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Neurology

BY CHRISTY WEST

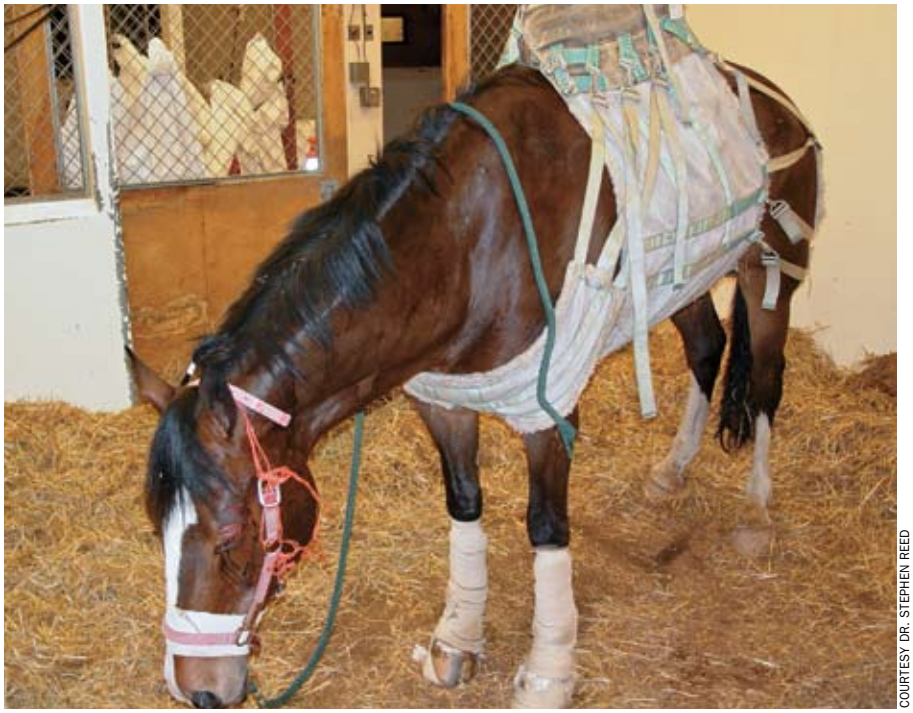
EHV-1: Minimizing Costs, Dispelling Myths

Equine herpesvirus-1 (EHV-1) disease is "one of the costliest equine diseases worldwide," said Rebecca McConnico, DVM, PhD, Dipl. ACVIM, associate professor of veterinary medicine at Louisiana State University. She and Paul Lunn, BVSc, MS, PhD, Dipl. ACVIM, professor of equine medicine at Colorado State University, presented a discussion of controversial issues and myths surrounding the neurologic form of equine herpesvirus-1 (also called equine herpesvirus-1 myeloencephalitis, or EHM).

EHV-1 can cause a variety of problems including respiratory disease, abortion, and neurologic problems. The virus is highly contagious among horses, asymptomatic carriers can shed it readily, and the disease is endemic worldwide; the neurologic form was declared an emerging disease in the United States in 2007 based on increasing incidence of outbreaks. Cases in such neurologic outbreaks are often characterized by fever, weakness, ataxia (incoordination), difficulty urinating and moving the bowels, tail and anal-tone deficits, and a dog-sitting posture.

McConnico and Lunn first detailed several aspects of EHV-1 neurologic disease/infection and control as follows:

- There is no definitive test for EHV-related neurologic disease in live horses; diagnosis is generally based on a history of acute-onset myeloencephalopathy, an outbreak scenario, and the presence of EHV-1 in blood and/or nasal swab samples.
- The incubation period for the disease (time between exposure and clinically apparent illness) is one to 14 days.
- Infected horses usually will shed virus into the environment for seven days or less, but in some cases they can shed for two weeks or longer.
- Horses can be infected with EHV-1 without showing signs of disease, but they can still shed the virus and infect other horses (as asymptomatic carriers).
- Equine herpesvirus can become latent (inactive) in the horse's body, but reactivate in response to stress and cause disease at a later time.
- The disease can be treated successfully.



COURTESY DR. STEPHEN REED

EHV-1 can cause respiratory disease, abortion, and neurologic problems. The latter is seen here in this slinged patient.

Minimizing economic losses associated with EHM outbreaks requires agreement among veterinarians and officials on disease/strain nomenclature, case definition, test interpretation, and appropriate biosecurity response, said McConnico and Lunn. They addressed several myths surrounding the disease and drove home the following points:

- Two strains of EHV-1 (D_{752} and N_{752}) have been termed "neuropathogenic" and "non-neuropathogenic" in the past. The D_{752} strain appears to be more commonly detected in neurologic disease outbreaks, causes higher levels of viremia (virus in the bloodstream), and appears to cause disease more readily than the N_{752} strain. However, both can cause neurologic disease and the response in outbreaks of each is the same (isolate and treat ill horses, quarantine ill and exposed horses, and monitor fevers every 12 hours for at least two weeks).
- Perform testing via polymerase chain reaction (PCR, preferably real-time) and viral isolation when possible to help diagnose disease and document which strain(s) are present.
- The D_{752} strain has been more commonly isolated in recent years from Central Kentucky populations. Whether this means this strain's prevalence is increasing in the general EHV-1 viral pool is not yet clear.
- Neither strain is definitively considered to be a "wild-type" or original strain, and these viruses do not spontaneously mutate from one strain to the other.
- Since the virus is recovered from ill horses for up to 16 days after infection,

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the AAEP recommends a 28-day quarantine period for ill/exposed animals. In some states, officials might allow a shortened quarantine period of 14 days if animals "test clean" via real-time PCR. However, it might be cheaper to simply continue to board horses at the quarantine location until 21 days have passed since the latest clinical case was identified or became asymptomatic (not re-testing if no new cases have presented).

"In conclusion, EHV-1 testing plays a vital role in managing equine neurologic disease," said McConnico. "Outbreaks are manageable, and testing should be done to document which … strain(s) are present; this could change the situation's risk assessment."

Neuroaxonal Dystrophy in Quarter Horses: Case Series

Neuroaxonal dystrophy, or NAD, is a neurologic disease that can affect horses as well as humans, sheep, cats, and dogs. The condition is not yet fully understood, although researchers believe there might be a genetic component. Carrie Finno, DVM, Dipl. ACVIM, a resident in large animal medicine at the University of California, Davis (UC Davis) discussed findings in a series of cases in Quarter Horses at a single cutting horse breeding farm.

"Neuroaxonal dystrophy is a degenerative disease of selected neurons and their axonal processes in the nervous system," explained Finno. Clinical signs include:

- Symmetric ataxia (incoordination) that can appear much like wobbler syndrome,
- A base-wide stance at rest,
- Abnormal circling,
- Dull mentation,
- Often laterally odd foot placement (inappropriate proprioception, or the horse not knowing where his feet are),
- Toe stabbing when walking up inclines,
- Weakness behind when going downhill, and
- Trouble walking over curbs (such as those in parking areas/on road edges).

Mild cases can present with performance issues, said corresponding author John Madigan, DVM, MS, Dipl. ACVIM, a professor of veterinary medicine at UC Davis.

"This disease is clinically indistinguishable from equine degenerative myeloencephalopathy," Finno noted. "The lesions (in the nervous system) are the same, just distributed differently."

The disease is not restricted to Quarter Horses, she added; she mentioned another study in which half of one farm's Lusitano foal crop was affected with NAD.

The case series Finno described involved a cutting horse farm with 148 Quarter Horses from two months to 34 years of age (but mostly yearlings), 59% of which had ataxia of Grade 1 or greater on a five-point ataxia scale.

"These cases showed symmetric ataxia of all four limbs, with the pelvic (hind) limbs more severely affected than the thoracic (front) limbs," she reported. "They also often had an inconsistent menace response (not always flinching from quick hand movement towards their eyes), dull mentation almost as if they were sedated, and we could induce this sleepiness by raising their heads for a short time."

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>
> DR. CARRIE FINNO

Also, many cases had low blood levels of vitamin E; Finno suggested that affected horses might have an underlying susceptibility to developing this disease if they don't receive enough vitamin E.

"Why a cluster (of cases) in cutting horses?" commented Madigan. "Could it be that horses with the genetic mutation for NAD who get adequate vitamin E have an ability to be tolerant of extreme limb position relative to their body (away from the midline)? Are the exceptional movements of the cutting horse related to this trait and disease simply occurs when vitamin E is low? The future will tell. For the meantime, feed plenty of vitamin E beginning in early pregnancy and the first few years of life of at-risk horses."

All three index (initial) cases from that farm that were euthanized showed characteristic NAD lesions in their nervous systems, strongly suggesting that the same process was at work in other affected horses. Lesions can be subtle and easy to miss when tissues are examined, Finno commented. Additionally, she is working to determine the underlying genetic basis for the disease.

"This disease is probably an autosomal dominant trait," she went on. "After genetic counseling (and breeding selection modification), 10% of this farm's 2009 foals were affected (compared to the 59% found in 2007).

"Neuroaxonal dystrophy is an important rule-out for any breed of horse with proprioceptive deficits," she concluded.

Vitamin E for Neurologic Disease

You might know that vitamin E is a powerful antioxidant that helps protect cell membranes and tissues from damage by reactive free radical molecules. You might even know that it's been recommended to help treat several neurologic diseases in horses. But did you also know that just feeding vitamin E might not be enough, and that having the right source of that vitamin E is also key?

Ed Kane, PhD, a researcher and consultant in animal nutrition, presented a review of literature on vitamin E and its effects on horses with neurologic disease.

"Horses on pasture or those that have access to fresh green forage get enough vitamin E," he began. "But most horses these days are fed stored forages and grains, and they might not get enough. Confined horses, or those on poor or winter pasture, often need vitamin E supplementation.

"All sources of vitamin E are not the same," he went on. "Natural and synthetic forms have chemically different structures. Synthetic vitamin E contains equal amounts of eight stereiosomers (different chemical structures) of vitamin E, of which only one is identical to the natural RRR-isomer. The body preferentially transports and incorporates the natural isomer, thereby making the bioavailability of natural vitamin E greater than an equal quantity of synthetic vitamin E."

Vitamin E deficiency has been linked to equine degenerative myeloencephalopathy (EDM) and equine motor neuron disease. Also, Kane noted that possibly due to underlying oxidant damage from their neurologic disease, affected horses might have greater need for vitamin E than unaffected horses. Thus, promoting high enough levels of alpha-tocopherol (a specific form of vitamin E) in a horse's blood and cerebrospinal fluid (CSF, the fluid around

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the brain and spinal cord) is important for preventing and treating these neurologic diseases and potentially others.

"It's highly recommended that young horses at risk for these neurologic diseases, or mature horses with neurologic disease, be supplemented with vitamin E," said Kane. "Supplementing stallions might help their foals, too." (This practice reduced EDM incidence by 75% in one study he referenced.)

He discussed two studies of water-soluble vitamin E supplementation in horses (completed at UC Davis); in the first study researchers found that giving horses 10,000 IU (international units) of natural micellized (processed for greater bioavailability) vitamin E compared to 1,000 IU unsurprisingly resulted in higher concentrations of vitamin E in both blood and cerebrospinal fluid. However, the 10x dose did not give 10 times the serum/CSF concentrations of vitamin E; the increase in E concentration in each horse was 1.3-3.4-fold across both groups.

In the second study investigators evaluated natural micellized vs. synthetic vitamin E use by comparing blood serum and CSF levels of α-tocopherol before and during 14 days of supplementation with 10,000 IU of natural vitamin E, 10,000 units of synthetic vitamin E, or 5,000 IU of natural vitamin E daily. The natural vitamin E came out on top, yielding higher levels of α-tocopherol in study horses' blood and CSF even when given at half the synthetic dose. Indeed, the synthetic form did not even significantly raise α-tocopherol levels in CSF above baseline at the 14-day mark.

"Supplementation of a water-soluble natural micellized α-tocopherol should be used instead of synthetic vitamin E when treating horses with neurologic disorders," Kane concluded. "Consider giving this to horses with neurologic disease at 5-10 IU/lb, to reach serum α-tocopherol levels greater than 6 µg/mL."

EPM Incidence in Horses: Holding Steady

Some say the incidence of equine protozoal myeloencephalitis (EPM) is increasing, while others say it's decreasing. Who's right? Frank Andrews, DVM, MS, Dipl. ACVIM, director of the Louisiana State University Equine Health Studies Program, discussed a retrospective evaluation of 17 years' worth of horses' records from 15 university equine hospitals, coupled with an online survey of veterinarians.

The research team found that the incidence of EPM diagnosis (confirmed by positive test results for the protozoa) in those university hospitals' populations has not increased from 1990 to 2007 (despite a spike from 1995 to 1997, when the Western blot test first came into use). The proportional EPM morbidity rate, or rate of EPM cases within the hospital population, was found to be 0.88% over the study period.

The rate of EPM diagnosis "peaked in 1997 with a 1.95% incidence," commented Andrews. "This is very common in epidemiology, when the number of cases goes way up when a new test is found. Also, at least two pharmaceutical companies were working on products to treat EPM at that time, so more horses were potentially being enrolled in university studies of the disease.

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>
> DR. AMY JOHNSON

"The actual incidence could be higher if you consider nonclinical or subclinical infection, or horses that have the disease but are not diagnosed," he added.

Andrews noted that Standardbreds, Thoroughbreds, Tennessee Walking Horses, and males were more likely to be diagnosed with the disease. Most of the affected horses in the study were 2-15 years old.

The second part of the study involved a recent survey of 221 veterinarians, 76% of whom felt that the incidence of EPM in their practices had decreased or stayed the same over the last two to four years. More than 43% of those veterinarians said they diagnose EPM without using laboratory testing, relying instead on neurologic exam results alone or in conjunction with the horse's response to EPM medication.

Andrews said the group's next goals are to document the incidence of EPM since 2007 and conduct a more thorough survey study of veterinarians on EPM incidence, diagnosis, and treatment.

How to Perform a Neurologic Exam in the Field

What does a veterinarian look for when evaluating a horse for neurologic disease? Hint: The neurologic exam starts with simple field tests, not sophisticated imaging equipment. Amy Johnson, DVM, Dipl. ACVIM-LAIM, lecturer in clinical studies at the University of Pennsylvania, discussed field neurologic examination of horses.

"Each clinician has his or her own method of performing a neurologic exam; the most important aspect (of the neurologic exam) is to develop a system and use it consistently to avoid overlooking abnormalities," she began.

She described four sections of the neurologic exam as follows:

- Evaluation of mental status;
- Cranial nerve examination;
- Spinal reflexes and muscle evaluation; and
- Gait and postural examination.

Under-saddle evaluation isn't required, and in fact Johnson recommended against this practice for safety reasons if a horse is showing neurologic signs.

Evaluating a Horse's Mental Status First, Johnson watches the horse in its stall or paddock to see any encephalopathic behavior such as head-pressing, compulsive circling, blindness, seizures, or changes in mental status (these are generally obvious without handling the horse). If any of these signs are present, this leads to suspicion of neurologic disease and further investigation to rule out other causes of the behavior (such as pain or systemic disease.

Handling the horse further will require additional caution and might also lead her to modify her exam for safety reasons, she noted. Additionally, if a symptomatic horse has not been vaccinated for rabies or its rabies vaccination history is unknown, she recommended using gloves and limiting contact with the horse.

Cranial Nerve Examination This phase of the exam evaluates the horse's cranial (head) nerves by looking at whether the horse has normal function of the head and related structures, such as head position, eye function, menace response (flinching

from quick hand movement toward the eye), normal tongue movement/retraction, chewing ability, etc.

Signs such as nystagmus (repetitive eye twitching), a head tilt, weak tongue, jaw deviation, food coming out of the nose, weak eyelid function, drooping ear, or abnormal pupil response to light suggest compromised neurologic function.

Spinal Reflex, Muscle Evaluation The next stage of the exam is to evaluate tail/anal tone and go over the horse systematically, usually testing with something like a pen, car key, or hemostats, to see if any nerve reflexes (skin flinching from the prodding) are abnormal. Neurologic disease signs could include excessive reaction (hyperesthesia) or areas of analgesia (no sensation), areas of abnormal sweating, and/or areas of muscle atrophy.

Gait/Posture Examination Finally, Johnson evaluates the horse standing and in motion with a combination of straight-line walking, curves, serpentines, circles, backing, walking while the tail is pulled to either side, and walking up and down off curbs. Spastic motion, loss of balance, irregular or inappropriate foot placement, foot dragging, and inappropriate limb crossing all can indicate neurologic problems.

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Learn how to spot neuroaxonal dystrophy in this case series video, described by Dr. Carrie Finno.

"This exam is designed to start with relatively easy maneuvers and increase in complexity to highlight subtle neurologic deficits," Johnson noted. Neurologic problems might cause the veterinarian to halt the exam for safety reasons.

If the veterinarian finds any abnormalities during any phase of the neurologic exam, Johnson said the vet should determine the most likely location of the neurologic problem based on the abnormalities observed and follow up with more advanced diagnostics targeting that area. She commented that recording the exam on video can help monitor the horse's progress, refresh your memory later, and allow slow-motion evaluation, which can help pick up subtleties.

"After abnormalities are confirmed and localized, construction of a differential diagnostic list becomes much easier, and both the diagnostic and therapeutic plans will fall into place," she concluded.

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- Watch the Neurology/Opthamology in Horses video, TheHorse.com/Video.aspx?vID=486.