OCTOBER 2023 VOLUME 32, NO.4

EQUINE DISEASE QUARTERLY

A PUBLICATION BY: THE UNIVERSITY OF KENTUCKY DEPARTMENT OF VETERINARY SCIENCE,
MAXWELL H. GLUCK EQUINE RESEARCH CENTER
FUNDED BY: EQUUS / STANDARDBRED STATION, INC. M&J INSURANCE

IN THIS ISSUE

RESEARCH SPOTLIGHT

The impact of short-term transportation stress on endocrine and immune function in horses.

Horses are routinely transported for equestrian events as well as medical care. It is well recognized that long-distance transportation is a risk factor for the development of pleuropneumonia. Results from a nationwide survey showed that horses are most commonly trailered short distances of three hours or less. The Adams Lab at the Gluck Equine Research Center within the University of Kentucky Martin-Gatton College of Agriculture, Food and Environment is currently working to investigate the impact of acute transportation stress on immune function in different groups of horses. Previous research has shown that transporting horses one to three hours can elicit a stress response as seen through increased heart rate. Our lab has previously shown that short-term transportation stress can cause changes in whole blood gene expression of cytokines in aged horses. Following these findings, we wanted to know if similar responses occur in young horses. Additionally, since horses are often transported to veterinary clinics for diagnostic testing, we have investigated the effect of transportation on endocrine responses and testing for insulin dysregulation.

Two studies where horses were transported one and one-half hours (55 miles) round trip were performed. Study #1 focused on evaluating age-differences in stress and immune response following short-term transportation. Horses were grouped by age with six horses in each group. Group one had an average age of two years old and group two an average age of 22 years old.

Study #2 evaluated differences in endocrine responses to transportation between seven insulin dysregulated (ID) and seven age-matched non-insulin dysregulated (non-ID) horses. For both studies blood, saliva, heart rate and temperature were collected before and after transportation.

Transportation stress led to various physiological changes in both studies. For both studies, heart rate and cortisol increased in response to transportation, with the highest heart rates recorded at loading and both serum and salivary cortisol being highest directly after transport. There were no differences based on age or whether a horse was insulin dysregulated. In Study #1, all horses had increased ACTH following transportation, with three out of five aged horses having ACTH concentrations above the cutoff for pituitary pars intermedia dysfunction (PPID) 15 minutes after transportation. While rectal temperature was not influenced by short-term transportation stress in either study, these studies were conducted in mild weather during the spring and fall.

Study #1 also showed increased gene expression of the pro-inflammatory cytokine IL-6 post-transport in aged horses and increased salivary IL-6 in aged horses compared to young horses. Additionally, aged horses had increased cytokine production from lymphocytes compared with young horses. These results are all indicative of the older horses being in a state of "inflamm-aging" where they have increased inflammatory markers, putting them at higher risk for development of diseases.

Serum insulin was measured in both studies. In Study 1, insulin was increased one to three hours post-transportation in aged horses and followed a similar trend in ID horses in Study #2, although not statistically different from pre-transportation insulin levels. In Study #2, performing an oral sugar test (OST; current standard for diagnosing ID in horses) post-transportation caused insulin concentrations to be above the recommended diagnostic cutoff for insulin dysregulation in non-ID horses and were twofold greater than pre-transportation OST results in some ID horses.

The results of these studies show that there are significant changes in immune and endocrine function following short periods of transportation. Additionally, caution should be used when performing endocrine testing for metabolic diseases post-transportation as ACTH and insulin may be elevated in horses without endocrine disease. It is recommended that ACTH should be collected for PPID testing at least 30 minutes after transportation. Furthermore, performing an OST with in the first few hours following transportation could lead to inaccurate diagnostic findings, particularly in non-ID horses. Given the importance of PPID in the aging horse population, we are currently evaluating if short-term transportation stress alters endocrine function and diagnostic results of horses with PPID and plan to report on those findings in the near future.

Erica Jacquay, PhD Student
Gluck Equine Research Center

Supervisor: Dr. Amanda Adams

Third Quarter 2023

International report on equine infectious diseases.

The following report was composed with information provided by laboratories in Lexington, Kentucky, the University of Kentucky Veterinary Diagnostic Laboratory and by Equine Diagnostic Solutions, Inc. We are also grateful to IDEXX laboratories, Germany, for sharing their quarterly PCR respiratory panel results with this community.

We included information from the International Thoroughbred Breeders' Federation; the International Collating Centre in Newmarket, United Kingdom; and from the American Association of Equine Practitioners' Equine Disease Communication Center. This report is retrospective and does not claim to be complete. However, it provides an indication of heightened activity of several considered relevant contagious or environment-linked diseases among equids. To further improve this data set, we encourage everyone in/outside the United States to report laboratory-confirmed (toxico)infectious disease of *Equidae* to the ICC in Newmarket, UK, or EDCC, USA.

We received a single report of Hendra infection in a horse from Australia. Libya reported an outbreak of Equine Influenza on a premises south of Tripoli.

Summer and early Fall is typically the season where mosquito-borne diseases are more prevalent. Hence, cases of Eastern equine encephalitis virus infections have increased. What is worrisome is that there is increased reporting of EEE from the Midwest United States and from eastern Canada provinces (12 cases in Ontario). Summer is also the season for West Nile virus infections. Both EEEV and WNV infections are known causes of clinical neurologic disease in horses. During the past quarter, we witnessed a surge of equine WNV cases, particularly in the Western United States. The surge began with cases in Colorado's more densely populated Front Range; followed by unusually high numbers reported from the neighboring states of Wyoming, Nebraska, Utah, Idaho and Montana. Additionally, California reported a surge of clinical WNV cases. Many affected horses were unvaccinated or 'not current' on their vaccinations. France (Europe) also reported WNV cases, while other parts of Europe with endemic WNV have not yet provided information.

EQUINE DISEASE QUARTERLY

EDITORS
Rebecca Ruby
Lutz Goehring
Allen Page

STAFF
Holly Wiemers
Hendri Smeenk

North America reported scattered cases of EIA positive horses, with six unrelated cases in Texas. In Europe, France and Italy reported incidental EIA cases.

Canada reported an outbreak of Equine Arteritis virus on a stud farm in the province of Prince Edward Island, where a number of newborn foals apparently died of (interstitial) pneumonitis.

North America and Europe (France, Sweden and Switzerland) reported Strangles (*Streptococcus equi spp. equi*) cases and outbreaks in several locations. It is currently the most consistently reported pathogen for both continents. For North America, the majority of cases have been reported from several distinct regions. For the USA, hot spots have been Florida, Michigan and Washington. For Canada, reports primarily originated from the Province of Ontario. There have been a few reports of Equine Influenza outbreaks/cases in the UK, France, Sweden and the Netherlands.

We already mentioned the EI outbreak in Libya. USA reports two EI outbreaks, one in the Pacific Northwest and one in the Mid-Atlantic region.

Few equid alphaherpesvirus respiratory infections (fewer EHV-1 than -4) were reported from North America and continental Europe. A single abortion caused by EHV-4 (Europe-France) and two isolated cases of EHV-1 neurologic disease in North America (with the remainder of the herd in quarantine) were reported.

Vesicular Stomatitis virus (*Rhabdoviridae)* infections in horses in the USA have not been contained. New cases were reported from California, Texas and Nevada, although the numbers are decreasing.

Miscellaneous:

A case of Rabies infection was reported from Oklahoma, USA.

Kentucky laboratories and the laboratory in Germany reported high incidences of *Strep. equi spp equi* and EHV-4 positive samples with positive EHV-1 samples submitted on rare occasions. EDS (Kentucky) reports a moderate number of EI positive samples with origin from the Eastern United States, while there were no EI reports from the German laboratory. UK-VDL (Kentucky) reported three samples positive for Equine Viral Arteritis; however, there is apparently no link to the EAV outbreak in Canada.

Lutz Goehring
University of Kentucky
Gluck Equine Research Center – Department of Veterinary Science

l.goehring@uky.edu

Maxwell H. Gluck
Equine Research Center
Lexington, Kentucky USA, 40546-0099
Telephone (859) 257-4757
Fax (859) 257-8542
gluck.ca.uky.edu

Recent Advances in Lameness Detection and Localization in the Horse

Many horses are affected by lameness each year with a large number of these horses being examined and treated by veterinarians. According to the 2015 USDA National Animal Health Monitoring System (NAHMS) study on equine management and select equine health conditions in the United States, 67% of horse operations reported one or more lame horses within the past year. In this survey, about 60% of lame horses had lameness examination performed by a veterinarian. Low grade lameness is usually of less concern to horses that perform lower levels of athletic function; although, early detection and identification of the cause of low level lameness can lead to earlier treatment, resolution of lameness and return to previous function. Low grade lameness is more concerning in horses that perform at speed (i.e., racehorses), jump over large obstacles over uneven footing (three-day event horses) or work over extended distances (i.e. endurance horses). Low grade lameness may indicate the beginning of a larger problem, and if untreated, could lead to a catastrophic injury, which could result in end of career or end of the horse's life. Thus, good screening tools are needed to identify early, subtle lameness to prevent low grade injury/lameness from developing into a catastrophic injury.

The mainstay of lameness and musculoskeletal injury diagnosis begins with a complete lameness evaluation. However, agreement among veterinarians on the affected leg and degree of lameness is poor for horses with low grade lameness. Within the past 20 years, horse mounted gait analysis devices have been developed and have been shown to have better accuracy in the identification of low grade lameness compared to visual examination by experienced veterinarians. Benefits of these systems are ease of use and the ability to be used on the farm.

The Lameness Locator® is one of the first of these systems developed. It is an easy to use, accurate system that is currently used by veterinarians around the world. This system is composed of three small sensors that can be easily attached to the horse and provide real-time information about a horse's lameness, by identifying asymmetric head and pelvis movements. This system has the ability to record type of footing and can make comparisons between trials, such as before and after flexion tests and/or blocking.

More recently, additional horse mounted motion analysis systems have been developed. Two such systems are the Pegasus® system and EquiMoves®, both of which were developed in Europe. While these systems are newer, they provide some of the same symmetry indices of the head and pelvis as the Lameness Locator® system. In addition to evaluating movements of the head and pelvis, these two systems also allow evaluation of limb movement since they also include limb mounted sensors. For instance, with the Pegasus®, hock range of motion can be measured. Protraction and retraction, as well as abduction and adduction of all four limbs can also be determined with these systems.

Even more recently, the use of artificial intelligence has provided even more advancements in equine lameness detection and monitoring. A video-based system has been developed for use on a smart-phone, which is called Sleip. This is a subscription based program for veterinarians that allows horse owners to upload videos to a cloud for analysis. This system provides the opportunity for objective follow-up in horses without the need for sensor application.

In addition to improvements in objective lameness assessment, which allows regionalization of lameness, there have also been recent improvements in diagnostic imaging tools that can help with localization of lameness to specific bony and soft tissue structures. Within the past decade, computed tomography has been adapted so that it can be used in standing horses. A CT scan provides 3D imaging of a section of the horse's body. This type of imaging provides more information about bony structures compared to standard radiographs and with contrast injection, can also be used to image soft tissue structures. The standing CT scanners now available have the same high resolution as previous CT scanners that were only available for use under general anesthesia. Additionally, these new standing CT scanners can be safely used to obtain 3D imaging of the horse's limbs from the level of the carpus (knee) and tarsus (hock) down through the foot.

In addition to standing CT, positron emission tomography scan is becoming available in horses, which can also be performed in the standing horse. PET allows functional information about bone and/or soft tissue structures within the scanned area, which can indicate if an imaging abnormality is currently active.

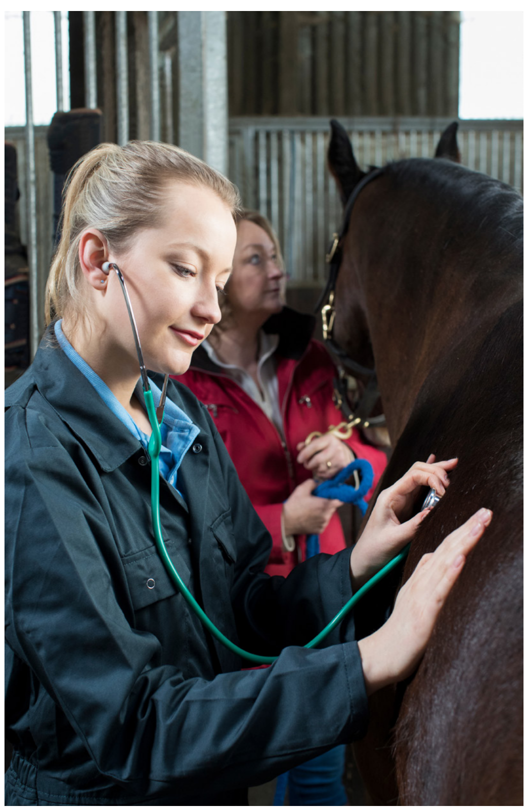
Maxwell H. Gluck
Equine Research Center
Lexington, Kentucky USA, 40546-0099
Telephone (859) 257-4757
Fax (859) 257-8542
gluck.ca.uky.edu

The PET scan is performed after a radioactive tracer is administered intravenously, similar to a bone scan. The PET scan is combined with another type of imaging (typically MRI or CT) so that the radioactivity can be matched up with specific anatomic structures.

These advances in lameness detection and localization will aid equine veterinarians in early identification of disease processes in horses, which will advance equine welfare, minimize catastrophic injury and prolong the athletic capabilities of horses.

Valerie J Moorman, DVM, MS, DACVS-LA, PhD
Clinical Associate Professor
Large Animal Surgery and Lameness
University of Georgia
College of Veterinary Medicine
Athens, GA

valerie.moorman@uga.edu



Equine neuroaxonal dystrophy / equine degenerative myeloencephalopathy

Equine neuroaxonal dystrophy (eNAD) and equine degenerative myeloencephalopathy (EDM) have become some of the most common postmortem diagnoses in neurologic horses in the United States. They are two diseases that can have identical clinical signs, with both conditions involving degeneration of the central nervous system. They are distinguished by the location within the central nervous system that this degeneration occurs, as eNAD affects the brainstem (specifically the medulla), and EDM affects the spinal cord in addition to the brainstem.

The clinical signs associated with eNAD/EDM can be variable, but most commonly involve an element of proprioceptive ataxia (incoordination of limbs), and, described more recently, signs may also be accompanied by behavior changes. The ataxia is typically symmetric and often has a slower onset, as opposed to beginning suddenly. The severity of the ataxia is most often mild-to-moderate. The behavior changes observed can range significantly from the horse seeming more quiet-to-dull, all the way to a horse that is extremely excitable and not one the owner or trainer can claim to behaviorally recognize. Many owner accounts describe a “switch flip” in such horses. The behavior changes may be noted under saddle and/or when handling the horse on the ground. In some cases, descriptions of changes in herd behavior, inter-horse aggression or bouts of unpredictability and explosivity have been reported.

Reasons for the development of eNAD/EDM are not fully understood, but may involve a variety of genetic, nutritional and/or environmental factors. The disease can affect many breeds and a variety of ages. While younger horses (less than 12 months old) were historically the classic age-of-onset description, more recently at the author’s institution, 5-15 years of age and predominantly Warmblood breeds seem overrepresented (unpublished data). Data suggest that deficiencies in antioxidant vitamin E may play a role in the development of eNAD/EDM, but the underlying mechanisms remain to be fully understood. Some horses that are diagnosed with eNAD/EDM have low blood vitamin E levels, but it is also possible that the vitamin E deficiency associated with the disease could have occurred early in the horse’s life or development, even if their blood levels are normal at the time of evaluation. Research is ongoing to better understand this aspect of eNAD/EDM.

Unfortunately, at the time of this publication, eNAD/EDM does not have an available, definitive diagnostic test that can be performed in the living horse to confirm its presence. eNAD/EDM can only be diagnosed postmortem via microscopic evaluation of the brain and spinal cord by an experienced pathologist. This means that eNAD/EDM is a "diagnosis of exclusion" in the living horse. Put simply, we are tasked with trying to ensure that there are no alternative diseases that may be contributing to the clinical signs of concern. In horses that we suspect have eNAD/EDM, if we are able to "rule out" these alternative diseases through diagnostics and observations, we are left with an increased suspicion of eNAD/EDM which we then term our "working diagnosis" until it can be confirmed postmortem.

The clinical signs observed in horses with eNAD/EDM are often similar to those seen in other neurologic conditions; ataxia is commonly attributable to cervical vertebral stenotic myelopathy (CVSM, colloquially known as Wobblers), or equine protozoal myeloencephalitis (EPM), two conditions which are also frequently diagnosed in neurologic horses in the United States. Determining if a horse has CVSM is best approached using imaging (radiographs, myelography, computed tomography). Determining if a horse has EPM or other infectious diseases is most comprehensively approached through analysis of cerebrospinal fluid (CSF) and blood, where CSF is obtained through a spinal tap. Importantly, other causes of unpredictable and abnormal behavior as well as gait abnormalities should be considered (i.e. musculoskeletal sources of pain, like lameness, back pain or muscle diseases; equine gastric ulcer syndrome, among other sources of discomfort and reactivity). Your veterinarian will use a combination of history and examination findings to determine the most likely possibilities and formulate an appropriate diagnostic plan.

If alternative sources for the ataxia and behavior change in eNAD/EDM suspect horses have been ruled out, horses with this working diagnosis have a variable prognosis. Some horses will stabilize in their ataxia and/or behavior abnormalities for months-to-years without progression. Still others will progress in their signs. Recommendations are made based on the severity of disease and are generally limited. Depending on risks to safety of the horse and/or his handlers, a tailored exercise plan may be recommended or the horse may need to be retired from riding. Those horses with severe clinical signs may pose a safety hazard to themselves or their handlers and ultimately require euthanasia. In conclusion, eNAD/EDM is a frustrating spectrum of chronic neurodegenerative disease currently without antemortem confirmatory diagnostics, making it challenging for the horse, the horse's connections and veterinarians alike. Research is ongoing into understanding the pathophysiology, diagnostics and, hopefully, eventual treatment and prevention options for these diseases.

Sarah F. Colmer, VMD, DACVIM
Fellow, Large Animal Neurology
Penn Vet New Bolton Center
University of Pennsylvania
School of Veterinary Medicine
Kennett Square, PA

Colms@vet.upenn.edu
610-444-5800

Why do we need genomes and how do we use them?

For centuries, horse breeders have chosen to mate specific sires and dams based on information in pedigrees and traits that they find desirable within them. The goal of pedigree analyses, and the resulting breeding pair selection, is production of successful offspring through the propagation of beneficial genes. Although this has worked well, there are problems associated with breeding within a closed book that will not be well managed by pedigree analyses. For example, genes associated with disease may be selected for when linked to desirable traits. Additionally, inbreeding may result in important copies of genes being removed from the population.

The first reference genome for the horse was published in 2007. Since then, the equine research community has been able to use this resource to catalog genetic variants (called alleles) that occur in the horse and measure their frequencies across breeds. This has been a powerful tool for identifying disease-causing genetic variants. Additionally, animals who are carriers can be identified and therefore the passing of these alleles to the next generation can be managed.

Inbreeding is a practice used to “fix” gene alleles that produce the most desirable traits, removing the copies of the genes that don’t produce the trait. It is how we create breeds with distinguishing characteristics. However, there is a chance that animals can become too inbred, and that many important genes with benefits that are not as obvious are also purged, resulting in an unexpected increase in less fit animals in the population.

An inbreeding value quantifies exactly how much genetic diversity an animal has inherited. This number can be calculated exactly with genetic data. Inbreeding values derived from pedigrees however are not going to be as accurate. Excluding the sex and mitochondrial chromosomes, a foal will inherit exactly half of its genomic content from its sire, and the other half from its dam. What is inherited from the respective grand-sires and grand-dams is going to be roughly 25%, but not exactly. This inaccuracy makes pedigree based inbreeding calculations unreliable for an animal, and by extension for the population. By performing whole genome sequencing on an animal and quantifying the density of homozygous regions of the genome (regions inherited from each parent that are identical at the nucleotide level), the actual measure of inbreeding can be assessed. Once measured, a rate of change for inbreeding can be monitored. Although a so-called tipping point for inbreeding, i.e., when genetic diversity becomes too low to maintain a healthy population is almost impossible to assess, changes of rate of inbreeding can be easily measured and changes in that rate can be addressed.

Likewise, when a seemingly inherited trait emerges, whether negative or positive, genome sequencing is the best tool for identifying the gene alleles associated with, and perhaps responsible for, that trait. This is not to say that it will easily provide the answers, as many traits are genetically complex in nature, but it is the best approach for analyzing the genetics of an animal or population to gain an understanding of the underlying genetic cause.

Having a reference genome and being able to inexpensively look at an animal’s genetic composition is by no means a complete solution to the genetic problems that affect horse health. They are, however, essential components among the resources we need to understand the genetic basis of health and wellbeing in these animals.

Ted Kalbfleisch, Ph.D.
Associate Professor
Department of Veterinary Science
Gluck Equine Research Center
University of Kentucky
Lexington, KY 40546-0099

ted.kalbfleisch@uky.edu
1-502-424-7795