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EQUINE DISEASE QUARTERLY

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RESEARCH SPOTLIGHT

Evaluating the impact of CBD on equine joint inflammation

Joint pain and osteoarthritis (OA) represent one of the leading causes of performance loss in equine athletes, affecting around 60% of the overall population. Chronic inflammation may cause permanent changes in joint function, leading to long-term pain, swelling and decreased range of motion, among other debilitating symptoms.

Many of the current OA treatments are management tools that prolong function, generally without modifying OA progression. The most common treatments include non-steroidal anti-inflammatory drugs (NSAIDs) and oral joint supplements that target cartilage repair or protective pathways, as well as joint injections with corticosteroids or newer orthobiologics, both of which are anti-inflammatory. Unfortunately, many of these treatments are associated with other adverse effects, especially when used long-term.

Several novel treatments to reduce joint inflammation with minimal side effects have been proposed within the scientific community. One such treatment is cannabidiol (CBD), a non-psychoactive chemical compound found in *Cannabis sativa* (colloquially known as hemp). CBD is known to target the endocannabinoid system, a complex network of several biological systems that affects many physiological processes, including but not limited to, pain perception, appetite, mood, learning and immune function. Within the context of OA, CBD has been found to inhibit the production of substances that increase inflammation, decrease sensitivity of pain-associated receptors and modulate an overactive immune system. Anecdotally, many people claim the benefits of CBD, but more research is required to accurately quantify and qualify its potential benefits and risks. This is especially true within the equine community.

Our work in the Page Laboratory is interested in understanding the potential anti-inflammatory effects of CBD in joints via the implementation of a three-phase project. We aim to improve a chemically induced joint inflammation model such that it will be repeatable and reversible, while still accurately mimicking the body's physical and biochemical response to inflammation.

Phase one involves refining the dosage of a pro-inflammatory compound which will be injected into one knee (carpal) joint, inducing temporary inflammation. Defining an appropriate dosage protocol and taking note of individual horse variability is an important step for developing a reliable experimental procedure.

Following phase one, the aim of phase two is to identify an appropriate CBD formulation for oral administration. Due to its chemical composition, CBD is not well absorbed by the equine GI tract, with a bioavailability around 10% (e.g. horses will only absorb about 10% of the CBD administered to them). Previous research has found what a drug is dissolved in can make a large difference in systemic CBD levels, and the most effective candidates are usually composed of fats, such as sesame or canola oil. An optimized formulation is necessary to both maximize therapeutic benefit while keeping palatability in mind for horses.

In phase three, we will combine the findings from the first two phases and analyze the effects of CBD on the drug-induced inflammatory response. A control group will receive no CBD, and the differences between the treated and untreated group will be evaluated. Horses will be evaluated for several parameters, including the presence of biomarkers associated with inflammation both within the joint and systemically throughout the body. The mild lameness that is induced will be quantified via an objective evaluation system that can better detect the subtleties of gait asymmetries when compared to the human eye.

While other researchers have shown that CBD represents an exciting prospect for the treatment of chronic joint pain, our research should provide additional information on its efficacy for the horse. Our findings may find applications for human medicine given the mechanisms of OA and joint pain in humans often mimic those seen in horses, which is important given that approximately 45% of people will develop some form of OA within their lifetimes. In the end, we hope to provide a better research model for joint inflammation while simultaneously evaluating CBD as a way to manage joint pain in horses.

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Tick-Borne Diseases of Concern in U.S. Horses

Spring has officially sprung in Kentucky with flowers in full bloom and the horses off to the races! While we may be excited to get outdoors and enjoy the sunshine after a long winter, the warm weather also draws out other critters… ticks. Often overlooked compared to mosquito-borne pathogens, ticks are capable vectors of several equine diseases and can cause adverse effects ranging from local irritation to acute and chronic disease. Proactive tick management is an essential component of equine preventive care, particularly as many regions continue to report increased numbers of tick bites and changes in tick species distributions.

In the United States, notable tick-borne diseases affecting horses include:

- Equine Granulocytic Anaplasmosis (*Anaplasma phagocytophilum*) – most commonly observed signs of infection include fever, lethargy, limb edema and ataxia. In equines, *A. phagocytophilum* is most commonly transmitted by the blacklegged tick (*Ixodes scapularis*) in the Northeast, Midwest and parts of the Southeast, but may be transmissible by the Western blacklegged tick (*Ixodes pacificus*) on the West Coast.
- Lyme Disease (*Borrelia burgdorferi*) – although horses are less susceptible than dogs or humans infection can result in chronic weight loss, shifting lameness, behavioral changes, and neurological signs. This disease can be difficult to diagnose in equines, as a positive blood test indicates exposure to the pathogen but not necessarily current disease status. Lyme Disease is also transmitted by *I. scapularis.*
- Equine Piroplasmosis (EP) – caused by *Babesia caballi* and *Theileria equi*. This disease is reportable in the mainland U.S., but endemic in Puerto Rico and the U.S. Virgin Islands. Transmission can occur through tick bites (most commonly from *Dermacentor* or *Rhipicephalus* spp.), but most U.S. outbreaks or reports of disease are associated with iatrogenic transmission from contaminated equipment during unsanctioned racing events or through illegal importation of infected Quarter Horse racehorses.
- Tularemia (*Francisella tularensis*) – a rare tick-borne zoonotic disease in horses, associated with *Dermacentor* spp. and *Amblyomma* spp. ticks. This pathogen can be transmitted through bites from fleas and flies and through contaminated water sources, but is most commonly associated with tick bites. While rare in horses, it is of veterinary and public health significance due to its ability to persist in the environment, multiple modes of transmission and zoonotic disease potential.
- Tick Paralysis and Hypersensitivity – Toxins in tick saliva may cause neuromuscular dysfunction or localized inflammatory responses in sensitive animals.

Emerging Tick Species: Asian Longhorned Tick

The Asian longhorned tick (*Haemaphysalis longicornis*) is an invasive species that has been detected in numerous U.S. states along the East Coast and Appalachian Mountains, including Kentucky, where it has been detected on wildlife, cattle, equines, dogs and people.

- It reproduces asexually via parthenogenesis, enabling rapid population growth and large infestations, particularly on livestock.
- This tick has been documented on horses in the U.S., although no confirmed cases of equine disease have been associated with it.
- Internationally, *H. longicornis* can transmit pathogens of veterinary and medical concern, causing diseases such as anaplasmosis, babesiosis, ehrlichiosis, theileriosis and rickettsiosis.
- Its ability to cause anemia and death in cattle raises concern for similar effects in heavily infested horses, particularly if infestations go unnoticed, though such cases have not yet been reported.
- As horses can develop hypersensitivity reactions to tick and other arthropod bites, even mild infestations of *H. longicornis* could exacerbate stress, pruritus and allergic dermatitis, affecting welfare and performance even in the absence of pathogen transmission.

Asian longhorned tick. Photo by James Gathany, CDC

EQUINE DISEASE QUARTERLY

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Most Common Equine-Associated Tick Species in the U.S.

- *Amblyomma americanum* (lone star tick)
- *Amblyomma maculatum* (Gulf Coast tick)
- *Amblyomma mixtum* (Cayenne tick)
- *Dermacentor albipictus* (winter tick)
- *Dermacentor andersoni* (Rocky Mountain wood tick)
- *Dermacentor variabilis* (American dog tick)
- *Haemaphysalis longicornis* (Asian longhorned tick)
- *Ixodes scapularis* (blacklegged tick)

Integrated Tick Prevention and Property Management

Most tick species tend to prefer habitats with shade, moisture and vegetation, including wooded edges, brush and tall grasses commonly found on or adjacent to horse properties, or along trail riding locations. To reduce equine tick exposure, there are environmental, behavioral and chemical strategies available to reduce the number of ticks on the property and reduce equine exposure to areas where ticks may be more common. This can include pasture and property management to reduce areas that are more likely to harbor ticks and reduce wildlife from bringing ticks onto the property. Integrated management also includes on-animal prevention strategies to reduce ticks from attaching to animals and removing ticks quickly when they do attach to animals.

Pasture and Property Management

- Mow and maintain pastures frequently to reduce habitat more likely to harbor ticks.
- Create buffer zones between wooded or brushy areas and paddocks.
- Remove brush, leaf litter and overgrown field margins.
- Exclude wildlife (e.g., deer, raccoons) via fencing or deterrents to reduce tick introduction and movement of disease-causing pathogens.
- Control rodents through exclusion and secure feed storage; rodents serve as reservoirs for immature ticks and several tick-borne pathogens.

On-Horse Prevention

- Perform daily tick checks, focusing on thin-skinned, less-visible areas such as ears, eyelids, muzzle, chest, belly, mane and tail. Full body tick checks are recommended after equines have been in areas where ticks may be more common, such as after trail rides in brushy habitat.
- Apply EPA-registered pyrethroid-based sprays labeled for equine use. Reapplication may be needed based on rainfall or sweat exposure and is typically only effective for short-term applications.
- Fly sheets or insect barriers may provide partial protection from both biting flies and ticks.
- Avoid off-label or overuse of pesticide products to prevent skin irritation or systemic absorption. Consultation with a veterinarian before application of on-animal chemical products is highly recommended.

When to Heighten Vigilance

- After trail rides or turnout in brushy or wooded areas.
- During peak tick activity months: spring through fall, although milder winters may support year-round activity in parts of the Southeast and South Central U.S.

Veterinary Role in Surveillance and Education

Veterinarians are well-positioned to contribute to equine welfare through owner and caretaker education on tick-borne diseases and bites and preventative approaches for tick and other arthropod-borne diseases and associated conditions. In many states, ticks can be submitted for identification through the state's Departments of Agriculture, Environmental Health or Public Health Departments, or through state Extension services. In Kentucky, suspected Asian longhorned ticks can be submitted through the University of Kentucky Cooperative Extension Service by bringing them to your county Extension office, mailing them to the Entomology Department through the contact information below or by contacting the Office of the State Veterinarian at statevet@ky.gov.

For identification of suspected Asian longhorned tick in Kentucky, please preserve specimens in ethanol or hand sanitizer (*without* additives like aloe), or in a ziplocked bag after freezing specimens (to kill ticks). Mail specimens to University of Kentucky Veterinary Entomologist, Dr. Hannah Tiffin, at the address below along with information on date of collection, host animal collected from, county of collection and follow-up contact information.

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Florescent ticks can be seen on this horse hoof as part of anti-tick research trials on horses conducted at Penn State University. Photo by Hannah Tiffin

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First Quarter 2025

International report on equine infectious diseases

This report collates information on equine infectious diseases provided by diagnostic laboratories in Lexington, Kentucky, the University of Kentucky Veterinary Diagnostic Laboratory (UKVDL), and Equine Diagnostic Solutions (EDS), Inc. We further included information from the International Thoroughbred Breeders Federation, the International Collating Centre (ICC) in Newmarket/Cambridge, United Kingdom, and information from the American Association of Equine Practitioners' Equine Disease Communication Center (EDCC). Some information became available by word-of-mouth and is likely incomplete or (yet) unconfirmed by official sources. We will provide updates accordingly.

Lexington and Kentucky

For the first quarter of 2025, nearly 200 aborted fetuses or stillbirths were examined by the UKVDL. Over 80% of the exams were conducted in Thoroughbreds, followed by Standardbreds. Two EHV-1 and two *Leptospira* spp. abortions were reported.

Approximately 50 foal diarrhea samples, analyzed by EDS, were found positive for Rotavirus B (Rota B) antigen. Rotavirus A (Rota A) antigen detection, so far, has been negative. We observed this in previous years, where Rota B had an early appearance in neonates, while Rota A appeared in older foals with waning colostrum derived immunity.

Few nasal swabs submitted to EDS were positive for EHV-4 antigen or *Strep. equi spp. equi* (Strangles). Equine Influenza positive samples have not surfaced in Kentucky.

North America

Across the continent there have been incidental Equine Influenza reports (Pacific Northwest, Wyoming, Florida) and numerous *Strep. equi spp. equi* (Strangles) reports.

An ongoing outbreak investigation on Contagious Equine Metritis (CEM) caused by the bacterium *Taylorella equigenitalis* in the United States is in a back-tracing phase (for more information please visit https://www.aphis.usda.gov/livestock-poultry-disease/equine/contagious-equine-metritis).
An Equine Infectious Anemia virus nidus has been detected in an endemic area of Canada, where 16 horses on a single farm have been found positive for virus-induced antibodies. Nineteen new cases on individual farms have been identified in Texas.

Arbovirus activities have decreased dramatically due to vector inactivity, and only a single case of West Nile virus (WNV) and a case of Eastern Equine Encephalitis virus has been reported from Florida (for more information on WNV, please find Dr. Long's article in this volume of the EDQ).

We believe that there is an underreporting of EHV-1 abortions, as the first and second quarter of a year typically corresponds with the third trimester of pregnancy, the most vulnerable period of EHV-1 abortion. For this quarter, we report a single EHV-1 abortion from Utah (in addition to two abortions from Kentucky). The first and second quarters of a year, winter and spring, are also heydays for neurologic EHV-1 (or Equine Herpesvirus-associated Myeloencephalopathy – EHM), and EHM is a reportable disease in many states and provinces. Therefore, it is not surprising that we report a total of 20 cases of EHM from across the continent, and north of the Gulf of Mexico. In addition, reports of EHV-1 respiratory disease that typically accompany EHM cases on premises have increased, too. The report summary on the EDCC diseases alert page (https://equinediseasecc.org/alerts) also lists the number of in contact animals, in case the information is provided. A frequent comment in the reports is that the EHM affected horse has not traveled during the past two weeks. As a comment and in our opinion, the index case with clinical signs of EHM is rarely the horse with a travel history but is more likely a horse exposed or in contact with those who traveled, either those who returned or were passing through. Furthermore, EHM is also the result of, at first, a respiratory tract infection with viral replication, and then followed by a cell-associated viremia (viral spread through the blood stream). An incubation period of one to two weeks between exposure and clinical EHM has to be taken into consideration. Alternatively, exposure to an EHV-1 abortion (fetus, fetal membranes and fluids) has been described as the initiating event of an EHM outbreak.

South America

While we do not routinely receive infectious diseases updates from the Southern Hemisphere, we received word on an EHM outbreak among polo horses in Chile. The venue has been described to us as a large training facility with several stable units and facilities on site. There were three horses in a first barn that showed clinical signs of EHM on Feb. 26, 27 and 28, respectively, that were admitted onto the premises a few days earlier. A swift diagnosis of EHM was made by the Chilean veterinary authorities and the premises were quarantined. We hope to tell you more about this outbreak in the future. These cases are unique and interesting as we don't see EHM outbreaks often in South America. In previous years we have been made aware of EHM outbreaks in Argentina and Brazil, but this is apparently a first EHV-1 outbreak with cases of EHM in Chile. Another aspect marks this outbreak as unusual. Outbreaks are typically, but not exclusively, associated with cooler temperatures of the Northern Hemisphere's winter and spring temperatures, while the Chilean cases started during late summer-early fall conditions of the Southern Hemisphere.

Europe and British Isles

Northern and Central Europe report several EHV-1 abortions. It is unclear whether there are additional cases of abortion on the premises with an index case. An abortion outbreak is ongoing on a larger horse breeding facility in Germany. In addition, there have been a few EHM cases in a connected training facility.

Several EHM outbreaks have been reported from Northern and Southern Germany and several EHM cases have been reported from France and the Netherlands. While most outbreaks occur in boarding facilities (liveries) we report one outbreak occurring in a veterinary care facility in Switzerland, without reports from equestrian events or from the horse racing industry.

There has been an increase in reporting of EHV-4 respiratory disease from across Northern Europe relative to previous years, and there is continuous reporting of numerous *Strep. equi spp. equi* (Strangles) cases from across Europe.

Equine Influenza has been detected in Ireland and the Netherlands.

Asia

Japan reports EHM in two Thoroughbreds-in-training.

There have been no reports on equine infectious diseases from Africa or Australia.

Adobe Stock

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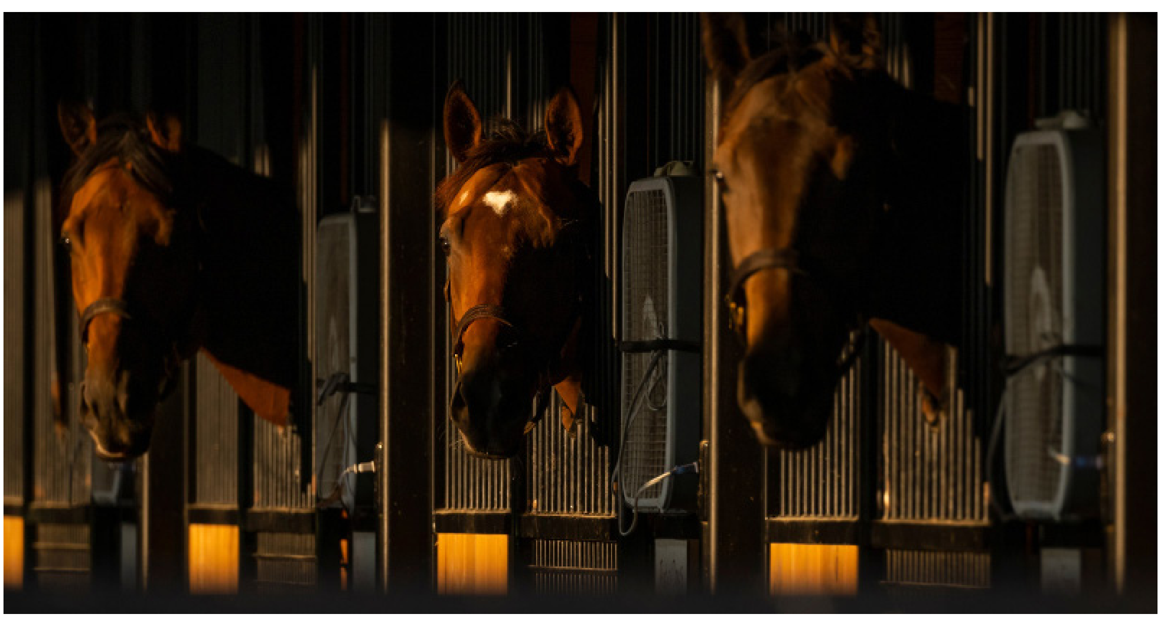

Photo Courtesy Mark Pearson Photography

West Nile Virus in Horses – Not Gone and Should Not Be Forgotten

Over the last two decades, West Nile virus (WNV), an orthoflavivirus transmitted by mosquitoes, has become endemic on all continents except Antarctic and continues to be a major threat to the health and well-being of both horses and humans. The virus had an explosive emergence in North America in 1999, followed by rapid expansion throughout the U.S. and parts of Canada over the first five years, which resulted in often catastrophic disease in over 25,000 U.S. horses. With the rapid deployment of vaccines, the U.S. equine caseload decreased dramatically by 2006.

Once established in a new area, reported cases in humans and horses, depending on vaccine status, will occur yearly but can vary in intensity from year to year. The virus can also cause explosive outbreaks in new locations or among those that have only experienced sporadic cases.

While most mosquito borne viruses are typically associated with tropical or subtropical climates with high precipitation, WNV is endemic in a variety of climates, including temperate, continental and semi-arid areas. The continental U.S. and Europe are two great illustrative examples of the adaptability of this wide-ranging virus. During the last 10 years, 2,484 cases of equine WNV were reported in 46 U.S. states. Climate did not appear to be an issue since the states reporting the highest number of cases of WNV infection (Texas, Pennsylvania, California, Colorado, Utah and Montana) spanned all six U.S. National Oceanic and Atmospheric Administration defined climate regions. In Europe, most WNV activity in equids was initially reported in regions around the Mediterranean basin, however, during the past two decades, WNV activity was reported in more central and northern countries and regions such as Western France (Landes), Eastern Austria (Vienna), Hungary, and Northeastern Germany (Berlin). In 2024, a spike in the number of cases occurred with 494 affected premises reported in 10 countries, representing a 50% rise in reported equine cases over the two previous years. Northern Germany had the highest number of reported cases, approximately 200, with disease occurring in two federal states where activity had not been previously reported. There were 55 affected premises, typically with one or two cases, reported in Austria, a country in which the previous highest case count was four in 2019.

WNV outbreaks are not confined to North America and Europe. Outbreaks have been reported in Central and South America, the Middle East and Australia. Australia is home to WNV lineage denoted as Kunjin virus, or WNV subtype 1b, which underwent a change in virulence resulting in a severe WNV outbreak in 2011 affecting over 1,000 horses.

Nine lineages are now recognized with at least three (Lineage 1a, L1b and L2) associated with neurological disease in horses and cause similar clinical signs and pathology. When data is analyzed across multiple studies, mortality is about 30-40% for all lineages. Neurological disease, often with severe outcomes, remains the primary clinical presentation in the nonvaccinated horse.

Contrary to observations for other viral epidemics, the virulence of this virus has not declined over time. West Nile fever is not recognized in the horse and all clinical manifestations observed are neurological. Affected horses had one or more neurological abnormalities consisting of changes in mentation (30%), locomotion (70%) and/or cranial nerve deficits. A common feature (approximately 80%) of WNV in horses was the presence of muscle tremors or fasciculations. In an analysis of pooled data from 14 studies (2,182 horses), approximately 30% of horses became recumbent necessitating euthanasia for humane reasons.

Many studies examined risk factors for disease, including intrinsic factors such as age, sex or breed predilection with pooled analysis demonstrating no inherent bias. While early studies suggested an increased risk of mortality for older horses associated with underlying health issues, in fact all unvaccinated horses less than 1 year old infected with WNV died. Multiple extrinsic factors such as hair coat, housing, use of fans, etc. have been analyzed and were found equivocal to disease. Vaccination overrides all risk factors in terms of effect on susceptibility to disease.

With no specific antiviral therapies, vaccination is the only intervention that successfully prevents severe neurological disease in the horse. Currently all marketed vaccines have comparable efficacy (over 90%) against known lineages that infect horses, and vaccines are marketed in North America, the United Kingdom and Europe. The American Association of Equine Practitioners identifies WNV vaccination a core component, which indicates that horses should be immunized annually to prevent disease. Vaccination against WNV is considered a 'best practice' under the guidelines provided by The Equine Infectious Disease Surveillance of the United Kingdom. While annual boosters are recommended, horses are not fully protected unless the initial immunization consists of two injections given four weeks apart. Foals must receive an additional booster 10 to 12 months prior to the next mosquito season or eight weeks after the second dose.

With continuous expansion of this virus within and beyond an established endemic area, coupled with (international) travel of horses in and out of these areas, veterinarians and owners should consider all horses irrespective of location and climate at risk for WNV disease if not vaccinated.

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Image provided by the CDC

Highly pathogenic avian influenza (HPAI) H5N1 in U.S. horses

Equine influenza

Influenza in horses is typically caused by the H3N8 subtype of type A influenza virus. The H3N8 subtype circulates in equids worldwide and its infection often results in mild to severe respiratory disease. In addition to the H3N8 subtype, another influenza A subtype, H7N7, was also identified in horses in the 1950s. After a more than two-decade circulation in horses, H7N7 is believed to have become extinct, probably since 1979. In this regard, equids are unique in that only a single influenza virus, H3N8, is known to currently infect them. Humans and swine are infected by multiple subtypes of influenza A virus.

Current knowledge about highly pathogenic avian influenza virus (HPAI) H5N1 in equids

Despite the consensus in the equine infectious disease research field that equids are not normally a host species of highly pathogenic avian influenza (HPAI) H5N1, very rare spillover events of HPAI H5N1 in equids over the past few decades occurred in donkeys and horses, respectively. In 2009, HPAI H5N1 was successfully isolated from diseased donkeys with influenza-like symptoms in Egypt. The antibodies to HPAI H5N1 were also detected in 27 out of 105 donkeys involved in this H5N1 outbreak. The combination of seroconversion and virus isolation data provides good evidence that equids are susceptible to infection by HPAI H5N1. Furthermore, a serosurveillance study in 2020 showed low level titers of H5 specific antibodies in wild asses *(Equus hemonius hemonius)* in Mongolia. Most recently, a comprehensive serosurveillance study of 2,160 equine blood samples collected from July to October 2021 from Mongolian horses, confirmed two samples positive for antibodies against H5N1 by using an array of different antibody assays. This latest serology data appears to continue a theme that equids are susceptible to HPAI H5N1 infection. Considering the low prevalence, it is very likely that HPAI H5N1 may not undergo an efficient transmission in horses, and horse-to-horse transmission may not occur.

Possibly, horses infected with HPAI H5N1 may not show any clinical symptoms. If so, despite the silent infection, HPAI H5N1 virus, when replicating in horses, may encounter seasonal H3N8 virus in the same horse. Such co-infections can create an environment to facilitate swapping genetic segments between the two subtypes and generate a new variant. Such a variant might have the transmissibility of the H3N8 parent and the virulence and novelty to the immune system of the H5N1 parent, which would enable the new virus to escape vaccination-mediated immunity, readily spread among horses, and could cause severe respiratory disease in horses and, potentially, in in-contact humans as well. To

protect equine health, HPAI H5N1 research and diagnosis in horses is critically needed so a potential threat of HPAI H5N1 can be identified before it can jump and spread in horses.

Rapid response to HPAI H5N1's threat in U.S. horses by the University of Kentucky Gluck Equine Research Center

Since late March 2024, the unprecedented spread of HPAI H5N1 in U.S. dairy cows raises critical questions about the virus's potential to cross species barriers to infect and cause disease in other agricultural animals, including horses.

To investigate whether U.S. horses are susceptible to HPAI H5N1 infection, we and our collaborators across the country conducted a nationwide serosurveillance study involving 1,462 equine serum samples that were collected between July 2024 and February 2025. Samples were obtained from diverse geographic locations, with most samples from Minnesota, Nebraska, Kansas, Indiana and Kentucky, as well as 23 other states.

Using the IDEXX influenza nucleoprotein (NP) antibody competition ELISA, we found 653 samples (45%) tested positive for NP antibodies (produced by either H5N1 or H3N8). When these NP antibody positive samples were screened in the ID Screen influenza H5 antibody competition ELISA, we identified one sample positive for H5 antibodies. Further validation of the 653 NP antibody-positive samples with the hemagglutination inhibition (HI) assay showed that 641 out of 653 NP antibody-positive samples had detectable HI antibody titers against equine H3N8 virus, indicating these horses were previously vaccinated or infected with this subtype. Finally, none of the 653 NP antibody-positive equine serum samples were positive in the H5N1 HI assay whereas bovine H5N1-positive reference sera were successfully detected.

The current data from our study that is still in progress show that only one out of 1,462 equine serum samples is positive for antibodies to H5 antibodies, indicating that the chance of HPAI H5N1 spillover to U.S. horses is very low. Nevertheless, considering an extremely expanded list of host species that can be infected by HPAI H5N1 with fatal outcomes plus the fact that the HPAI H5N1 virus is mutating rapidly, scaling up H5N1 surveillance efforts in U.S. horses especially in regions where H5N1 has extensively circulated in bovines, is critically needed towards better understanding of equine susceptibility to HPAI H5N1 infection.

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