefit horses?
We now know that the common practice of combining some types of pharmaceuticals to treat orthopedic injuries in horses is not compatible with treatment with mesenchymal stem cells. However, these stem cells tolerate co-incubation with hyaluronic acid. Mixing mesencymal stem cells with aminoglycoside antibiotics causes rapid cell death and is not recommended for clinical use. Cultured MSCs are tested for sterility prior to distribution, which mitigates the need for concurrent antibiotic injection.

Investigators: Laurie Bohannon, Naomi Walker, Danielle Carrade, Julie Burges, Sean Owens, Larry Galuppo, and Dori Borjesson
Study ID: 10-04R

Improved Methods for Freezing and Recovery of Equine Stem Cells

Funded by the Patterson Foundation

Current methods of preserving equine stem cells, such as cryopreservation in liquid nitrogen, are inadequate for the long-term storage of some types of stem cells. Advances in stem cell preservation in other species have been made using substances that stabilize cells, such as trehalose, and minimize damage during thawing, such as epigallocatechin gallate (EGCG). This study will test alternate freezing media for the long-term storage of both types of stem cells, mesenchymal (MSC) and hematopoietic (HSC).

How does this research benefit horses?
There is a high demand for stem cell therapy in horses, and many of the techniques and advances made with cell collection, processing and expansion have been equine-driven. The labor-intensive process of stem cell collection and processing yields many potential doses of stem cells. The goal of this study was to compare current storage methods (freezing in serum and DMSO) with alternative preservation agents (trehalose and EGCG). If both types of equine stem cells could be successfully frozen, then they could be stored for future use, expanding their availability and increasing their potential applications in equine regenerative medicine.

In this study, we found that both hematopoietic and mesenchymal stem cells can be stored using the freeze-drying method. Our results also showed that the use of EGCG and trehalose as cryopreservation agents are not superior to the conventionally used fetal calf serum and 10% DMSO.

Investigators: Isabelle Kilcoyne, Johanna Watson, Dori Borjesson, and Fern Tablin
Study ID: 10-10R

Dose-Dependent Alteration in Early Host Immune Response to *Rhodococcus equi* Infection

Funded by The Patterson Foundation

Rhodococcus equi is one of the most important causes of pneumonia in foals between 3 weeks and 5 months of age. Unlike adults, the foals often fail to mount effective immune reaction to the *R.equi* infection and become clinically ill. A complete understanding of the immune reaction of the

foals against *R. equi* will be necessary to develop an effective vaccine.

In this study, we investigated the hypothesis that *R. equi* alters the initial immune response of foals and adult horses in a dose-dependent manner. We found that high infective doses of *R. equi* suppress gene expression for a chemokine that may play an important role in the development of a protective immune response to *R. equi* infection. High infective doses of R. equi were found to be immunosuppressive in foals when compared with adult horses. An early lag in response by foals may play a role in the development of this disease.

How does this research benefit horses?
The dose-dependent effect of *R. equi* infection on innate immune responses highlights the importance of optimal antigen dose determination for future vaccine development. The results of this study added novel information that can be used for the design of effective prophylactic measures against *R. equi* infection.

Investigators: Seika Hashimoto-Hill, Johanna Watson, Meera Heller, and Ken Jackson
Study ID: 09-09R

Use of N-Butylscopolammonium Bromide in the Field to Facilitate Complete Ophthalmic Examination in Horses

Funded by the Dan Evans Memorial Endowment

A complete ophthalmic exam, as is often performed on grossly normal eyes during a pre-purchase exam, involves examining the retina in the back of the eye to assess for lesions, which could affect a horse's vision and limit their ability to perform. In order to adequately examine the retina, temporary but effective pupil dilation is necessary. Current practice involves the use of topical medications that may take up to 40 minutes to reach full effect and may cause unnecessary pupil dilation in the horse for several hours.

In this study, we evaluated the use of N-butylscopolammonium bromide (NBB) for rapid pupillary dilation with minimal side effects, providing an alternative to currently available topical medications. We found that the use of NBB at the label dose may represent an effective faster-acting and shorter duration dilating agent in some horses.

How does this research benefit horses?
NBB represents a viable alternative medication for pupil dilation that may result in less discomfort post-dilation and decreased time spent per call for veterinarians.

Future Work
Further research is warranted to determine a safe yet reliable dose that results in pupillary dilation in a majority of horses.

Investigators: Joanie Palmero, Steven Hollingsworth, Stephanie Moore, and Nicola Pusterla
Study ID: 10-06H

Evaluation of Different Sedation Protocols for Neurologic Horses For Spinal Fluid Collection

Funded by the John Hughes Memorial Endowment

Spinal fluid collection is an essential part of the diagnostic workup in neurologic horses. This procedure requires heavy sedation to facilitate safe performance, which can often exacerbate the neurologic status of the horse and result in severe ataxia. Objective evaluation of the different sedation techniques for lumbosacral spinal fluid collection can help to identify the safest and most effective protocol that can be used as a standard in the future.

The objective of the study was to find the most effective and safest sedation protocol for lumbosacral spinal fluid collection in ataxic horses. Detomidine alone, romifidine alone, or these agents combined with butorphanol were evaluated. Out of the 16 attempts to collect spinal fluid, the tap was successful in 15 cases. All horses tolerated the procedure well and had an uneventful recovery from the sedation. When evaluating the feasibility of the tap, mainly determined by the level of sedation, we found all protocols to be the same, suggesting that the type of sedation does not necessarily determine the feasibility of the procedure.

How does this research benefit horses?
The sedation protocol did not seem to determine the feasibility of the spinal fluid collection, suggesting that it more likely depends on the horse's personality and response to any of the sedatives used.

Future Work
Our observation that one of the sedation protocols tested provided a better quality tap compared with the other protocols is interesting and warrants further studies in this area.

Investigators: Nora Nogradi and Nicola Pusterla
Study ID: 10-07H

Measurement of Oxidative Damage in the Cerebrospinal Fluid of Foals Affected with Neuroaxonal Dystrophy/ Equine Degeneratie Myeloencephalopathy (10-08H)

Funded by the John Hughes Memorial Foundation

Neuroaxonal dystrophy (NAD) is a disease seen in horses that is characterized by the development of neurologic disease at 4 to 6 months of age. It is clinically indistinguishable from equine degenerative myeloencephalopathy (EDM) and therefore is referred to as NAD/EDM. A definitive diagnosis of NAD/EDM can only be made upon examination of the spinal cord and brainstem once the horse has died; therefore, the disease may be under-diagnosed since a test is not readily available prior to euthanasia.

There is evidence of oxidative damage on postmortem in horses diagnosed with NAD/EDM. In human neurodegenerative diseases, F2 isoprostanes have been used as markers of oxidative damage and could serve as a potential marker in cases of equine NAD/EDM. Therefore, in this study, we investigated whether age-related variations in cerebrospinal fluid markers in normal foals during the first six months of life are elevated in foals affected by NAD/EDM as compared with age, sex and breed-matched controls. We also investigated whether there was a correlation with the onset of neurologic defects and the rise of these markers.

We found that there was no significant age-associated variation between one to six months of age in cerebrospinal fluid F8 isoprostane concentrations in healthy Quarter horse foals. There was no difference between NAD/EDM-affected and healthy, age-matched Quarter horse cerebrospinal fluid F8-isoprostane concentrations. Finally, at one month of age, cerebrospinal fluid F4-neuroisoprostane concentrations tended to be higher in NAD/EDM-affected Quarter horses vs. age-matched controls. However, cerebrospinal fluid F4-neuroprostane concentrations were below the detection limit in the majority of additional samples, precluding further analysis.

How does this research benefit horses?
During the first year of life, age does not appear to influence F8-isoprostane concentrations in the cerebrospinal fluid of Quarter horse foals. NAD/EDM-affected Quarter horse foals may demonstrate increased F4-neuroprostane concentrations in the cerebrospinal fluid; however, additional horses are required to verify this finding.

Future Work
Studies are continuing at UC Davis to identify a diagnostic test for NAD/EDM and to develop treatment recommendations for affected foals.

Investigators: Danika Bannasch, Carrie Finno, and Laramie Winfield
Study ID: 10-08H

Clinical Comparison of Two Drugs for Postoperative Recovery in Horses

Funded by The Kelly Foundation

In recovering from inhalation anesthesia, horses experience excitement and uncoordinated attempts to stand that can lead to injury. The drugs xylazine and romifidine are used to sedate horses during anesthetic recovery and improve the overall recovery experience. However, there are currently no studies to compare these two sedative drugs or their dose effects in clinical equine anesthetic cases.

In this study, we compared xylazine and romifidine in horses during postanesthetic recovery at the William R. Pritchard Veterinary Medical Teaching Hospital. We hypothesized that romifidine would be associated with better recovery quality than an equivalent dose of xylazine, and that there would be a dose-dependent effect on recovery quality for both drugs.

We found that painful procedures, longer anesthesia times, and the Arabian horse breed were associated with poorer recovery scores. Adjustment for these factors revealed an improved recovery score was associated with the use of a romifidine dose of 20 µg/kg.

In healthy adult horses anesthetized with isoflurane for > 1 hour, the results of this study supported the use of 20 µg of romifidine/kg intravenously, rather than lower romifidine doses or xylazine, for postanesthetic sedation to improve recovery quality. This information can be used by veterinarians to reduce post-anesthetic morbidity in horses.

How does this research benefit horses?
The mortality rate for horses during the perianesthetic period is 1.9%. The anesthetic recovery period represents the greatest risk to equine patients. If sedative drugs and doses can be optimized to improve recovery, it may be possible to decrease postanesthetic morbidity and mortality in horses.

Investigators: Kerry Robinson and Robert Brosnan
Study ID: 06-19R

Is Dummy Foal Syndrome Caused by a Failure in the Pathway that Signals the Transition from the In Utero Environment to the External Environment?

Funded by The Patterson Foundation

Neonatal maladjustment syndrome (NMS), or dummy foal syndrome, affects neonatal foals in the first 36 hours of life. Although the exact pathogenesis is unknown, it is thought to be caused by birth hypoxia (deficiency in the amount of oxygen reaching the tissues) or trauma to the central nervous system. We propose that the syndrome is caused by an abnormality in the pathway that leads to the conversion of cortisol in the newborn neonate. This causes high levels of neuroactive steroids that suppress the central nervous system. These neuroactive steroids are normally present in the late-term fetus and suppress the foal's movement during the birth process to prevent trauma to the mare. We suspect that the disease is caused by a failure of the neonatal foal to successfully make the transition to a state of readiness for the external environment.

In this study, foals were given an intravenous injection of a steroid synthesis inhibitor and their behavior was recorded continuously for 24 hours. The infusion produced signs compatible with NMS. From this study, we have developed a model for further studies of NMS which was previously thought to be caused by low oxygen and altered blood flow to the brain and other organs of newborn foals.

How does this research benefit horses?
With these findings, new treatments may be developed to rapidly reverse clinical signs in foals presented to veterinarians with neonatal maladjustment syndrome.

Future Work
UC Davis has led the nation in neonatal medicine and care. This critical area is underfunded at this time, and donations to support needed research could make a difference to the health and well being of foals.

Investigators: Emily Haggett, John Madigan, Balazs Toth, and Monica Aleman
Study ID: 07-15R

Field Evaluation of an Intrarectally Administered *Lawsonia intracellularis* Vaccine in the Protection Against Equine Proliferative Enteropathy

Funded by the Kelly Foundation

Equine proliferative enteropathy (EPE) caused by *Lawsonia intracellularis* has been identified in the last decade and has gained special attention as an endemic (native) and emerging disease in several regions of the United States, Europe, Australia and South Africa. No preventive measures have been identified yet. Previous research from our study group showed that the intra-rectally administered *Lawsonia intracellularis* vaccine created detectable immune response in healthy weanling foals, which may be compatible with protection.

In the current study, we determined the protective effect of intra-rectally administered avirulent (non disease-causing) live vaccine of *Lawsonia intracellularis* in preventing EPE in foals residing on endemic farms in Central Kentucky. We found no adverse effects in foals from the vaccination, and all tolerated the vaccine well. Of 184 foals in the study, only 4 became sick with EPE, resulting in a markedly decreased disease prevalence on the study farms compared with previous years. The overall disease prevalence in Central Kentucky did not change.

Although there was no statistically significant difference between the occurrence of EPE in the vaccinated and control groups, the overall decreased disease prevalence among the study foals was considered to be a success of the vaccine trial. Vaccinated foals demonstrated an increased daily weight gain compared with nonvaccinated, subclinically affected foals.

How does this research benefit horses?
The epidemiology of EPE certainly needs further study to identify the factors associated with the development of clinical disease. However, our study demonstrated that the intra-rectal vaccination of weanling foals is able to decrease

disease prevalence on endemic farms and also prevent subclinical disease.

Future Work
UC Davis has pioneered much of the work on equine proliferative enteropathy. Please contact Dr. Claudia Sonder at the Center for Equine Health if you wish to contribute to future studies.

Investigators: Nora Nogradi, Nathan Slovis, Connie Gebhart, Karen Wolfsdorf, Jeanette McCracken, Charles Scoggin, Phil Kass, Samantha Mapes, Balazs Toth, Megan Lundquist, and Nicola Pusterla
Study ID: 08-22R

Comparison of two anti-inflammatory drugs for the treatment of eye diseases in horses

Funded by The Patterson Foundation

Non-steroidal anti-inflammatory drugs such as banamine are used to treat eye diseases in horses. These drugs have systemic side effects that can cause kidney or gut disease in horses undergoing treatment. A newly licensed anti-inflammatory drug for use in horses, Equioxx (firocoxib), may have less systemic side effects than traditionally used drugs. The efficacy of this drug for the treatment of eye disease in horses is not known.

In this study, we evaluated the efficacy and eye penetration of Equioxx (firocoxib) and compared the results with those for Banamine (flunixin Meglumine) in reducing clinical and laboratory markers of eye inflammation. We found that Equioxx (firocoxib) had better penetration into the eye compared with Banamine (flunixin meglumine).

How does this research benefit horses?
This study suggests that orally administered Equioxx (firocoxib) penetrates into the aqueous humor to a greater extent than orally administered Banamine (flunixin meglumine) at labeled doses. Firocoxib should be considered for the treatment of inflammatory ophthalmic lesions in horses at risk for the development of adverse side effects associated with nonselective nonsteroidal anti-inflammatory drug administration.

Future Work
Further research to evaluate the clinical efficacy of firocoxib in the treatment of ocular disease in horses is warranted.

Investigators: Hugo Hilton, K. Gary Magdesian, Allyson Groth, Scott Stanley, Steven Hollingsworth, and Heather Knych
Study ID: 09-05R

Blood, Urine and Feces Concentrations of the Chemotherapeutic Agent Doxorubicin in Horses Undergoing Systemic Chemotherapy

Funded by The Patterson Foundation

Doxorubicin is a commonly used chemotherapy drug used to treat various cancers in horses. To date, there is no data examining the blood levels of doxorubicin in horses and, thus, no information on whether these doses are potentially effective or toxic. Furthermore, elimination of the drug via urine and/or feces in horses has never been documented in the literature, although it is known to be eliminated in the feces up to 7 days post administration in humans and is potentially a carcinogen exposure risk for handlers of treated horses.

In this study, we determined the blood concentrations over time of doxorubicin and how it is metabolized in horses following intravenous infusion. We also determined the length of time after drug administration that doxorubicin or its metabolites can be found in equine urine and feces, which would post a possible exposure danger to caregivers. We found that the maximum blood concentrations reached are lower than what is considered to be therapeutic concentrations in other animal species. No doxorubicin or its active metabolites could be measured in any of the fecal samples evaluated; however, both the drug and its metabolites were present in urine samples up to 3 days post therapy.

How does this research benefit horses?
The results of this study indiciate that higher doses of doxorubicin should be evaluated to improve its antitumor effects in horses. In addition, the study demonstrates that horse handlers should be aware of the potential risk of carcinogen exposure from the urine of treated horses for at least 3 days following treatment with doxorubicin. Proper protective gear (eye protection, gloves, boots) should be worn when handling the horse for a minimum of 3 days.

Stalls should be cleaned in a manner as to contain, dilute and inactivate the drug without aerosolization. Children and pregnant women should avoid contact with the animal while being treated.

Future Work
Further studies are indicated to test therapeutic dosages and safety of doxorubicin.

Investigators: Monique Marois, Tara Marmulak, Valerie Wiebe, Alain Théon, and Nicola Pusterla
Study ID: 09-07R

Temporal Antibody Concentration to *Sarcocystis neurona* in Serum from Normal Adult Horses Following Treatment with Antiprotozoal Drugs

Funded by The Patterson Foundation

Equine protozoal myeloencephalitis (EPM), often caused by the protozoan *Sarcocystis neurona*, is a neurologic condition in horses that continues to pose a diagnostic and therapeutic dilemma. For example, we do not know how long horses should be treated for EPM or whether they can be completely cured or if it is possible to maintain a latent or subclinical state of disease. The diagnosis of EPM is often based on the presence of antibodies to *S. neurona* in serum and/or cerebrospinal fluid (CSF) on the Indirect Fluorescent Antibody Test (IFAT). It is unknown how long specific antibodies to *S. neurona* persist in peripheral blood following treatment with antiprotozoal drugs.

In this study, we determined the length of time antibodies to *S. neurona* will persist in the serum from non-neurologic horses treated for 60 days with ponazuril in order to better understand whether treatment could effectively eliminate the organism. Seven seropositive (IFAT) horses were treated with ponazuril and seven horses with similar IFAT titers were not treated. Titers were monitored monthly for six months. We found that antibody half-time to *S. neurona* is approximately 30 days, as long as re-exposure does not occur. Seroreversion took 60 to 120 days in seropositive-treated and nontreated hoses, with no difference between the two groups.

How does this research benefit horses?
This information suggests that persistent infection following exposure is unlikely to occur in horses. Serum antibody titers to *S. neurona* are expected to decline following treatment with antiprotozoal drugs.

Investigators: Anna Renier and Nicola Pusterla
Study ID: 10-03R

Solubility Differences of Anesthetics in Equine Blood and Their Potential Effect on Equine Anesthesia

Funded by The Patterson Foundation

Inhaled anesthetics are transported in blood from the lungs to the brain where they produce unconsciousness; this process is reversed during recovery from anesthesia. The blood solubility of different agents helps determine how quickly a particular drug will act and how long it will take for a horse to recover from anesthesia. Previous studies suggest that at least some anesthetics may have different solubility in horse blood compared to blood from other species. Solubility differences may alter how quickly anesthetic drugs are delivered and removed from the horse brain, and they may alter the pharmacologic effects caused by factors that modify anesthetic blood solubility.

Understanding how anesthetic solubility differs in horses is important to understanding how uptake and elimination of these drugs may be different in horses compared to other species. This information is essential to the safe use of these agents in horses requiring anesthesia for surgical or diagnostic procedures.

In this study, we measured the solubility of four anesthetics (isoflurane, sevoflurane, desflurane and methoxyglurane) in equine blood. We also measured the same solubilities in human blood using identical laboratory methods to generate the first comparative physical data ever available for these agents between humans and horses. This is very important because the pharmaco-kinetics and physical properties of anesthetics are much better understood in humans than they are in horses.

We found that the relative solubilities of these agents in blood varies between species; hence, the kinetics between agents will vary by species as well. Of all animals studied, the horse exhibits the largest difference between the blood solubilities of the two least soluble anesthetic agents currently used (desflurane and sevoflurane). Therefore, the horse may benefit from a more rapid desflurane washout

during anesthetic recovery (versus other inhaled anesthetics) than other species.

How does this research benefit horses?
Data from this study suggest that desflurane may be an inhaled anesthetic agent ideally suited to facilitating rapid drug washout in horses. Since residual anesthetic drugs may predispose to excitement, delirium, and injury during recovery, rapid desflurane elimination kinetics might improve anesthetic recovery in horses and reduce the risk of perianesthetic morbidity and mortality. UC Davis continues to study equine anesthetic protocols with the goal of improving the safety of equine general anesthesia.

Investigators: Joao Soares, Robert Brosnan, and Sean Owens
Study ID: 10-05R

Comparison of Chemistry Results Derived from Unclotted and Clotted Blood Samples Using Different Collection Tubes

Funded by the Patterson Foundation

Laboratory biochemical tests are traditionally run on serum obtained from clotted blood. However, equine clinicians often need laboratory results quickly and horse blood is slow to clot, which may delay testing and reporting of results. Because of this, some clinicians submit unclotted blood to the laboratory for testing, but use serum-derived (clotted) reference ranges for interpretation.

It is unknown if the results generated from plasma and serum samples are interchangeable. This knowledge is fundamental to accurate interpretation and optimal patient care. Furthermore, there is no research assessing whether alternative collection tubes with additives, such as clot activator and gel separator, will accelerate clot formation in horses or affect measurement of biochemical analytes.

In this study, we evaluated the interchangeability of routine chemistry results generated using different blood sample types as well as the effect of collection tube additives. We found that biochemical results obtained from serum and plasma samples were interchangeable and that interpretation of results from heparinized plasma compared with serum-derived reference intervals is valid. Serum separator tubes clot faster than standard serum tubes, and biochemistry results are also interchangeable.

How does this research benefit horses?
The faster turnaround time for biochemical results using either heparinized plasma or serum separator tubes will help optimize patient care, especially in emergency and critical situations.

Investigators: Connie Wu, Philip Kass, William Vernau, and Jeanne George
Study ID: 10-09R

Preliminary Evaluation of Magnetic Resonance Imaging for the Characterization of Early Fetlock Injury Including Bone Bruising or Edema of Thoroughbred Racehorses in Training

Funded by The Patterson Foundation

Magnetic resonance imaging (MRI) can be used to identify specific imaging characteristics, termed "bone edema", that precede stress fractures induced by excessive training in human athletes. Similar to human athletes, racehorses are subjected to repetitive forces that induce bone remodeling and can eventually lead to stress fractures or fetlock breakdown injuries. MRI has not yet been used for identifying early bone injury in racehorses. We speculate that edema occurs in the distal cannon bone of racehorses in the acute stage of repetitive, exercise-induced injury and can be detected using MRI since similar changes have been documented in human athletes.

In this study, our goals were to optimize MRI sequences for evaluation of equine fetlock joints and identification of third metacarpal (cannon) bone edema. We also wanted to compare the images obtained in a low-field standing MRI and high-field MRI to high-detail radiographs, gross and histopathology. The third aim was to describe the underlying pathology in regions of bone edema as identified using MRI.

We found that bone edema could not be identified in any fetlock on standing low-field MRI or on high-field MRI. A single fetlock that suffered breakdown was investigated using the same imaging techniques and bone edema was identified at all fracture sites. Scan parameters for optimal fetlock imaging were developed. Although it is difficult to draw any conclusions from this study, several possibilities exist. The group of horses investigated in this study may not have had areas of bone edema, or postmortem scanning may not have accurately reflected the bone edema that was present in life, or the techniques used may not detect bone edema.

How does this research benefit horses?
The ability to identify horses at risk for breakdown prior to racing is a goal veterinary medicine should continue toward. Standing MRI presents an attractive, noninvasive option for this purpose. At the outset of this project, it was predicted that MRI would be able to identify bone edema as a result of race training. This prediction proved untrue. Based on the limited number of horses in this study and the fact that bone edema was identified at fracture margins in a breakdown fetlock, bone edema can be identified post-mortem but is associated with injury and not training. This study should not dissuade investigators from working toward the development of MRI as a tool for the early identification of bone injury.

Investigators: Ryan Schultz, Sarah Puchalski, Larry Galuppo, and Susan Stover
Study ID: 06-21R

Pre-Existing Lesions and Race Characteristics of Racehorses That Have Died Due to a Scapula Fracture

Funded by The Patterson Foundation

Musculoskeletal injuries are the primary cause of death in 79% of California racehorses. Scapula fractures account for 2% of Thoroughbred and 6% of Quarter horse musculoskeletal injuries. There are no reports that describe scapular fracture characteristics, evidence of pre-existing bone pathology, or analysis of race characteristics for racehorses.

In this study, we investigated whether scapular fractures occur in repeatable sites and are secondary to pre-existing bone pathology that may be related to affected horses previous racing history. This involved reviewing the racing records of Thoroughbred and Quarter horse racehorses that died due to scapular fracture in racing or training and examining affected and normal bone specimens. Computed tomography was used to look within bones to determine the presence of pre-existing bone pathology that may have predisposed the scapula to fracture.

We found that with catastrophic scapular fractures, there was a consistent fracture configuration among Thoroughbred and Quarter horse racehorses. Pre-existing pathology (stress fracture disease) was noted at the fracture site and in the other nonfractured scapula. These changes were seen less frequently in control scapulae from horses that died for another reason. Computed tomography revealed that fractured scapulae had lower density bone at the fracture site more frequently than control scapulae.

With complete scapular fractures, there were more males and 2- or 5-year-olds. Scapular fractures commonly occurred in the right forelimb and during racing. Affected Quarter horses were more likely to finish the race than Thoroughbreds.

Quarter horses tended to have shorter exercise distances and fewer official timed workouts compared with Thoroughbreds. Thoroughbred horses with scapular fractures had fewer events (races or workouts), less total distance, fewer active days in training, and lower frequency of events than their matched controls.

How does this research benefit horses?
Thoroughbred and Quarter horse racehorses have a characteristic scapular fracture configuration that is associated with pre-existing pathology at the site of fracture. This location is consistent with scapular stress fractures diagnosed in lame Thoroughbred racehorses. Catastrophic fracture is the acute manifestation of a more chronic process, which is related to exercise history variables. Consequently, there are opportunities for early detection and prevention of fatalities.

Investigators: Stuart Vallance, Mathieu Spriet, Rachel Entwistle, Jim Case, and Susan Stover
Study ID: 08-25R

Do Joint Abnormalities Detected on Radiographs at "2-year-old in Training Sales" Affect Thoroughbred Race Performance?

Jointly funded by CEH and the Southern California Equine Foundation (SCEF)

Evaluation of radiographs for abnormalities is standard practice when selling racehorses. However, this evaluation is currently based on opinion and anecdotal information, and there is no actual data comparing which abnormalities lead to future problems in race performance. We believe that some abnormalities will have a much greater impact on race performance than other abnormalities. Those that have a significantly small impact on race performance can thus be considered less relevant when evaluating radiographs for potential buyers.

In this study, we determined the relationship between joint abnormalities detected on radiographs at "2-year-old in training sales" (980 horses) and subsequent race performance of the horses during their career to determine which abnormalities were most and least likely to reduce performance. We found that none of the identified radiographic abnormalities prevented all of the affected horses from racing. However, affected horses with some specific radiographic abnormalities had lower performance than unaffected horses. A smaller proportion of horses with fetlock chips, sesamoid bone fractures, or sesamoiditis earned money. Horses that had a faster one-furlong work time (< 11 seconds) were more likely to have more starts, earn >$25,000 as a 2-year-old, and earn >$100,000 as a 3-year-old.

How does this research benefit horses?
The results of this study provide veterinarians with information to assist buyers of Thoroughbred racehorses at 2-year-old in training sales with the likely significance of radiographic abnormalities on future race performance.

Future Work
Similar studies in sport horses are needed to help veterinarians assign clinical significance of common radiographic findings to performance.

Investigators: Julia Labadie, Dennis Meagher, Ian Gardner, and Susan Stover
Study ID: 09-04R

Computed Tomographic Arthrography as a Method for Identifying Intercarpal Ligaments in the Equine Carpus

Funded by the Patterson Foundation

The equine carpus (knee) is an important source of lameness. The intercarpal ligaments, which help to stabilize the joint, have been implicated as a source of lameness but this finding has been identified usually in postmortem examinations. In the live horse, it is difficult to diagnose injury to these ligaments because of the lack of specific clinical signs, the complexity of the carpal anatomy, and limitations with our current diagnostic modalities.

Radiology and ultrasound are insensitive for diagnosing intercarpal injury, and only a small portion of the medial palmar intercarpal ligament is visible during arthoscopy (examination of the joint structures by inserting an arthroscope into the joint through a small incision). Currently, arthroscopic surgery is the preferred method to identify injury to the inercarpal ligaments.

In this study, we investigated computed tomographic arthrography for providing an accurate assessment of the overall carpal anatomy and contrast-enhanced computed tomography for specifically delineating the intercarpal ligaments. Arthrography is the injection of dye (contrast material) into joints to allow the visualization of anatomical structures that do not normally appear on x-rays. Our goal was to determine whether intercarpal ligaments can be identified consistently using this method by comparing CT arthrograms with high-field magnetic resonance imaging and gross anatomical specimens.

We found that CT arthrography delineated the intercarpal ligaments from origin to insertion, which correlated well with the MRI and anatomical images. An additional clinically relevant finding was that contrast enhancement was identified in the region of the origin of the proximal suspensory ligament in all eight cadaveric limbs.

How does this research benefit horses?
CT arthrography can be considered as an adjunctive imaging modality in cases of lameness localized to the carpus, specifically when there are little or no radiographic or ultrasonagraphic changes indicative of lameness. This modality is less invasive than the current standard of arthroscopy and yields greater visualization of the ligaments.

Investigators: Sarah Gray, Sarah Puchalski, and Larry Galuppo
Study ID: 10-12R

Retrospective Study on the Role of Androgen Production by the Adrenal Gland on Stallion-Like Behavior in Mares

The John Hughes Memorial Endowment

Stallion-like sexual behavior adversely affects a mare's utility for a variety of uses. Underlying causes of stallion-like or aggressive behavior in mares include granulosa/theca cell tumors (GCT), administration of anabolic steroids, or hormonal fluctuations. Although GCT tumors can cause elevated levels of testosterone, many cases submitted to the Clinical Endocrinology Laboratory do not have evidence of such tumors. In humans and in ruminants, adrenal gland stimulation has been shown to produce increases in serum testosterone and progesterone, respectively. Therefore, adrenal glands have been suggested to be a possible source for reproductive steroids in mares showing abnormal behavior and abnormal hormonal patterns.

The goal of this study was to provide a better understanding of the underlying endocrine profiles in mares with a history of aggressive or stallion-like behavior and compare them with mares with normal testosterone levels. Cortisol, progestin and testosterone levels were evaluated retrospectively using the database of the Clinical Endocrinology Laboratory. We found that mares with modestly elevated testosterone had higher cortisol concentrations than control mares and there was a significant, positive correlation between testosterone and cortisol concentrations.

How does this research benefit horses?
This study was the first to examine the relationship between stallion-like behavior in mares and adrenal steroid hormones. The results provide evidence that these behaviors are linked to adrenocortical function and therefore that changes to the environment may alleviate symptoms.

Investigators: Monica Morganti and Alan Conley
Study ID: 09-06H

Marcia MacDonald Rivas
RESEARCH GRANTS

The Marcia MacDonald Rivas Grant program has been in existence for over 20 years in the UC Davis School of Veterinary Medicine. Recently, this program was transferred to the Center for Equine Health for oversight and management of the selection of projects. These grants are awarded to new teaching and research personnel (less than 5 years in the School of Veterinary Medicine).

Study of the Platelet Secretion Defects from Horses with a Hereditary Bleeding Problem

Thoroughbred horses have bleeding tendencies ranging from mild to severe that can result in diminished performance or death. We have identified a congenital defect in the blood clotting cells (platelets) of Thoroughbred horses that is characterized by reduced platelet binding of the major blood clotting molecule (fibrinogen) in response to the major platelet-activating stimulus (thrombin). Several protein-mediated cellular events associated with the platelet secretion process that is required for fibrinogen binding do not occur normally in platelets from the affected horses.

In this study, we investigated this defect in the platelet secretion process by characterizing protein interactions needed to regulate the process. We also determined the nature and extent of the secretory defect by examining three key proteins. We found that half the amount of the protein Factor V was secreted by platelets from horses with the bleeding disorder compared with normal horses. Factor V is necessary for the rapid assembly of a blood clot. The lower amounts of the protein secreted by the platelets is consistent with the excess bleeding seen in affected horses.

How does this research benefit horses?
We now have a better understanding of the causes for bleeding in horses with this disorder and it pushes us closer to knowing the ultimate cause of the disorder. With the eventual determination of genetic differences between affected and normal horses, this information will also be used to help determine which mutation causes poor platelet function in affected horses. The results of this research are critical in our ongoing efforts to develop a genetic test for this disorder.

Investigators: Jeffrey Norris, Fern Tablin, Monica Pombo, and Meagan Drescher
Study ID: 08-01M

Newly Funded
RESEARCH STUDIES

Study of Equine Proliferative Enteropathy in Weanling Foals

Equine proliferative enteropathy is an emerging disease of weanling foals caused by the obligate intracellular organism *Lawsonia intracellularis*. The disease has almost reached a worldwide occurrence. Affected foals develop anorexia, fever, peripheral edema, colic, diarrhea and weight loss. Infections in foals have in the past been linked to exposure to swine feces, since proliferative enteropathy in pigs is widespread.

However, a preliminary investigation into the epidemiological relationship between *L. intracellularis* isolates from pigs and horses suggest that they represent different strains and therefore may be species specific. This study will aim to clarify this relationship.

How will this research benefit horses?
The epidemiology of equine proliferatie enteropathy has been poorly characterized due to the emerging nature of this disease. The information generated by this study will help us better understand the epidemiology of this devastating disease and better prevent its occurrence.

Investigators: Nicola Pusterla and Connie Gebhart
Study ID: 11-01

Study of an Antiprotozoal Treatment Against *Sarcocystis neurona*, an Agent of Equine Protozoal Myeloencephalitis

Equine Protozoal Myeloencephalitis (EPM) is a protozoal disease of the central nervous system that is typically caused by infection with *Sarcocystis neurona*. It is often a progressively debilitating disease affecting anywhere from the front part of the cerebrum to the end of the spinal cord. Clinical signs are dependent on the area of the central nervous system that is parasitized.

Although the epidemiology of *S. neurona* has been well characterized, the diagnostic modalities, long-term implications and response to treatment are not fully understood. The diagnosis of EPM is often based on the presence of antibodies against *S. neurona* in serum and/or cerebrospinal fluid (CSF). The recent introduction of a quantitative indirect fluorescent antibody test (IFAT) for the detection of specific antibodies against *S. neurona* has enabled equine veterinarians to better determine the likelihood of infection in a neurological equine patient.

However, the temporal variation of specific antibodies to *S. neurona* following treatment with antiprotozoal drugs has yet not been investigated. This information is crucial in order to determine if the indirect fluorescent antibody test (IFAT) to *S. neurona* can be used to judiciously determine successful cure.

How will this research benefit horses?
This study will help us better understand the reactions of antibodies specific to *S. neurona* in healthy, nonneurologic horses. The researchers expect to then extrapolate the results to horses with clinical EPM, increasing the accuracy of the IFAT in helping veterinarians better assess the effectiveness of antiprotozoal treatment.

Investigators: Nicola Pusterla, W. David Wilson, Patricia Conrad, Anna Renier, and Andrea Packham
Study ID: 11-02

Does Guaifenesin, a Muscle Relaxant, Decrease the Concentration of Desflurane Required for General Anesthesia in Horses?

The muscle relaxant guaifenesin is commonly used in horses to help induce and maintain general anesthesia. However, it is not known whether guaifenesin contributes to immobility during anesthesia because it has never been measured. In order to use this drug most appropriately during anesthesia, the effect of guaifenesin on anesthetic requirement must first be determined.

We believe that guaifenesin decreases general anesthetic requirements (as measured by a decrease in desflurane requirement) in direct proportion to its blood concentration in horses. In this study, we will measure the desflurane concentration required to prevent movement in anesthetized horses during different plasma concentrations of guaifenesin.

How will this research benefit horses?
General anesthesia in horses is associated with a 0.9% mortality rate, which is much higher than in dogs, cats or humans. In order for equine anesthetics such as guaifenesin to be used most effectively and safely, their contributions (or lack thereof) to immobility during general anesthesia must be known. Understanding of equine anesthetic drug actions should improve the safety of equine anesthetic practice.

Investigators: Robert Brosnan, Eugene Steffey, Alonso Guedes, Scott Stanley, and Heather Knych
Study ID: 11-03M

Identification of the Unique Molecular Fingerprint of Equine Blood-Derived Stem Cells

The promise of regenerative medicine includes the potential transfer of disease- resistant genes into animals that do not carry them. This could be accomplished by taking an animal's own blood-derived stem cells, introducing the required form of the gene, and then transplanting these cells back to the animal.

The first step toward blood-derived stem cell transfer in the horse is identification and purification of these cells. While there are useful surface markers (CD34, Sca-1) in mice and humans, no such markers have been identified for the horse. Before we can realize the benefits of these cells in regenerative medicine we will need to develop molecular markers for their unique identity.

In this study, we hope to identify the unique molecular "fingerprint" of blood-derived stem cells from bone marrow, peripheral blood and umbilical cord blood and determine the most suitable source tissue for future stem cell applications.

How will this research benefit horses?
Regenerative medicine holds great promise for the treatment of diseases and injuries in horses. However, before we can harness these new therapeutic options, more information about stem cells is needed and a means to identify pure stem cell populations is a crucial step.

Investigators: Johanna Watson, Dori Borjesson, and Kenneth Jackson
Study ID: 11-04

Improving the Quality of Cryopreserved Sperm

The fertility of frozen semen is poor compared with that of freshly collected or cooled, shipped semen. Oxidative stress is a major reason that cryopreservation of stallion sperm fails. Heat shock proteins protect sperm from adverse conditions, but we do not know if these proteins play any role in the survival of sperm after cryopreservation.

In this study, we will attempt to identify the mechanism by which these proteins become activated during the various stages of cryopreservation so that we can better understand their role and ultimately develop improved cryopreservation techniques.

How will this research benefit horses?
This study will benefit a variety of breed registries in the United States and abroad, as improvement in preservation of stallion genetics will allow more stallions within breeds to contribute to breeding programs and progeny production.

Investigators: Stuart Meyers and Katie Klooster
Study ID: 11-05

Genetic Investigation of a Neurologic Disorder Affecting Foals

During the first year of life, genetically predisposed foals may develop a neurologic disorder known as Neuroaxonal Dystrophy/Equine Degeneratie Myeloencephalopathy (NAD/EDM). The only way to diagnose NAD/EDM is by examination of the spinal cord and brainstem once the horse has died. In evaluating horses that were euthanized due to neurologic disease, NAD/EDM was diagnosed in 23/96 (24%) of cases at Cornell University.

It appears that the disease is inherited based on breeding studies in Morgans and Appaloosas. Preliminary investigations indicate that there are five candidate regions that may be responsible for a genetic mutation responsible for the disease. In this study, we will conduct further studies to identify a major region and subsequently candidate genes that may contain a mutation causing NAD/EDM.

How will this research benefit horses?
The discovery of a genetic mutation for NAD/EDM would allow veterinarians to test for the disease in neurologically abnormal horses in order to diagnose the condition. A genetic test would aid breeders in making decisions designed to decrease the overall prevalence of this disease.

Investigators: Danika Bannasch and Carrie Finno
Study ID: 11-06

Development of an X-Ray Technique to Detect a Fetlock Injury Before Breakdown

Fetlock breakdown injuries are the cause of death in 34% of Thoroughbred and 40% of Quarter Horse racehorses that die from injuries. The mild injury that predisposes racehorses to fetlock breakdown was recently discovered in the research laboratory, but this injury is not detectable using routine x-rays in live horses. There is a need to develop an x-ray technique that can be used in live horses for detection of this injury before catastrophic breakdown.

In this study, we will investigate whether a new radiographic angle projection through the fetlock will allow visualization of the mild injury that predisposes to catastrophic fetlock breakdown. This x-ray technique could be used to detect affected horses so these horses could be treated and return to performance.

How will this research benefit horses?
A new x-ray technique to detect the mild injury that predisposes horses to fetlock breakdown will assist in early detection of horses with mild injuries. Affected horses can be treated and returned to normal performance, thus preventing racehorse deaths due to fetlock breakdowns.

Investigators: Susan Stover, Sarah Puchalski, Tanya Garcia, and Daniel Luethy
Study ID: 11-07

Investigation of Trigeminal Nerve Testing as a Diagnostic Aid in Equine Headshaking

Headshaking is a painful disease of adult horses that is currently diagnosed by suggestive history, clinical signs and the exclusion of other diseases rather than by any specific test. The trigeminal nerve is the chief nerve of sensation for the face and controls the muscles used for chewing. It is thought that pain arising from abnormal firing of the trigeminal nerve is the likely cause of equine headshaking.

Preliminary studies have shown that this nerve is irritable in headshaking horses and is triggered with only one-tenth of a normal stimulus. Humans with trigeminal nerve pain show altered sensory function, which can be assessed by very specific testing of perception using touch and thermal receptors.

In the proposed study, we will further characterize the trigeminal nerve in healthy control and in affected horses by conducting sensory testing. Identification of altered sensory function of the trigeminal nerve in headshaking horses could provide a useful noninvasive diagnostic technique.

How will this research benefit horses?
Sensory testing of the trigeminal nerve will allow further characterization of equine headshaking and increase understanding of this frustrating disease, which limits the utility of many horses worldwide. Additionally, development of a non-invasive, practical test to aid diagnosis of headshaking would be beneficial to horses, horse owners and veterinarians.

Investigators: John Madigan, Kristie Pickles, and Linda Barter
Study ID: 11-08

Derivation of Stem Cells from Equine Embryos

Embryonic stem cell therapy has the potential to treat a great number of athletic injuries including, laminitis, navicular disease, chronic obstructive pulmonary disease and neurological diseases, among others. Current reports about the isolation of equine embryonic stem cells have failed to demonstrate complete pluripotency (the ability of a cell to generate all tissues in the body). In this project, a novel approach to derive genuine equine embryonic stem cells will be implemented.

We hypothesize that authentic equine embryonic stem cells can be isolated from horse embryos using a novel culture system based on external stimuli inhibition, and that the use of equine recombinant hormones for superovulation will substantially increase the number of equine embryos available for embryonic stem cell derivation. In this study, we will collect horse blastocyst-stage embryos after superovulation using equine recombinant hormones and isolate equine embryonic stem cells using a novel culture system. We will then characterize the properties of equine embryonic stem cells.

How will this research benefit?
Isolation of genuine equine embryonic stem cells may facilitate the development of "off-the-shelf" cell treatments for musculoskeletal tissue injuries. It may also foster development of new therapies for currently incurable diseases such as spinal cord injury and blindness and

improve current stem cell laboratory research capabilities. Moreover, availability of equine embryonic stem cells and optimization of culture conditions for genuinely pluripotent equine cells will facilitate the derivation of patient-specific pluripotent stem cells (e.g. iPSC).

Investigators: Janet Roser, Pablo Ross, Geraldine Meyers-Brown, and James Chitwood
Study ID: 11-09M

Evaluation of Tramadol (a Painkiller) for Pain Relief in Horses with Chronic Hoof Pain

Chronic laminitis (long-term inflammation of the foot) is a common and prominent cause of pain and suffering in horses, yet effective options for pain relief are very limited. Tramadol, a painkiller used in other species, has the potential to be useful to treat pain in horses. Recent studies by one of the investigators (Guedes) showed that tramadol indeed produces effective pain relief but only initially and not later in the course of treatment, suggesting the dose used may have been inadequate and that a higher dose may produce sustained pain relief.

In this study, we will test whether or not tramadol is able to produce sustained pain relief in horses with chronic hoof pain due to laminitis (e.g., pain due to long-term inflammation of the foot).

How will this research benefit horses?
Pain is a debilitating factor associated with laminitis in horses and its effective control is one of the greatest challenges in equine clinical practice. In many instances, humane euthanasia is the only option to alleviate suffering in affected horses, underscoring how critical the need is for the development of effective pain-relieving medications for horses. The studies proposed here have been designed to improve and expand the currently limited number of effective pain-relieving medications in horses, which directly impacts all branches of the equine industry.

Investigators: Alonso Guedes, Heather Knych, and David Hood
Study ID: 11-10M

Optimizing the Derivation of Stem Cells from Equine Embryos

Embryonic stem cell therapy has the potential to treat a great number of athletic injuries, laminitis, navicular disease, chronic obstructive pulmonary disease and neurological diseases, among others. Current reports about the isolation of equine embryonic stem cells have failed to demonstrate complete pluripotency (the ability of a cell to generate all tissues in the body). In this project, we will continue to optimize conditions aimed at deriving genuine equine embryonic stem cells.

We believe that authentic equine embryonic stem cells can be isolated from horse embryos by optimizing isolation conditions and feeder cell composition. The use of equine recombinant hormones for superovulation can substantially increase the number of equine embryos available for embryonic stem cell derivation.

How will this research benefit horses?
Isolation of genuine equine embryonic stem cells will facilitate the development of cell treatments for musculoskeletal tissue injuries. It will also allow development of new therapies for currently incurable diseases such as spinal cord injury and blindness.

Investigators: Janet Roser, Pablo Ross, Geraldine Meyers-Brown, and James Chitwood
Study ID: 12-01

Does Compression and/or Damage to the Trigeminal Nerve Occur in Equine Headshaking?

Headshaking is a common distressing and painful disease of adult horses and, in severe cases, horses may be euthanized on welfare grounds. Headshaking behaviors include sudden, violent flicks of the head (described by owners "as if a bee had stung the horse's nose") and excessive snorting and rubbing of the nose on the foreleg or ground. The cause of headshaking is currently unknown, although inappropriate activation and pain of the trigeminal nerve (which innervates much of the face) is suspected. Headshaking shares many similarities with the human condition "trigeminal neuralgia".

Compression and damage of the trigeminal nerve is believed to be the most common cause of human trigeminal neuralgia. Understanding the biological cause of equine headshaking is essential for improved understanding of this

disease and the development of more rational and successful therapies. We therefore propose to investigate trigeminal nerve compression and damage as the cause of equine headshaking.

How will this research benefit horses?
A thorough investigation of the equine trigeminal nerve system for damage has not been undertaken previously. Understanding the biological cause of equine headshaking is vital to determine more successful therapeutic strategies and reduce wastage due to this distressing disease. As such, horses, horse owners and veterinarians alike would benefit from this study. Additionally, if causal factors are similar, headshaking horses would provide the only naturally occurring animal model of human trigeminal neuralgia.

Investigators: John Madigan, Kirstie Pickles, Silvia Siso, Robert Higgins, Sarah Puchalski, Monica Aleman, Doug Herthel, and Carter Judy
Study ID: 12-02

The Effect of Storage (Time and Temperature) on the Stability of Adrenocorticotropic Hormone in the Blood of Horses With and Without Cushing's Disease

Equine Cushing's disease is one of the most common diseases of horses greater than 15 years of age. The clinical signs are associated with abnormally elevated hormone concentrations in the blood and, along with other hormones, cortisol plays an important role in this disease. This syndrome is better defined as Equine Pituitary Pars Intermedia Dysfunction (PPID) because it reflects the location within the brain that is abnormal.

The best indication of PPID is the clinical sign of hirsuitism (excessive hair growth) in the aged horse. The sensitivity of this clinical sign is better at predicting an abnormal pituitary than any diagnostic test available. Horses that have subtle signs of PPID need to be tested to confirm the disease. Of the tests available, no single test is 100 percent accurate. The most commonly used tests in the field are the dexamethasone suppression test and the measurement of resting plasma adrenocorticotropic hormone (ACTH) concentration. The dexamethasone suppression test can be contraindicated in horses suffering from laminitis, which can occur secondarily to elevated cortisol levels.

ACTH in blood is considered highly unstable because of proteolytic degradation. Recent studies from companion animals have shown that pre-analytical factors, such as time to centrifugation and temperature storage of blood samples, can influence the pre-analytical stability of ACTH. Equine ambulatory practitioners are faced with several challenges, including the inability to centrifuge samples in the field and to keep samples on ice until processed for plasma collection. Unfortunately, the combined effect of time to centrifugation and storage of sample prior to centrifugation has not been determined for equine blood.

We hypothesize that samples processed for plasma separation within 1 and 4 hours will yield significantly higher ACTH values than samples processed at 8, 24 or 48 hours. We also hypothesize that storage temperature and time to analysis will significantly influence the ACTH results.

How will this research benefit horses?
Horses 18 years of age and older are at higher risk of developing pituitary pars intermedia dysfunction. With the recent introduction of a labeled drug for the control of PPID, it is important that any diagnostic modality leading to the diagnosis of PPID be as accurate as possible. The information gained from this study will help equine veterinarians to accurately process and store blood from horses with suspected PPID.

Investigators: Nicola Pusterla, Sean Owens, Johanna Watson, and Joanne Hodges
Study ID: 12-03

Investigation of Mechanisms of Bone Loss (Osteoporosis) in Horses from Geographic Regions with Soils High in Toxic Silicates

Bone fragility syndrome is a devastating disease that causes nonspecific chronic lameness, skeletal deformities, bone fractures, death or humane euthanasia of horses that are exposed to soil containing toxic silicates (cristobalite). Most horses have concurrent lung disease caused by cristobalite, but the reason for the skeletal disease in horses with this lung disease is unknown. If the mechanism that links the bone disease to the lung disease can be discovered, further research into targets for treatment and prevention of the bone disease can be pursued.

We hypothesize that bone loss can be attributed to changes in numbers or activity of bone forming and/or bone resorbing cells. The objective of our study is to quantify

differences in bone tissues and cell activities in the ribs of diseased and nondiseased horses.

How will this research benefit horses?
Bone fragility syndrome is a chronic, devastating disease that affects horses' performance, quality of life and usually culminates in pathological fractures, death or humane euthanasia. Horse owners incur financial and emotional burdens and in some instances devaluation of real estate with soil containing toxic substances. We hope that by determining the major cellular dysfunction in the disease, the information gained will guide future studies into disease mechanisms that might serve as targets for treatment and preventive strategies.

Investigators: Regina Zavodovskaya, Susan Stover, Bradd Barr, and Brian Murphy
Study ID: 12-04

Comparison of Drug Elimination Rates and Recovery Characteristics in Horses Anesthetized with Sevoflurane vs. Desflurane

Horses recovering from anesthesia with inhaled agents often experience excitement and difficulty standing, which can increase the risk of severe injuries. Anesthetic drugs that have low solubility in blood undergo rapid elimination that should shorten recovery time and may reduce risks of post-anesthetic injury. Desflurane solubility is lower in horse blood than for any other domestic species, and it is significantly less soluble than the next closest agent, sevoflurane. Properties of desflurane may make this drug particularly advantageous to equine anesthetic practice.

We hypothesize that the elimination rate of desflurane is significantly faster than that of sevoflurane in horses, and that anesthetic recovery will be faster and of better quality than that from sevoflurane in horses. To investigate this, we will model the pharmacokinetics (the speed of drug elimination) of sevoflurane and desflurane in horses and measure the effects of each drug on time to standing recovery and indices of recovery quality.

How will this research benefit horses?
The greatest risk associated with general anesthesia in horses is the potential for injury upon an excited recovery. Use of agents that shorten recovery time and improve the quality of recovery will improve anesthetic safety for all horses.

Investigators: Robert Brosnan, Caitlin Tearney, Alonso Guedes, and Trung Pham
Study ID: 12-05

Control of Oxygen Byproducts During the Early Phase of Cryopreservation Increases Sperm Survival and Improves Cryopreservation Success for Stallions

Semen freezing for stallions has been growing rapidly worldwide, although certain stallions with highly desirable genetics have been unable to benefit from frozen semen due to poor survival of frozen sperm. When sperm are frozen, they are more susceptible to oxidative attack from metabolic byproducts than unfrozen sperm. Oxidative byproducts are believed to be the major contributing factor to sperm cell death and poor fertility of frozen sperm.

We hypothesize that most of the oxygen-derived byproducts come directly from sperm mitochondria and that they are generated during the initial phases of cooling below ambient temperature and well before the sperm are exposed to ice formation. If oxidative attack can be prevented during the initial phase of cooling, then sperm are likely to better withstand very low temperature storage. In this study, we will investigate whether stallion sperm are actually susceptible to freezing damage in the above-zero phase of freezing and whether treatment by restricting oxygen in that period will allow improvement in sperm survival.

How will this research benefit horses?
The ability to understand the ability of sperm to cope with stress is critical for the development of improved cryopreservation techniques for sperm. This study will benefit a variety of breed registries in the U.S. and abroad since improvement in preservation of stallion genetics will allow more stallions within breeds to contribute to breeding programs and progeny production.

Investigators: Stuart Meyers, Kelly Martorana, and Katie Klooster
Study ID: 12-06

Changes in the Sensitivity of *Corynebacterium pseudotuberculosis* to Antibiotics Over Time

Corynebacterium pseudotuberculosis (*C. pseudotuberculosis)* may cause external abscesses, internal abscesses, or ulcerative lymphangitis in horses. While treating external abscesses with antibiotics remains controversial, internal abscesses are fatal without long-term treatment with antibiotics. There are no reports describing the susceptibility of equine *C. pseudotuberculosis* to our commonly used antibiotics over time.

We believe that there have been changes in the antibiotic susceptibility patterns of *C. pseudotuberculosis* to commonly used antibiotics over time. More specifically, we predict that that *C. pseudotuberculosis* has become more resistant to the commonly administered antimicrobials over the past 15 years. The objective of this study is to document changes in antimicrobial susceptibility patterns of *C. pseudotuberculosis* isolated from horses over a 15-year period to 16 antimicrobial agents. The secondary objective is to determine if resistance is related to abscess location (internal vs. external).

How will this research benefit horses?
Corynebacterium pseudotuberculosis infections often require treatment with antibiotics. The ability to select an appropriate antibiotic is paramount to a successful outcome. The information we hope to gain from this study of antimicrobial susceptibility patterns will help guide clinicians in treatment and determination of prognosis for success when dealing with internal abscesses.

Investigators: Sharon Spier, Diane Rhodes, Barbara Byrne, Judy Edman, Philip Kass, and Gary Magdesian
Study ID: 12-07

Evaluation of Blood Levels and Pain-Relieving Effects of a Novel Painkiller (t-TUCB) in a Reversible Model of Joint Pain in Horses

Effective options for pain relief in horses with inflammatory painful conditions are limited. An experimental painkiller, t-TUCB, has the potential to be useful to treat pain in horses. In preliminary studies, two horses with inflammatory pain due to acute lamintis who were non-responsive to traditional painkillers showed marked improvement in pain levels with the addition of t-TUCB in the treatment protocol.

We predict that t-TUCB will produce significant pain relief in a model of joint inflammation and pain in horses. The specific objectives of this study are to determine the blood concentration of a t-TUCB in healthy horses and to test the pain-relieving efficacy, demonstration of target engagement, dose-effect relationships and mechanisms of this drug in a reversible model of joint pain in horses.

How will this research benefit horses?
In horses, safe and effective drugs for pain relief of painful inflammatory diseases (osteoarthritis, laminitis, etc.) are very limited. The studies proposed here have been designed to improve and expand the currently limited options for pain relief in horses, which directly impacts all branches of the equine industry.

Investigators: Alonso Guedes, Heather Knych, Robert Brosnan, Martin Vidal, Christophe Morisseau, and Bruce Hammock
Study ID: 12-08M

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The research studies described in this publication are driven by ideas and by the researchers who pursue them: individual scientists who pursue hypotheses and are dedicated to following rigorous research methods that eventually lead to a new discovery.

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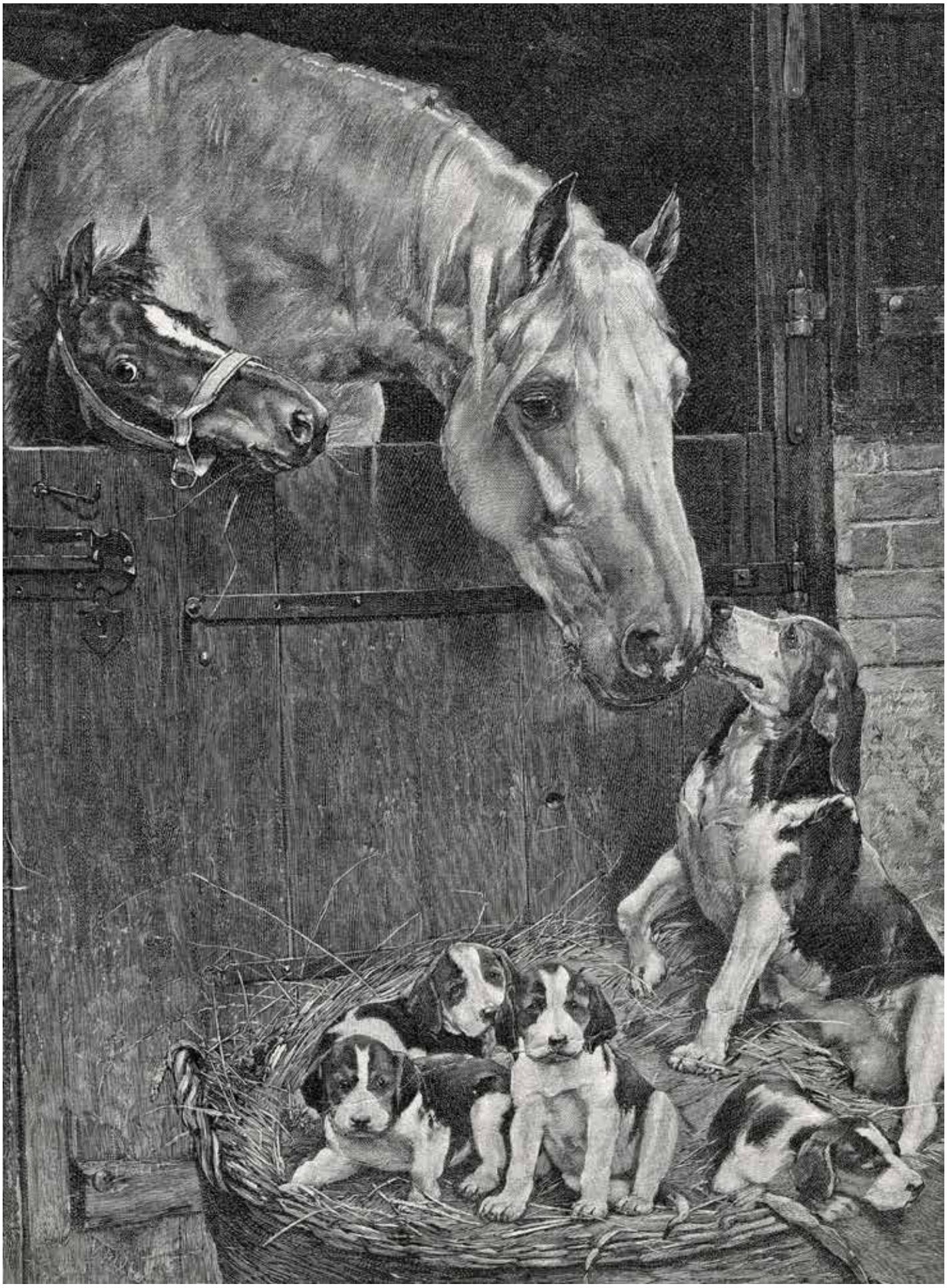

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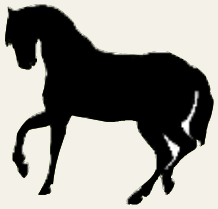

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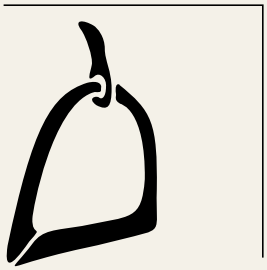

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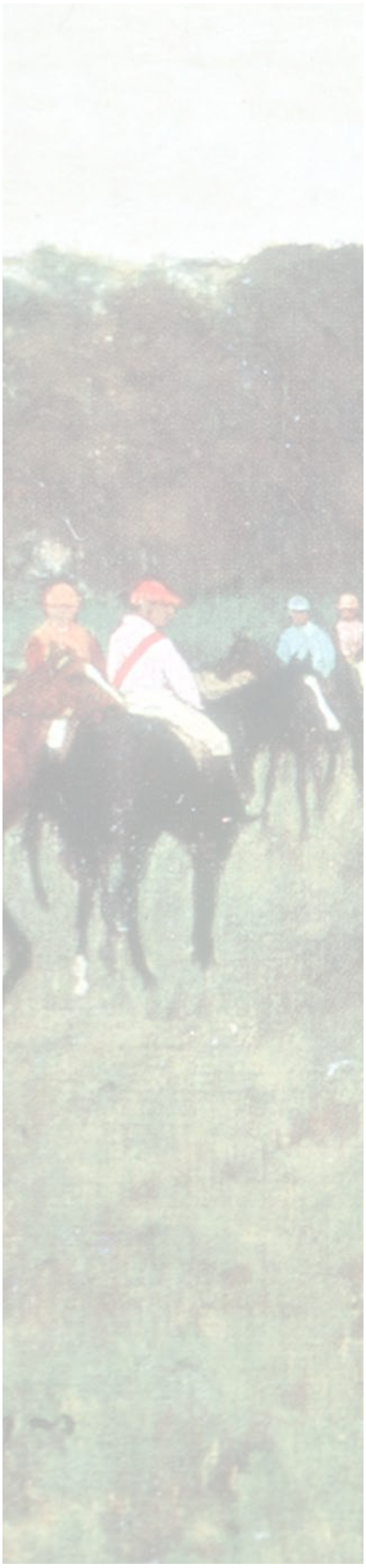

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