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EQUINE DISEASE QUARTERLY

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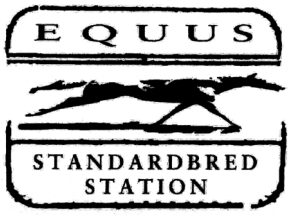

COMMENTARY

Breeders in the northern hemisphere are anxiously awaiting the upcoming foaling season and the potential arrival of a future Triple Crown winner, or second Totilas. Foaling is the culmination of 11 months of preparation involving a team of the mare's owner, stud farm personnel, and veterinarians, who have supported and navigated the mare through pregnancy. This often involves carefully monitoring the fetal-placental unit, which maintains an intricate balance involving nutrients, oxygen, and waste products between the foal and the mare's uterus. This complicated interaction steers and regulates fetal growth and development. Any disturbance can affect fetal growth and development and may result in abnormal behavior, adaptation, or configuration. These abnormalities are often observed in the first minutes or hours after birth and dictate the need to closely observe the mare prior to and during parturition and the foal within hours after birth.

A foal born under normal circumstances should function with the precision of a Swiss wristwatch. Within minutes after parturition, the foal should exhibit a righting response, in which the foal maneuvers into a sternal position, and attempts to get up on its spindly legs in quest of the dam's teat(s) and udder. The foal should stand within an hour of birth and suckle within two hours. This is succeeded by a routine of sleeping, getting up, stretching, suckling, passing urine (and feces), exploring, and then sleeping again. Any deviation from this routine, subtle or profound, can be a sign of developmental abnormalities. Poor nursing can lead to decreased colostrum or milk consumption and inappropriate swallowing that can result in milk aspiration into the lungs due to fatigue of the pharyngeal musculature. Inability to stand or a lack of strength results in an increased ground/floor contact that increases the risk of infection from the environment. As soon as abnormal behavior is noted, a reason for the abnormality should be identified and appropriate intervention initiated. Tendon laxity or limb contracture will make it difficult for a foal to stand or ambulate. This is not a generalized illness. Conversely, sepsis (as discussed by Dr. Christie in this issue) carries the risk of infection and inflammation in many organ systems.

Importantly, a poor start is not the end of the foal's career. Mild abnormalities may only need a little jumpstart by experienced farm personnel and an expedited examination by a veterinarian. More severely affected foals often require referral to a veterinary hospital and placed under intensive care. The sooner a foal is referred, the better the outcome. All foaling units should be prepared for complications and have a plan in place to rapidly transport the mare and foal to a veterinary hospital. Transportation should include a warm, dry space for the foal and ample space for the broodmare.

CONTACT:
Lutz S. Goehring DVM, MS, PhD
l.goehring@uky.edu
Maxwell H. Gluck Equine Research Center
University of Kentucky
Lexington, Kentucky

University of Kentucky
College of Agriculture, Food and Environment

REMINDER: This is the final printed Equine Disease Quarterly publication you will receive. Visit https://tinyurl.com/EDQemail to enroll in our electronic publication, or scan the QR code. If you have already responded with your e-mail address, please be aware that we are still receiving responses and are continuing to update.

Third Quarter 2021

The International Thoroughbred Breeders Federation, International Collating Centre, Newmarket, United Kingdom, and other sources reported the following equine disease events.

African horse sickness was reported as endemic in the Republic of South Africa (RSA). One case was confirmed in Gauteng Province.

Canada, the UK and the USA recorded equine influenza. The number of outbreaks ranged from one (Canada), three (the UK), to single or multiple outbreaks in 23 states in the USA, where the disease is endemic.

Outbreaks of strangles were reported by Belgium (one), France (22), Germany and the Netherlands (two apiece), Switzerland (five) and the USA (25), where the disease was diagnosed in eight states and is considered endemic.

Equine herpesvirus 1 (EHV-1) respiratory disease is endemic in most countries. Infection was confirmed by Germany (two outbreaks), the RSA (nine cases involving outbreaks on three premises), and the USA (one outbreak).

Outbreaks of EHV-1 abortion were reported by Germany (one) and the USA (two), all represented by individual cases. Cases of EHV-1 neurologic disease were confirmed by Argentina (four on one premises), Canada (one), Germany (two outbreaks, one involving five cases), the RSA (one of nosocomial infection), and the USA (six outbreaks, one involving several animals that had attended a show and the remainder by individual cases).

Equine herpesvirus 4 (EHV-4) respiratory disease was recorded by France, Germany, Italy, the Netherlands, RSA, and Switzerland. The number of outbreaks ranged from one (Italy, RSA), two (Germany, the Netherlands, and Switzerland) to four (France). The majority of outbreaks involved a single case.

The USA reported cases of infection with equine herpesvirus-2 and -5 (EHV-2/EHV-5). EHV-2 (18) and EHV-5 (25) infections were diagnosed in five states, some associated with respiratory disease.

Infection with equine arteritis virus was recorded by France. A three-year-old colt and a stallion were involved.

The USA diagnosed 11 single cases of *Rhodococcus equi* related respiratory disease.

Equine infectious anemia was confirmed by Canada, Italy, and the USA. The number of outbreaks varied from three (Canada), six (USA), to eight (Italy). The majority of outbreaks comprised single cases. The outbreaks in the USA involved American Quarterhorses in Texas and feral horses in Utah.

Equine piroplasmosis was reported by Japan (single clinical case of *Theileria equi* infection at the Olympic Games in Tokyo) and the RSA. The disease is considered endemic in the RSA, with a total of 38 cases confirmed in five premises, of which 26 were recorded in Gauteng Province.

Multiple outbreaks of contagious equine metritis (CEM) were recorded by Germany, three had two cases each, and the remaining 10 had a single case. Six of the outbreaks involved stallions, and seven outbreaks involved mares.

The USA reported a case of equine coital exanthema (equine herpesvirus 3) and single cases of leptospiral abortion and renal disease in Kentucky.

The USA also diagnosed 20 cases of *Salmonella* infection involving serogroup B and five cases of untyped *Salmonella* spp.

Clostridial enterocolitis associated with *Clostridium perfringens* was reported by Switzerland (one case). The USA recorded 11 cases of *C. perfringens* and three cases of *Clostridiodes difficile*, the majority in Kentucky.

The USA confirmed nine outbreaks of *Neorickettsia risticii* infection involving four states.

Rotavirus diarrhea in foals was reported by France (six outbreaks, primarily single cases) and the USA (two cases of rotavirus Type A infection).

One case of rabies was confirmed in Montana, USA. This marked the 12th case in the state in 2021.

Canada and the USA recorded cases of eastern equine encephalomyelitis (EEE). Five outbreaks were diagnosed in Canada and 28 in the USA. With two exceptions, the outbreaks consisted of single cases. The majority of cases were in unvaccinated horses.

Outbreaks of West Nile encephalitis were reported by Canada (three), Germany (seven), Italy (two, one involving lineage 2 virus), Portugal (three), Spain (six), United Arab Emirates (one), and the USA (58 cases in 15 states).

Equine encephalosis is considered endemic in the RSA, and two cases were confirmed in the Western Cape Province.

Three cases of equine protozoal myeloencephalitis were diagnosed in Kentucky, USA.

Kazakhstan, Spain and the USA reported cases of anthrax. The disease affected horses, cattle and sheep on a farm in Kazakhstan. Of 115 horses, 10 developed disease and nine died. Three cases were confirmed in Spain and one in Texas; the latter represented the third case in Texas in 2021.

Switzerland diagnosed three outbreaks of intercurrent anaplasmosis and ehrlichiosis in separate Cantons.

EQUINE DISEASE QUARTERLY

EDITORS
Alan Loynachan
Rebecca Ruby
Lutz Goehring

STAFF
Tawana Brown

EDQ@uky.edu

Whole Genome Sequencing in 101 Thoroughbreds

Breeders have always used pedigrees to manage the genetics of Thoroughbred horses. Pedigree analysis is firmly rooted in our understanding of classical, Mendelian genetics. However, pedigrees only track relationships. The actual genetic variation present in any animal can only be assessed by reading the DNA itself. In 2006, the whole genome sequence of the horse was first reported. It was an expensive undertaking, but since then the costs of doing this work decreased dramatically such that sequencing the whole genome of a horse is a routine activity in research laboratories. The DNA sequence contains information about the extent of genetic variation, relationship to other horses, relationship to other breeds, levels of inbreeding and can even provide raw material for discovery to potentially deleterious genes that interfer with the success of the breeder.

On August 6, 2021, Teruaki Tozaki and colleagues from the Laboratory of Racing Chemistry and Japan Racing Association published a landmark paper describing whole genome sequencing of 101 Thoroughbreds in Japan (https://nature.com/articles/s41598-021-95669-1). While scientists have been identifying DNA variation in short regions for the last three decades, this study is unique in that these scientists collected data on all 2.41 billion DNA nucleotides of the 101 horses.

This work provides a baseline for comparison of different populations of Thoroughbreds as well as a benchmark to assess changes over time. In addition, we can compare the variation found in this study to variation found in other breeds. Jagannathan and colleagues (2019 *Anim. Genet.* 50, 74–77) sequenced the whole genomes of 88 horses of diverse breeds including Warmblood, Standardbred, Quarter Horse, Arabian, Morgan, Franches-Montagne, Paint, Icelandic, Shetland, Akhal-Teke, Noriker, Welsh ponies, and one Thoroughbred. The two studies were similar in design, so we can directly compare their results such as those shown in Table 1.

The total numbers of single nucleotide variants (SNVs) found in the Jagannathan study was almost twice as large as those found in the Tozaki study. This illustrates the great amount of diversity existing among horses of all breeds. However, when we examine the number of SNVs found in each horse (Max-Min), Thoroughbred horses fall within the range for the diversity of breeds. Specifically, while the Jagannathan study reported a range of 4.4 million-6.6 million SNV per animal, the Thoroughbred counts fall within that range, 4.8 million-5.3 million.

Two technical caveats bear mentioning here. SNVs are just one type of DNA variant. Other types of variants exist, including DNA insertions, deletions, and repeats. Therefore, the total number of variants including those in other categories is certainly greater than the number of SNVs reported. Another—and perhaps very consequential—caveat is that the number of SNVs were determined through comparisons with reference to the genome of a Thoroughbred mare (the equine reference genome). If we were to use a different breed as a reference, say a Shire horse, we will see a larger number of variants for Thoroughbred horses when compared to this new reference, but less for Shires.

Regardless of how we count the variants these results suggest that the amount of variation found among Thoroughbreds is not exceptionally depleted when compared to the range of variation among other horse breeds.

Arguably, some of the most important outcomes of this study are yet-to-be generated products of these data. For instance:

- The information serves as a baseline of diversity to assess and model/predict changes in the future population resulting from current and evolving breeding practices.
- The 12.1 million genetic variants identified among these 101 Thoroughbreds can be assessed to determine which may cause fitness problems, and those desirable for health and racing performance.
- These data can be applied to assist in detecting inappropriate modifications of DNA, called gene doping, done in order to enhance racing performance.

CONTACTS:
Ernest Bailey, PhD
ebailey@uky.edu, (859) 218-1105
Maxwell H. Gluck Equine Research Center
University of Kentucky, Lexington, Kentucky

Ted Kalbfleisch, PhD
ted.kalbfleisch@uky.edu, (859) 218-1147
Maxwell H. Gluck Equine Research Center
University of Kentucky, Lexington, Kentucky

Jessica Petersen, PhD
Jessica.petersen@unl.edu, (402) 472-6328
Department of Animal Science
University of Nebraska-Lincoln, Lincoln, Nebraska

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

Table 1. Comparison of the number of single nucleotide variants (SNV) among horse breeds in two studies.

Study	# Horses	Total # SNV	Range of SNV/Horse	Average # SNV/Horse
Tozaki *et al*. 2021	101 Thoroughbreds	12.1M	4.8M-5.3M	5.1M
Jagannathan *et al*. 2018	88 from Diverse Breeds	23.5M	4.4M-6.6M	5.9M

Eight Tips for Equine Winter Care

Caring for horses in winter can be challenging. Horses may need additional feed, water, and close monitoring of body condition. Additionally, changes in exercise routines, hoof care and blanketing are needed. As conditions become icy, increased risk of injury can occur if paddocks and barn areas are not properly maintained. This article discusses eight key areas to focus on to help ensure the horse's needs are met during winter.

Water is important. Most adult horses need 10 to 12 gallons of water daily. During the summer months, pastures contain about 80% moisture and can contribute to your horse's water requirement. In contrast, dried hay contains less than 15% moisture, therefore, your horse will require more water in winter. To encourage drinking, keep your horse's water temperature between 45° to 65°F, regularly clean waterers, make sure tank heaters are in working condition, and check waterers for electrical sensations or shocks. Remember, snow and ice are not adequate water sources for horses.

Monitor feed intake. Lower critical temperature is defined as the temperature below which a horse needs additional energy to maintain body warmth. The lower critical temperature estimate for horses is 41°F with a summer coat and 18°F with a winter coat; however, younger horses may reach their lower critical temperature before a mature horse. For every degree below 18°F the horse requires an additional 1% energy intake in their diet to help maintain body temperature and condition. The best source of additional dietary energy is silage, frequently grass that is fermented by microbes which produce heat and keep the horse warm. Other nutrient requirements don't change during cold weather.

Track body condition and weight. During winter months, heavy hair coats can hide weight loss or gain. Body condition and weight should be assessed monthly to help track horse health and to note purposeful or unwanted changes. Body weight can be tracked using weight tapes, the Healthy Horse mobile device application, or mathematical equations that use various body measurements.

Blanketing a horse is necessary to reduce the effects of cold or inclement weather when shelter is not available during turnout periods; temperatures or wind chill drop below 5°F; and when the horse has become wet, had its winter coat clipped, is very young or very old, isn't acclimated to the cold, and/or has a body condition score of three or less. Make sure blankets fit, because poorly fitted blankets can cause sores and rub marks. Remove the blanket daily, inspect it for damage, reposition it, and make sure it stays dry.

Provide access to shelter. In the absence of wind and moisture, most horses tolerate temperatures at or slightly below 0°F. If horses have access to shelter, they can tolerate temperatures as low as -40°F. Researchers found that in mild winter weather, horses housed outdoors tended to use very little shelter. However, shelter usage increased to 62% when it snowed and wind speed was greater than 11 miles per hour. Although frostbite of the ears is uncommonly reported in horses, there is the potential for it to occur under very adverse, sub-zero weather conditions.

Provide exercise with turnout, or as often as possible. One challenge with winter riding is the process of cooling down a horse with a winter coat. A hair clipping technique, known as a trace clip, can be used on regularly exercised horses to help speed the cooling process. However, clipped hair doesn't grow back rapidly in winter; therefore, use appropriate shelter and blankets throughout the winter and into the early spring months. Take caution when riding in deep, heavy, or wet snow to prevent tendon injuries and avoid icy areas.

Maintain regular hoof care. Horse hooves generally grow slower in the winter; however, trimming should still occur every 6 to 12 weeks. Horse hooves are prone to "ice or snowballs" during the winter. These balls of packed ice or snow make it hard for a horse to walk, increase the chance of slipping and falling, and put stress on tendons and joints. Make sure to pick your horse's hooves daily, especially after a heavy snow and consider fitting snow grips.

Keep paddocks in working order. Icy paddocks cause slips and falls that can lead to serious injury. Use sand to increase traction on ice, but don't feed horses near sand as they may accidentally ingest it. Straight salt can speed the melting of ice if temperatures aren't too cold. Research has not documented the effect of salt on horse hooves, but to be safe, use pure salt in moderation. Don't use a mixture of sand and salt in paddocks since horses may accidentally ingest the sand due to their interest in the salt. Additionally, a thin layer of wood ash or fresh manure can help improve traction. Avoid shavings, hay, and straw as they tend to slide over ice and provide little traction.

By paying attention to these eight areas, owners can provide a safe environment for their horses throughout cold weather months.

CONTACT:
Krishona Martinson, PhD
krishona@umn.edu
(612) 625-6776
Department of Animal Science
University of Minnesota, St. Paul, Minnesota

Equine Vertebral Column Pathology

As technology associated with advanced imaging and diagnostic modalities progresses, more attention is being given to equine vertebral column pathology. The vertebral column serves important roles in protection of the spinal cord and locomotion. Therefore, diseases that impact the vertebral column can have a significant impact on equine health and rider safety.

Equine submissions to the University of Kentucky Veterinary Diagnostic Laboratory over a 10-year period (2011-2021) were queried for diagnoses related to significant vertebral column pathology. A total of 426 cases were identified. Distribution of diseases included equine cervical vertebral stenotic myelopathy (n=224), fracture/subluxation (n=123), abnormal spinal curvature (n=51), osteomyelitis (n=13), intervertebral disk disease (n=7), congenital vertebral anomaly (n=5) and neoplasia (n=3).

Vertebral pathology associated with equine cervical vertebral stenotic myelopathy (wobbler syndrome) comprised the majority of cases. This is no surprise given the density of Thoroughbreds in the central Kentucky area and their documented breed predisposition to develop the disease. Wobbler syndrome occurs when malformation of the cervical vertebrae results in spinal canal narrowing and cervical spinal cord compression. In general, wobbler syndrome is categorized as affecting two groups of horses. The first being young, growing horses with complex multifactorial interactions between gender, growth rate, diet and genetic determinants. The second group is seen in older horses with age related changes in the neck, mainly osteoarthritis. In this retrospective, males were more commonly affected (male n=182; female n=34), the average age was 23.1 months (4 months-168 months) and Thoroughbreds were the most common breed (n=165). Vertebrae are classified as irregular bones due to their complex shape. Therefore, changes in different locations of the bone itself can result in spinal cord compression. Articular process joint lesions were the most frequent cause of spinal cord compression (n=71) followed by subluxation of the vertebral body (n=67), generalized narrowing of the canal (n=27) and thickening or elongation of the dorsal lamina (n=13). Articular process lesions were largely due to osteoarthritis, followed by osteochondrosis.

The cervical column was the most commonly reported site of fracture/subluxation (n=69), with the vertebral body being most frequently affected. In eleven cases, partial spinal cord transection was described. While a clinical history of trauma was reported in all identified cases, six cases had evidence of underlying neurologic disease (wobbler syndrome or equine protozoal myeloencephalitis).

Acquired spinal curvature disorders (i.e., scoliosis, lordosis, or kyphosis) were identified in 51 cases, with 50 considered congenital and one case of acquired scoliosis. Of the congenital cases, 71% had other skeletal abnormalities including limb contracture or facial malformations. Dystocia was described in 66% of the submitted histories. The thoracic column was the most common location (n=27) followed by the lumbar column.

All vertebral osteomyelitis cases occurred in horses under one year of age. The lumbar vertebrae were the most frequent location. *Rhodococcus equi* and *Streptococcus zooepidemicus* were common bacterial isolates. Secondary pathologic fracture was noted in six cases.

Clinically significant intervertebral disk disease is a more recent area of interest. In this review, intervertebral disk disease cases exhibited yellowing of the disk material with varying degrees of fibrillation, clefting and loss. All cases had a clinical history of ataxia. Secondary spinal cord compression was noted in four cases.

Of the remaining disease categories, congenital vertebral anomalies included cystic vertebral body or vertebral fusion. Neoplastic processes impacting the vertebral column included primary vertebral body sarcoma, metastatic lymphosarcoma and metastatic melanoma.

A variety of disease processes can impact the equine vertebral column. Pathologic evaluation of the equine vertebral column in conjunction with clinical information will continue to help better our understanding of these processes and their impact on equine health.

CONTACT:
Jennifer Janes, DVM, PhD, Dipl. ACVP
jennifer.janes@uky.edu (859) 257-8283
University of Kentucky Veterinary Diagnostic Laboratory
Lexington, Kentucky

Sepsis in the Newborn Foal

The newborn foal is a remarkable animal, born with the ability to stand and run within hours of birth. Despite this, they are more at risk than adult horses for certain medical conditions, including sepsis. Sepsis is a major cause of illness and death in newborn foals and is caused by overwhelming inflammation in response to invasion of the bloodstream by bacteria. The septic foal is also at risk for infection at specific locations in the body, including the lungs, joints, growth plates, gastrointestinal tract, and central nervous system.

Unlike people, foals do not receive antibodies from the mare during gestation. They rely on absorption of antibodies from the mare's colostrum—the first milk that is produced following birth. Colostrum is rich in antibodies, which are absorbed across an "open" gut in the first twelve hours of the foal's life. These antibodies help provide protection against infection until the foal begins to make antibodies of its own. This open gastrointestinal tract leaves them more susceptible to infection as bacteria can move from the GI to the bloodstream. Other potential sites of infection include the respiratory tract, umbilicus, and dam's reproductive tract during gestation.

The biggest risk factor for sepsis is failure to receive enough antibodies from colostrum within the first 12 hours of life. This can be due to the foal not standing and nursing appropriately, or production of poor-quality colostrum by the mare. Failure of passive transfer (FPT) can be detected by your veterinarian and is one of the most important reasons to have newborn foals evaluated during the first 24 hours. A blood sample can be used to measure antibody or IgG as a marker of antibody transfer. FPT can be partial or complete, and both can leave the foal susceptible to infection. Additional risk factors include maternal illness, prematurity, and poor environmental conditions. Foals that experience FPT can receive alternate sources of antibodies; intravenous plasma transfusion is the most common and can be provided by your veterinarian, if needed.

As with most foal diseases, the sooner treatment is initiated, the better. Early detection of clinical signs and rapid intervention are key. Any foal not standing within an hour of birth and nursing well within two hours of birth should be immediately evaluated by a veterinarian. Initial clinical signs of foals that develop sepsis can be mild and non-specific including decreased nursing, lying down a lot, and diarrhea. The foal's gums and whites of the eyes (Figures 1 and 2) may become bright red, and the foal may have a fever or abnormally low temperature. Limbs and ears may be cool to the touch and the foal may become unable to stand as the illness progresses to septic shock (Figures 3 and 4).

Treatment of septic foals is often intensive and can require hospitalization in severe cases. Antibiotics are the mainstay of treatment, and a broad-spectrum approach is essential at onset to treat for common bacterial culprits. Longer courses of antibiotics may be necessary in foals that develop localized signs of infection. Intravenous fluids and a nutritional plan are also important aspects of treatment in severe cases. Good nursing care is essential for successful treatment in these patients as they are often unable to stand; unable to handle enteral feeding including difficulties with swallowing, and are prone to urine scald and bed sores.

Survival rates have improved with advancements in treatment and are reported to be as high as 72% at discharge. Factors associated with decreased survival rate include duration of illness prior to admission, inability to stand at presentation, severity of clinical signs, and certain blood work abnormalities. The development of infection of one or more joints can also decrease overall survival rates in these foals.

Prevention can be the most important aspect of ensuring health of newborn foals and includes maintaining a clean foaling environment, ensuring adequate nursing of good-quality colostrum, treating the umbilicus appropriately, and having your veterinarian evaluate your foal within 24 hours of life. None of these can completely eliminate the risk of sepsis – early recognition of illness and rapid treatment by your veterinarian is essential for a good outcome.

CONTACT:
Katharine Christie, DVM, MS, DACVIM
kchristie@roodandriddle.com
(859) 233-0371
Rood and Riddle Equine Hospital
Lexington, Kentucky

Figure 1. Injected mucous membranes in a hospitalized foal—abnormal coloration of the mucous membranes is a common clinical sign associated with sepsis.

Figure 2. Injected sclera (whites of the eye) can be an early sign of sepsis in young foals.

Figure 3. Septic foals are often excessively lethargic and can be unable to stand without encouragement and assistance. Good nursing care is an essential part of treatment.

Figure 4. Neonatal foal showing abnormal behavior and response to stimulation.

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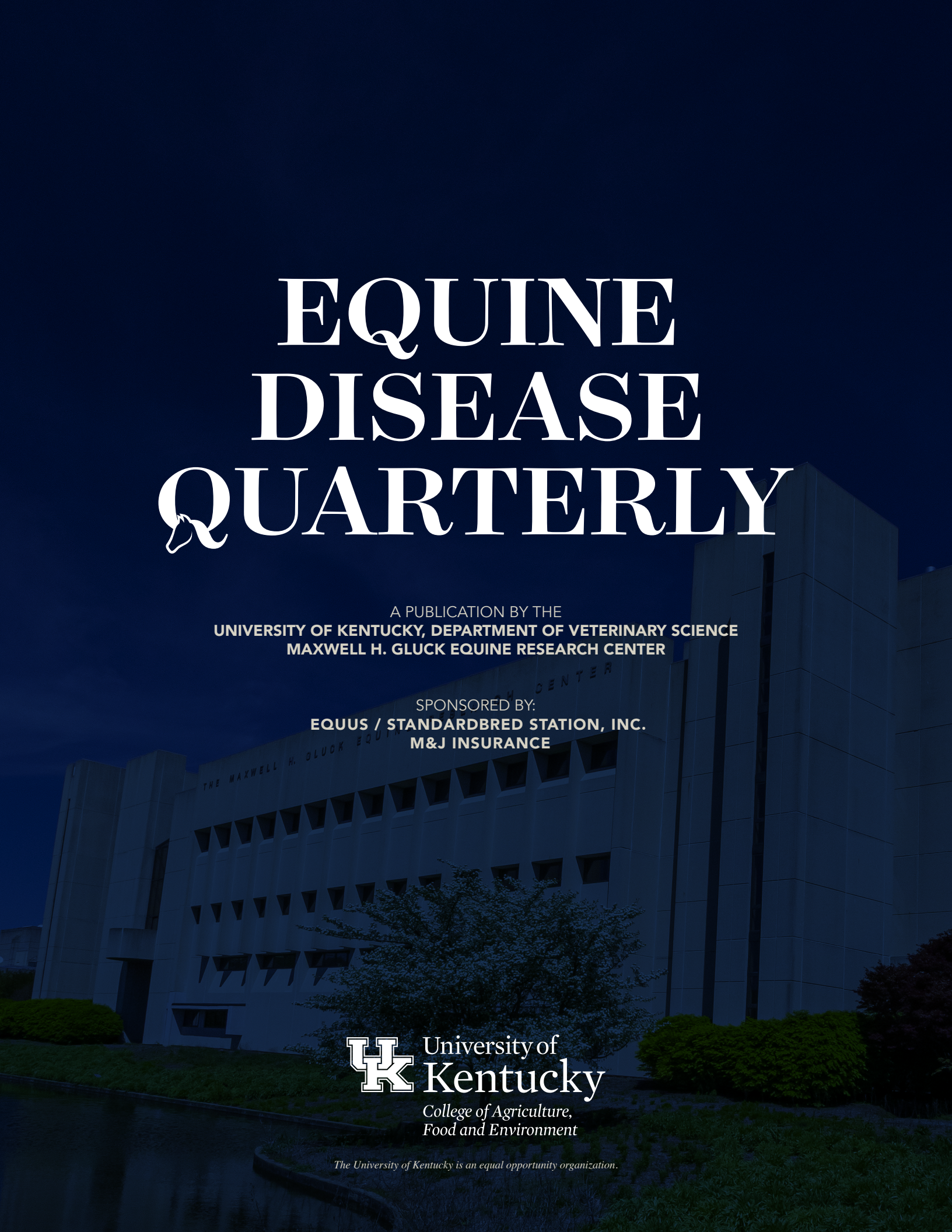

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